*Małgorzata Rumińska[1], Anna Majcher[1], Beata Pyrżak[1], Aneta Czerwonogrodzka-Senczyna[2], Ewelina Witkowska-Sędek[1], Danuta Janczarska[1]

Relationship between adiponectin levels and metabolic syndrome components in obese children and adolescents

Ocena zależności między stężeniem adiponektyny i składowymi zespołu metabolicznego u dzieci i młodzieży z otyłością prostą

[1]Department of Pediatrics and Endocrinology, Medical University of Warsaw
Head of Department: Beata Pyrżak, MD, PhD
[2]Department of Human Nutrition, Medical University of Warsaw
Head of Department: Dorota Szostak-Węgierek, MD, PhD

Key words
obesity, metabolic syndrome, adiponectin, HDL-C

Słowa kluczowe
otyłość, zespół metaboliczny, adiponektyna, HDL-C

Summary

Introduction. Adiponectin is an adipocyte-derived multiple function protein involved in metabolic syndrome pathogenesis of children.

Aim. The aim of the study was to assess the correlation between adiponectin levels and the metabolic syndrome and its components in obese children and adolescents.

Material and methods. The study included 122 obese children (52 girls, 70 boys, aged 5.3-17.9 years) and a control group of 58 normal-weight children. Obesity was defined according to IOTF criteria. Anthropometric measurements and blood samples were taken from each participant. Adiponectin levels were assessed using the radioimmunoassay (RIA) method. HOMA was calculated to estimate the degree of insulin resistance. Metabolic syndrome components were applied using the 2007 IDF criteria.

Results. The metabolic syndrome (MetS) was diagnosed in 20.2% of the study group. The plasma adiponectin levels were significantly lower in obese children than in the control group. Lower mean adiponectin levels were found in obese children with MetS criteria as compared to those without. In study and control groups of children considered as a whole the adiponectin levels were correlated with BMI, BMI SDS, HDL-C and CRP. The correlation with HDL-C was observed in the obese group only. Logistic regression analysis demonstrated that a 1 unit increase in adiponectin level results in a 0.9 fold reduction of the risk of a low < 40 mg/dl HDL-C level.

Conclusions. Adiponectin may be associated with the metabolic syndrome through its impact on HDL-C and inflammation.

Streszczenie

Wstęp. Adiponektyna jest białkiem tkanki tłuszczowej pełniącym wiele funkcji i odgrywającym istotną rolę w patogenezie zespołu metabolicznego u dzieci.

Cel pracy. Ocena zależności między stężeniem adiponektyny i zespołem metabolicznym oraz jego składowymi u dzieci i młodzieży z otyłością prostą.

Materiał i metody. Badaniami objęto 122 otyłych pacjentów (52 dziewczynki, 70 chłopców) w wieku 5,3-17,9 roku i 58 pacjentów grupy kontrolnej. Otyłość oceniano według kryteriów IOTF. U każdego pacjenta wykonano pomiary antropometryczne oraz badania laboratoryjne. Stężenie adiponektyny oznaczano metodą radioimmunologiczną (RIA). Wyliczono wskaźnik HOMA do oceny insulinooporności. Zespół metaboliczny definiowano na postawie kryteriów IDF (2007).

Wyniki. Zespół metaboliczny (MetS) stwierdzono u 20,2% otyłych dzieci. Średnie stężenie adiponektyny było statystycznie znamiennie niższe w grupie dzieci otyłych w porównaniu do dzieci z grupy kontrolnej. Niższe stężenie adiponektyny miały dzieci otyłe z zespołem metabolicznym w porównaniu do otyłych niespełniających kryteriów MetS. U dzieci z grup badanej i kontrolnej rozpatrywanych łącznie adiponektyna korelowała z BMI, BMI SDS, HDL-C i CRP. Związek adiponektyny z HDL-C stwierdzono również w grupie dzieci otyłych. W analizie regresji logistycznej wykazano, że wzrost adiponektyny o jedną jednostkę zmniejsza o 0,9 raza ryzyko wystąpienia obniżonego < 40 mg/dl stężenia HDL-C.

Wnioski. Adiponektyna może być związana z zespołem metabolicznym poprzez jej wpływ na HDL-C i proces zapalny.

Address/adres:
*Małgorzata Rumińska
Department of Pediatrics and Endocrinology
Medical University of Warsaw
ul. Marszałkowska 24, 00-576 Warszawa
tel. +48 (22) 522-73-60
malgorzata.ruminska@wum.edu.pl

INTRODUCTION

The observed epidemic of childhood and adolescent obesity has serious health consequences. Numerous concomitant metabolic and hemodynamic disturbances as well as chronic inflammation process result in diabetes type 2, arterial hypertension, atherogenic dyslipidemia, which are components of the metabolic syndrome (MetS). These ailments may accompany obesity in middle age and lead to cardiovascular disease (1, 2). Adipocytokines, biologically active substances produced by the adipose tissue play the key role in the induction of the above-mentioned changes.

Adiponectin is one of the adipocytokines and the only one the concentration of which decreases with the increase of the adipose tissue. It is the most abundantly expressed adipokine in adipose tissue which exerts pleiotropic insulin-sensitizing effects. Through activation of the adenosine monophosphate-induced protein kinase (AMPK) pathway and peroxisome proliferator activated receptor α (PPARγ) adiponectin regulates carbohydrate and fat metabolism. Adiponectin inhibits hepatic gluconeogenesis, increases glucose uptake and fatty acid oxidation in skeletal muscle (3, 4). The insulin-sensitizing effects of adiponectin participate in activating insulin-receptor substrate 1 – associated phosphatidylinositol 3-kinase (PI-3K) which improves intracellular insulin action pathway, enhancing fatty acid transport protein 1 mRNA expression and decreases TNF α production (5). Adiponectin has an anti-inflammatory effect on the vascular wall and reduces arteriosclerosis. It inhibits endothelial nuclear factor kβ signaling, reduces adhesion molecule expression and smooth muscle cell proliferation, suppresses macrophage transformation in foam cells as well as stimulates nitric oxide production. Dysregulation of adiponectin expression and secretion may affect pathogenesis of metabolic disease in children and adolescents. Lower levels of adiponectin are observed in obese children with insulin resistance and metabolic syndrome. Hipoadiponectinemia is predictive of development of type 2 diabetes and coronary artery disease (CAD) (3-5).

AIM

The aim of the study was to evaluate the correlation between adiponectin levels and metabolic syndrome and its components in obese children and adolescents.

MATERIAL AND METHODS

The study included 122 children with simple obesity (52 girls, 70 boys), aged 5.3-17.9 years (mean age 11.6 ± 3 years). The control group consisted of 58 children of the same age (mean age 11.7 ± 3 years) with normal somatic parameters.

Anthropometric measurements of all the children were taken, including body height (cm), body weight (kg), waist circumference and hip circumference (cm), thickness of 3 skinfolds (mm) and body composition using the bioelectrical impedance analysis (BIA) method. The results of these measurements were used to calculate BMI (Body Mass Index), waist to hip ratio (WHR), waist to height ratio (WHtR) and body fat percentage using the Slaughter equations based on skinfold measurements and the BIA method (7).

Obesity was assessed using the criteria developed by International Obesity Task Force (IOTF) (8). The threshold of obesity was set at BMI SDS $\geq +2$, expressed in values normalized for each patient using LMS method (9). WHtR exceeding 0.5 was assumed to be a value indicating abdominal obesity. The norms for body fat percentage were set at 19% for girls and 15% for boys.

After a 12-hour fast the following parameters were measured: fasting adiponectin concentration using the radioimmunoassay (RIA) method, glucose and insulin concentrations (fasting and at 30, 60, 90 and 120 minutes of the oral glucose tolerance test – OGTT; glucose levels were measured using the enzymatic method, whereas insulin concentrations were measured using the chemiluminescence and immunoenzymatic methods), total cholesterol (TG), high-density lipoprotein cholesterol (HDL-C), triglyceride (TG) and the acute-phase protein CRP using the standard enzymatic method. Light-density lipoprotein cholesterol (LDL-C) was calculated using the Friedewald formula (10). The resulting data was used to calculate indicators of insulin resistance HOMA. The resulting values of lipid metabolism were interpreted according to the 2007 American Heart Association (AHA) recommendations, and glucose levels were interpreted in accordance with the 2013 Polish Diabetes Association guidelines (10, 11). Hyperinsulinism was defined as fasting insulin level ≥ 15 μIU/ml, and/or maximum OGTT level ≥ 150 μIU/ml, and/or insulin level at 120 minutes of OGTT ≥ 75 μIU/ml Homoeostasis Model Assessment (HOMA) ≥ 3 testify to severe insulin resistance (12).

Each child's blood pressure was measured, and the results were evaluated using percentile charts for the population of children published by Nawarycz and Ostrowska-Nawarycz (13). Hypertension was diagnosed when the values of systolic or diastolic blood pressure were above the 95th percentile; mean blood pressure values between the 90th and 95th percentiles were defined as the border zone (13).

According to the 2007 International Diabetes Federation (IDF) consensus definition the metabolic syndrome criteria was applied (14).

The project received approval of the Ethical Committee at Medical University of Warsaw. The data were analyzed using the statistic package, SPSS. Statistical significance was considered to be $p = \text{value} < 0.05$.

RESULTS

The mean BMI of the obese children was 29.5 ± 4.9 kg/m^2, the mean BMI SDS was +2.8 ± 0.5. All the children were found to have high body fat percentage, averaging 38.1 ± 8.2%. The mean waist circumference was 90.3 ± 12.3 cm. In nearly all the children their WHtR met the criteria for diagnosing abdominal obesity. For most anthropometric parameters there

were statistically significant differences between the control group and the study group (tab. 1).

Table 1. Comparison of mean values and standard deviation of chosen anthropometric and biochemical parameters between the control group and the study group.

Variable	Control group	Study group	p-value
Height (cm)	158.2 ± 14.0	154.1 ± 16.2	0.148
Body weight (kg)	46.7 ± 12.9	72.2 ± 24.1	0.000
Body Mass Index (kg/m^2)	18.7 ± 2.7	29.5 ± 4.9	0.000
SDS BMI	0.0 ± 0.9	2.8 ± 0.5	0.000
Waist circumference (cm)	64.3 ± 6.6	90.3 ± 12.3	0.000
Hip circumference (cm)	82.4 ± 9.9	101.4 ± 14.0	0.000
WHR	0.78 ± 0.04	0.89 ± 0.05	0.000
WHtR	0.4 ± 0.02	0.58 ± 0.47	0.000
% FAT (skinfold)	19.5 ± 6.3	34.2 ± 5.0	0.000
Fasting glucose (mg/dl)	82.5 ± 10.4	83.6 ± 10.3	0.549
TC (mg/dl)	157.5 ± 22.4	176.9 ± 30	0.000
HDL-C (mg/dl)	56 ± 11.9	44.4 ± 11.2	0.000
LDL-C (mg/dl)	85.1 ± 24.2	105.8 ± 27.2	0.000
TG (mg/dl)	76.9 ± 33.6	133.2 ± 62.9	0.000
CRP (mg/dl)	0.49 ± 0.2	0.45 ± 0.3	0.446
Adiponectin (μg/ml)	15.9 ± 6.6	13.1 ± 5.9	0.004

WHR – waist to hip ratio, WHtR – waist to height ratio, % FAT – % of body mass, TC – total cholesterol, TG – triglycerides, CRP – C-reactive protein

The characteristics of anthropometric and biochemical parameters, blood pressure in obese children > 10 years old with and without metabolic syndrome IDF criteria are presented in table 2.

In the group of obese children 6.1% had systolic blood pressure (SBP) slightly above the 95th percentile, and 14.2% had diastolic blood pressure (DBP) slightly above the 95th percentile. Increased values of total cholesterol (TC ≥ 200 mg/dl) were found in 20% of obese girls and in 24% of obese boys (together they accounted for 22% of the study group). Raised LDL-C concentrations (≥ 130 mg/dl) were more frequent in males (17 vs. 14%). A higher percentage of boys showed low (< 40 mg/dl) levels of HDL-C (45 vs. 25.2%). TG levels exceeding 110 mg% were found in 76 children: 53% of girls and 73% of boys. Abnormal glucose tolerance was diagnosed in 26 obese patients, including 11 girls and 15 boys. Glucose levels ≥ 200 mg% were reported in a 12.5-year-old boy. Elevated fasting insulin levels ≥ 15 μIU/ml were found in 46.6% of the children (21 girls and 34 boys). Abnormal insulin levels in the OGTT (≥ 150 μIU/ml) were observed at 30 minutes in 19 patients, at 60 minutes in 21 patients, at 90 minutes in 18 patients, and/or at 120 minutes ≥ 75 μIU/ml in 55 obese children. The mean value of insulin resistance indicator HOMA was 3.3 ± 2.04 (46% of the group had HOMA values showing severe insulin resistance ≥ 3).

Table 2. Chosen anthropometric and biochemical parameters, adiponectin levels, blood pressure in the obese children > 10 years old with and without metabolic syndrome criteria.

Variable	Total (n = 84)	MetS (-) (n = 67)	MetS (+) (n = 17)	p-value
Age (years)	13.2 ± 2.04	12.9 ± 1.96	14.3 ± 2.03	0.010
Height (cm)	162.3 ± 11.09	160.8 ± 10.94	168.4 ± 9.74	0.010
Body weight (kg)	83.6 ± 19.84	81.4 ± 20.5	92.2 ± 14.52	0.044
BMI (kg/m^2)	31.3 ± 4.7	31 ± 4.99	32.4 ± 3.22	0.281
SDS BMI	4.1 ± 1.67	4.1 ± 1.76	4.3 ± 1.27	0.679
Waist circumference (cm)	95.5 ± 10.46	94.4 ± 10.92	100 ± 6.99	0.046
Hip circumference (cm)	108.1 ± 11.11	107.0 ± 11.6	112.1 ± 7.98	0.092
WHR	0.88 ± 0.06	0.88 ± 0.06	0.89 ± 0.04	0.429
WHtR	0.58 ± 0.05	0.58 ± 0.05	0.59 ± 0.04	0.558
% FAT (skinfold)	35.3 ± 5.41	35.1 ± 5.12	36.0 ± 6.5	0.531
% FAT (BIA)	40.1 ± 8.25	40.0 ± 7.93	40.2 ± 9.74	0.937
TC (mg/dl)	176.2 ± 31.59	175.2 ± 32.1	179.6 ± 30.33	0.611
HDL-C (mg/dl)	42.9 ± 9.6	45.4 ± 8.89	33.5 ± 5.44	0.000
LDL-C (mg/dl)	104.8 ± 28.4	104.3 ± 27.72	106.5 ± 31.75	0.781
TG (mg/dl)	141.4 ± 67.12	126.2 ± 50.95	197.8 ± 88.87	0.000
Fasting glucose (mg/dl)	83.9 ± 10.21	83.3 ± 10.19	86.2 ± 10.26	0.299
Fasting insulin (μIU/ml)	17.4 ± 9.54	16.7 ± 9.77	20 ± 8.4	0.209
HOMA	3.66 ± 2.21	3.48 ± 2.18	4.36 ± 2.25	0.143
CRP (mg/dl)	0.49 ± 0.31	0.51 ± 0.43	0.41 ± 0.12	0.227
Adiponectin (μg/ml)	112.76 ± 5.69	13.13 ± 6.0	11.32 ± 4.0	0.314
SBP (mmHg)	117.4 ± 10.25	115.5 ± 9.75	123.3 ± 9.76	0.007
DBP (mmHg)	73.9 ± 8.84	73.2 ± 8.46	76.0 ± 9.95	0.274

WHR – waist to hip ratio, WHtR – waist to height ratio, % FAT – % of body mass, TC – total cholesterol, TG – triglycerides, CRP – C-reactive protein, SBP – systolic blood pressure, DBP – diastolic blood pressure

According to International Diabetes Federation (IDF) criteria in obese children > 10 years old: 68 of those patients (81% of this group) had central obesity, 30 children (37.5%) had elevated levels of triglycerides (≥ 150 mg/dl) and 29 (36.3%) lower levels of HDL cholesterol (< 40 mg/dl). In 15 children (22.4%) increased levels of SBP (≥ 130 mg/dl) or decreased levels of DBP (< 85 mmHg) were recognized. Six obese children (7.4% of the study group) had impaired fasting glucose (≥ 100 mg/dl). The metabolic syndrome was diagnosed in 12 obese patients (20.2% of the group).

Mean adiponectin concentrations in the obese group were statistically significantly lower than in the control group (13.1 vs. 15.9 μg/ml; p = 0.004) (fig. 1).

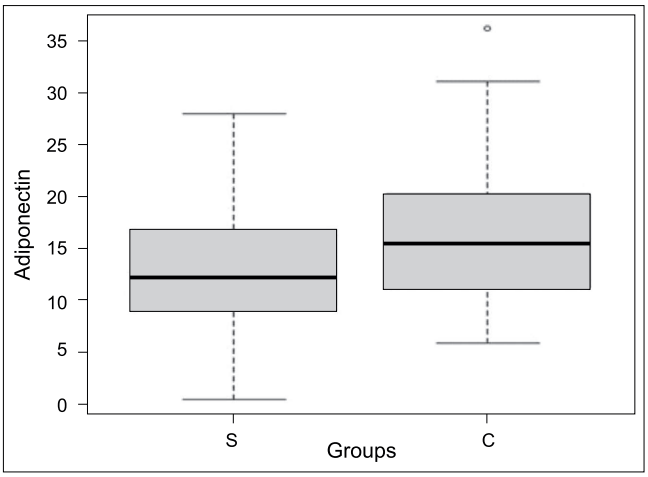

Fig. 1. Comparison of values of adiponectin level between study and control groups (13.1 vs. 15.9, p = 0.004).

Slightly higher values were found in obese girls as compared to obese boys (13.4 μg/ml vs. 12.9 μg/ml; p = 0.775). Children with metabolic syndrome were found to have lower mean adiponectin concentrations (11.32 vs. 13.13 μg/ml; p = 0.314) as compared to obese children who did not meet the criteria of the metabolic syndrome (fig. 2).

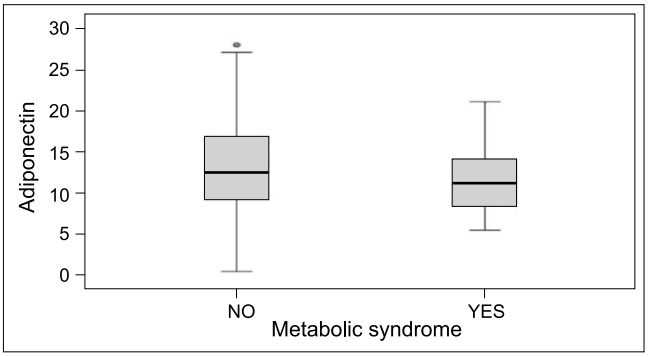

Fig. 2. Comparison of mean values of adiponectin levels in obese children > 10 years old with and without metabolic syndrome (11.32 vs. 13.13, p = 0.314).

In the group of obese children adiponectin did not correlate with any of the analyzed anthropometric parameters which assessed nutritional status. When the group of obese children was considered together with the control group of normal body weight children adiponectin concentration was negatively correlated with BMI (r = -0.182; p = 0.017) and BMI SDS (r = -0.159; p = 0.037). Negative correlations were found with waist circumference (r = -0.148; p = 0.059), body weight (r = -0.135; p = 0.086) and body fat percentage calculated using skinfold measurements (r = -0.134; p = 0.088) with a tendency for statistical significance. In all the children adiponectin concentration was positively correlated with HDL-C (r = 0.22; p = 0.005) and negatively correlated with triglicerides (r = -0.147; p = 0.067) and the acute-phase protein CRP (r = -0.194; p = 0.016). A positive correlation of adiponectin concentration with HDL-C concentration was also observed in the obese group (r = 0.183; p = 0.047).

In the obese group no statistically significant correlations were found between adiponectin concentration and fasting or OGTT glucose levels. For insulin, a negative correlation was found with adiponectin at 90 minutes (r = -0.183; p = 0.05) and 60 minutes (r = -0.160; p = 0.085) of the OGTT test. No statistically significant correlations were found between adiponectin and the analyzed indicators of insulin resistance and blood pressure. Logistic regression analysis showed that an increase of 1 unit in adiponectin reduces the risk of lowered < 40 mg/dl HDL-C levels (p = 0.008) by 0.9 times. A similar tendency was observed for hypertension (p = 0.096) (tab. 3). Logistic regression analysis demonstrated that increase in adiponectin level by 1 unit results in a 0.9 fold reduction of the risk of a low < 40 mg/dl HDL-C level.

Table 3. Evaluation of influence of adiponectin on the criteria of metabolic syndrome in the study group – logistic regression analysis.

Criteria of MetS	Beta	SE	p-value	OR
WC (G > 80 cm, B > 90 cm)	-0.034	0.025	0.168	0.996
TG ≥ 150 mg/dl	-0.030	0.030	0.317	0.970
HDL-C < 40 mg/dl	-0.085	0.032	0.008	0.919
Fasting glucose ≥ 100 mg/dl	0.061	0.043	0.153	1.063
Hypertension	-0.090	0.054	0.096	0.914
MS (children > 10 years)	-0.061	0.052	0.245	0.0941

WC – waist circumference, G – girls, B – boys, TG – triglycerides, HDL-C – HDL cholesterol, MS – metabolic syndrome, SE – standard error, OR – odds ratio

DISCUSSION

Childhood obesity pandemic is having a major impact on the incidence of metabolic, endocrine and hemodynamic disturbances at earlier ages. Based on The Bogalusa Heart Study the overweight (> 95th percentile) schoolchildren were 2.4 times as likely to have elevated level of total cholesterol (TC), 3.0 of low-lipoprotein cholesterol (LDL-C), 7.1 of triglycerides (TG) and 3.4 times as likely lower high-density lipoprotein cholesterol (HDL-C) as compared to normal weight schoolchildren. Odds ratios (OR) for other relationships were 12.6 for fasting insulin levels, 4.5 for systolic blood pressure (SBP) and 2.4 for diastolic blood

pressure (DBP) (1). Prevalence of obesity-related disturbances increase with higher fat mass. Among children and adolescents with Body Mass Index (BMI) > 95th percentile, 39% had at least two cardiovascular risk factors (59% in the case of children and adolescents with BMI > 99th percentile) (2). The present study also showed that obesity contributes to development of metabolic complications. Lipid profile levels varied significantly between obese and control groups. Obese children presented atherogenic lipids phenotype: 37.5% of the study group had elevated ≥ 150 mg/dl levels of TG and 36.3% lower < 40 mg/dl levels of HDL-C. These disturbances were more frequent in males. 6.1% and 14.2% of obese children had elevated systolic blood pressure and diastolic blood pressure respectively. Impaired fasting glucose was recognized in 9% of the obese children, abnormal glucose tolerance in 21.3 %. About half of the study group had severe insulin resistance estimated on insulin resistance indicator HOMA.

Dyslipidemia, insulin resistance, type 2 diabetes, hypertension and other metabolic abnormalities are risk factors of the atherosclerotic process, which may start early in life. The metabolic syndrome (MetS) is the pathophysiological description of metabolic and hemodynamic diseases which enhance the risk for CVD and type 2 diabetes development. Reaven was the first to describe the syndrome (1988) – and he presented it as a cluster of interrelated risk factors that increases the individual's susceptibility to cardiovascular morbidity and mortality. This problem is also observed in obese children and adolescents and has become a serious problem for public health. Various studies report different prevalence rates for MetS which results from studies being performed in different ethnic groups and according to different criteria. According to the International Diabetes Federation (2007) criteria the prevalence of MetS varied between 16-44% (15). In Mexico the MetS criteria applied to 13% of the obese population (16), in the Turkish population it was 33% (17), in the Polish population it was 37.7% (18) and 44.6% in Egyptian (19). In our study the metabolic syndrome was found in 20.2% children.

Understanding of the pathogenesis of obesity-related disturbances may contribute development of effective strategy for prevention of metabolic syndrome and atherosclerotic cardiovascular disease. Insulin resistance is thought to be the central abnormality MetS etiology. Apart from insulin resistance central obesity plays a very important part in the development of this disorder. In this study waist circumference surrogate for body fat centralization was the predominant anthropometric parameter which markedly differentiates obese children with metabolic syndrome from children with no such syndrome. Cizmecioglu et al. (20) in the study of 2491 adolescents aged 11-19 with BMI ≥ 85th percentile found that waist circumference was the best marker for MetS diagnosis. Visceral adipose tissue is an active endocrine organ that releases a number of bioactive molecules, known as adipokines. These play an important role in appetite regulation and energy homeostasis. Fat excess leads to imbalance in secretion of adipokines and negatively effects metabolism. The increase of proinflammatory cytokines such as tumor necrosis factor α (TNFα), interleukin 1, 6, 8 (IL-1, IL-6, IL-8) and decrease of adiponectin secretion in particular contribute to development of insulin resistance and other metabolic and vascular diseases characteristic for obese persons (16).

Adiponectin has multiple functions. This protein influences carbohydrate and fat metabolism, improves insulin sensitivity, plays an anti-inflammatory role and reduces arteriosclerosis. As opposed to other adipocytokines, its concentration decreases with the increase of the mass of adipose tissue and is lower in visceral vs. subcutaneous adipose tissue. Several studies have demonstrated adiponectin levels to be lower in overweight and obese children and adolescents as well as negatively correlated with anthropometric parameters representing body fatness (19, 21-23). The results of our study have also shown that obese children have significant lower adiponectin levels as compared to normal weight controls. When control and study groups were considered together adiponectin concentration was negatively correlated with BMI ($p = 0.017$) and BMI SDS ($p = 0.037$). Negative relationship was found with waist circumference ($p = 0.059$), body weight ($p = 0.086$) and body fat percentage calculated using skinfold measurements ($p = 0.088$) with a tendency for statistical significance. Furthermore, levels of adiponectin were higher in obese girls than obese boys, which is consistent with literature data (21-23).

Adiponectin levels are associated with the metabolic syndrome (MetS) and each of its components. Obese children to whom MetS criteria applied had lower levels of adiponectin than those without the syndrome (19, 24). The relationship between adiponectin levels and MetS prevalence is independent of the level of obesity, insulin resistance and inflammatory markers (21, 24). In Klünder-Klünder et al. study (16) obese children with lowest tertile of adiponectin levels exhibited the highest frequency of MetS components. With adiponectin levels in the high tertiles, each component improved. The odds ratio of MetS development was 10.3 as compared to the third tertile. The same relationship though less impact, was observed for eutrophic children. Matsushita et al. (25) found that the relationship between each component of MetS and the adiponectin levels was stronger than TNFα, IL-6 and CRP and they suggested that adiponectin could be the biomarker for identifying children at risk of MetS development. Also Shaibi (24) in a group of 175 Latino-youth confirmed that adiponectin independently predicts MetS and may participate in its pathogenesis. A 3-year prospective study of Korean children demonstrated adiponectin level as predictive for MetS development (26).

Our results demonstrate, that obese children above 10 years old with metabolic syndrome criteria of IDF have lower levels of adiponectin as compared to those to obese children without MetS. This differences were not significant and adiponectin levels correlated only with HDL-C component of metabolic syndrome. This finds confirmation in the study by Winer et al. (27). Logistic regression

analysis showed that an increase of adiponectin by 1 unit results in a 0.9 fold reduction of the risk of low < 40 mg/dl HDL-C levels (p = 0.008). Adiponectin participates in lipid metabolism regulation by increasing fatty acid oxidation in liver and muscle cells. In his study Magge et al. (28) used nuclear magnetic resonance and reported a relationship between adiponectin levels and atherogenic pattern of lipids and lipoproteins subclass particles which was independent of obesity and insulin resistance. Adiponectin was positively correlated with LDL-P size, HDL-P size and HDL-C and negatively correlated with small LDL-P and small HDL-P. Huang et al. (21) used different multivariate linear regression models and following adjustment of different anthropometric and biochemical variables demonstrated that only age and HDL-C were consistently correlated with plasma adiponectin. Other studies have confirmed that adiponectin is an independent predictor of low levels of HDL-C (29, 30).

There is mounting evidence that obesity is related to subclinical chronic inflammation, which may contribute to development of metabolic syndrome and vascular disease. Several studies suggest that adiponectin is the key molecular link between adiposity and inflammation. This protein modulates the immune system and inflammatory responses of endothelial cells through nuclear factor – κβ signaling pathway; it inhibits macrophage function and cytokine secretion from adipocytes. In clinical studies adiponectin serum levels negatively correlate with markers of systemic inflammation and endothelium dysfunction: hsCRP, TNFα, IL-1, sE-selectin, MCP-1 and positively with nitric oxide metabolites (31, 32). Ouchi et al. (33) found reciprocal relationship between CRP and adiponectin mRNA levels. Adiponectin knockout mice had higher levels of CRP mRNA in adipose tissue than wild-type mice. Winer et al. (27) demonstrated that the relationship between adiponectin and hsCRP levels is independent of insulin resistance and adiposity. In the present study we observed only a weak relationship between adiponectin and CRP levels in a group of both study children and controls (considered together) which might confirm the existing link between adiponectin and low grade inflammation. No differences in serum CRP levels between normal-weight children and obese children may result from the use of enzymatic standard assay. High sensitivity method for assessment of CRP levels in lower normal value-range allows to examine subclinical chronic inflammation.

CONCLUSIONS

In our study we demonstrated the relationship between adiponectin and metabolic syndrome, in particular with the HDL cholesterol levels and inflammation. Adiponectin may be the key molecular signal linking metabolic disturbances and low grade chronic inflammatory in development of metabolic syndrome. Hypoadiponectinemia may be a good risk factor for lower level of HDL cholesterol.

BIBLIOGRAPHY

1. Freedman DS, Dietz WH, Srinivasan SR et al.: The relation of overweight to cardiovascular risk factors among children and adolescents: The Bogalusa Heart Study. Pediatrics 1999; 103(6): 1175-1182.
2. Freedman DS, Mei Z, Srinivasan SR et al.: Cardiovascular risk factors and excess adiposity among overweight children and adolescents: The Bogalusa Heart Study. J Pediatr 2007; 150: 12-17.
3. Kadowaki T, Yamauchi T: Adiponectin and adiponectin receptors. Endocrine Reviews 2005; 26(3): 439-451.
4. Kadowaki T, Yamauchi T, Kubota N et al.: Adiponectin and adiponectin receptors in insulin resistance, diabetes and metabolic syndrome. J Clin Endocrinol Metab 2006; 16(7): 1784-1792.
5. Maeda N, Shimomura I, Kishida K et al.: Diet-induced insulin resistance in mike lacking adiponectin ACRP30. Nat Med 2002; 8: 731-737.
6. Pyrżak B, Rumińska M, Popko K et al.: Adiponectin as a biomarker of the metabolic syndrome in children and adolescents. Eur J Med Res 2010; 16 (suppl. II): 1-5.
7. Slaughter MH, Lohman TG, Christ CB et al.: Skinfold equations for estimation of body fitness in children and youth. Human Biology 1998; 60: 709-723.
8. Cole TJ, Lobstein T: Establish a standard definition for child overweight and obesity worldwide: international survey. BMJ 2000; 320: 1240-1243.
9. www.healthforallchildren.co.uk
10. Kłosiewicz-Latoszek L, Cybulska B: Diagnostyka i klasyfikacja dyslipidemii. [W:] Cybulska B, Kłosiewicz-Latoszek L (red.): Zaburzenia lipidowe. Termedia Wydawnictwo Medyczne, Poznań 2011: 45-53.
11. Polskie Towarzystwo Diabetologiczne: Zalecenia kliniczne dotyczące postępowania u chorych na cukrzycę. Diabetologia Doświadczana i Kliniczna 2013; 2 (suppl. A): A3.
12. Ten S, Maclaren N: Insulin resistance syndrome in children. J Clin Endocrinol Metab 2004; 89(6): 2526-2539.
13. Ostrowska-Nawarycz L, Nawarycz T: Normy ciśnienia tętniczego u dzieci i młodzieży – doświadczenia łódzkie. Arterial Hypertension 2007; 11(2): 138-150.
14. Zimmet P, Alberti K, George MM et al.: The metabolic syndrome in children and adolescents – an IDF consensus report. Pediatric Diabetes 2007; 8: 299-306.
15. Friend AJ, Craig LCA, Turner SW: The prevalence of metabolic syndrome in children – a systematic review. Arch Dis Child 2012; 97: 116-117.
16. Klünder-Klünder M, Flore-Huerta S, Garcia-Macedo R et al.: Adiponectin in eutrophic and obese children as a biomarker to predict metabolic syndrome and each components. BMC Public Health 2013; 13: 88.
17. Sanguan O, Dundar B, Kösker M: Prevalence of metabolic syndrome in obese children and adolescents using three different criteria and evaluation of risk factors. J Clin Res Ped Endo 2011; 3(2): 70-76.
18. Pyrżak B, Majcher A, Rumińska M et al.: Analiza częstości występowania zespołu metabolicznego z zastosowaniem kryteriów Cooke'a, de Ferranti i IDF u dzieci z otyłością. Endo Pediatr 2008; 2, 2(23): 21-32.
19. Atwa HM, Sad A: Adiponectin could be a comprehensive marker of metabolic syndrome in obese children. A Afr Clin Nutr 2012; 25(2): 53-56.
20. Cizmecioglu FM, Etiler N, Ergen A et al.: Associotion of adiponectin, resistin and high sensitive CRP level with the metabolic syndrome in childhood and adolescence. Exp Clin Endocrinol Diabetes 2009 Nov; 117(10): 622-627.
21. Huang KCh, Lue BH, Yen RF et al.: Plasma adiponectin levels and metabolic factors in nondiabetic adolescents. Obesity Research 2004; 12(1): 119-124.
22. Weiss R, Dufour S, Groszan A et al.: Low adiponectin levels in adolescent obesity: a marker of increased intramyocellular lipids accumulation. J Clin Endocrinol Metab 2003; 88: 2014-2018.
23. Stefan N, Bunt JC, Salbe AD et al.: Plasma adiponectin concentration in children: relationship with obesity and insulinemia. J Clin Endocrinol Metab 2002; 87: 4652-4656.
24. Shaibi GQ, Cruz ML, Weigensberg J et al.: Adiponectin independently predicts metabolic syndrome in overweight Latino youth. J Clin Endocrinol Metab 2007 May; 92(5): 1809-1813.
25. Matsushita K, Yatsuya H, Tamakoshi K et al.: Comparison of circulating adiponectin and proinflammatory markers regading their association with metabolic syndrome in Japanese men. Arteriscler Thromb Vasc Biol 2006; 26: 872-876.
26. Choi KM, Yannakoulia M, Park MS et al.: Serum adipocyte fatty acid-binding protein, retinol-binding protein 4, and adiponectin concentrations in relation to the development of the metabolic syndrome in Korean boys: a 3-years prospective study. Am J Clin Nutr 2011; 93(1): 19-26.
27. Winer JC, Zern TL, Taksali SE et al.: Adiponectin in childhood and adolescent obesity and its association with inflammatory markers and components of metabolic syndrome. J Clin Endocrinol Metab 2006; 91: 4415-4423.
28. Magge SN, Stettler N, Koren D et al.: Adiponectin is associated with favorable lipoprotein profile, independent of BMI and insulin resistance, in adolescents. J Clin Endocrinol Metab 2011; 96: 1549-1554.
29. Ong KK, Frystyk J, Flyvbjerg A et al.: Sex discordant association with adiponectin levels and lipids profiles in children. Diabetes 2006; 55: 1337-1341.
30. Gherlan L, Vladoiu S, Alexiu F et al.: Adipocytokine profile and insulin resistance in childhood obesity. Meadica J Clin Med 2012; 7(3): 205-213.
31. El-Mesallamy HO, Hamdy NM, Ibrahim SM: Adiponectin and pro-inflammatory cytokines in obese diabetic boys. Indian Pediatric 2011 Oct 17; 48: 815-816.
32. Głowińska-Olszewska B, Urban M, Koput A: Adipocytokiny i markery zapalenia w zespole metabolicznym u młodzieży. Endo Pediatr 7/2008; 2(23).
33. Ouchi N, Kihara S, Funahashi T: Reciprocal association of C-reactive protein with adiponectin in blood stream and adipose tissue. Circulation 2003;107: 671-674.

received/otrzymano: 02.07.2014
accepted/zaakceptowano: 19.09.2014