Original article

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Association of cardiac changes with serum adiponectin and resistin levels in obese and overweight children

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Objectives **To investigate serum adiponectin and resistin levels in childhood obesity and their relationship with cardiac changes and insulin resistance.**

Methods **Seventy-one obese and 24 overweight children and 40 healthy children and adolescents were selected for the study. Height and weight measurements, BMI values and BMI SD score values were obtained for each individual. After blood pressure measurement, left ventricular wall thickness, left ventricular mass, stroke volume, cardiac output, systolic and diastolic functions of the left ventricle were measured using an M-mode, two dimensional color-coded echocardiography device. Blood samples of the individuals were obtained for fasting blood sugar, total blood cholesterol, triglyceride, low-density lipoprotein (LDL) cholesterol, very low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, insulin, C-peptide, adiponectin and resistin values.**

Results **Cholesterol and LDL values, homeostasis model assessment of insulin resistance, fasting insulin and fasting C-peptide values of the obese and overweight groups were higher ($P<0.01$). Adiponectin level ($P<0.001$) and resistin level ($P<0.05$) of the obese and overweight groups were lower than those of the control group ($P<0.05$). Echocardiographic evaluation showed diastolic dysfunction in addition to increased left ventricular wall thickness and left ventricle mass values in the obese and overweight children. We also detected a significant positive correlation among left ventricular mass, interventricular septum systolic diameter and resistin in obese children. Among the factors, resistin level was determined as an independent predictor of left ventricular mass in obese children.**

Conclusion **In this study, even in asymptomatic obese and overweight children, cardiac structural and functional changes, such as increased left ventricular mass and diastolic dysfunction, were demonstrated. Although decreased adiponectin level was not related to cardiac changes, it was shown that decreased serum resistin levels in the obese cases lead to left ventricle hypertrophy.**

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Keywords: adiponectin, cardiac changes, childhood obesity, resistin

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Introduction

The prevalence of obesity in children has been dramatically increasing recently in both developed and developing countries. Obesity poses a crucial risk factor regarding cardiovascular morbidity and mortality.[1] The relationship between obesity and increased cardiovascular morbidity and mortality is thought to be related to a number of heterogeneous metabolic anomalies, such as dyslipidemia, insulin resistance and type-2 diabetes mellitus, and hypertension.[2–4]

Adipose tissue is an endocrine organ, which secretes several peptides such as leptin, resistin and adiponectin. These peptides, which have cytokine function, may at times be responsible for the development of cardiovascular disease.[5] Animal studies have shown that adiponectin increases insulin sensitivity and might also have antiadrenergic and anti-inflammatory effects.[6,7] Adiponectin has some positive effects on glucose and lipid metabolism, inflammation, endothelial functions and thrombogenesis. Therefore, decreased adiponectin levels may be responsible for the pathogenesis of cardiovascular diseases, which develop in the obese.

Resistin is a recently discovered, cysteine-rich hormone released by adipose tissue.[8] Resistin antagonizes the insulin effect by blocking glucose uptake independently of glucose production in the liver and glucose transporte-4 in the skeletal muscle.[9,10] Animal studies have shown that resistin levels in obesity are increased, and this may play a role in insulin resistance, which in turn increases cardiac hypertrophy; however, studies on humans have yielded varying results.[11–14]

In our study, we aimed to investigate serum adiponectin and resistin levels in childhood obesity and their relationship with cardiac changes and insulin resistance.

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Methods

Study groups

In this study, 71 obese and 24 overweight children and adolescents who had applied to the pediatric endocrinology department, Medical School of Inonu University were included. The control group consisted of 40 age- and sex-matched children and adolescents. Those with a chronic disease, those taking pills that may affect cardiac functions and those with a cardiac disease were excluded from the study. Before the study, the approval of the Ethics Committee of Medical School of Inonu University in accordance with Declaration of Helsinki was received.

Clinical evaluation

Height and weight measurements of each participant were made by the same person using the same tools. BMI values were calculated according to age and sex using the formula: BMI = weight (kilograms)/[height (meters)^2]. BMI SD score (SDS) (Z score) values were calculated by a computer program designed according to age and sex, using the formula:

BMI SDS = (calculated BMI value) − (average reference value of the population).

Standard deviation of the reference population

On the basis of age and sex, those with a BMI SDS of 2.00 and over were defined as obese, whereas those with a BMI SDS between 1.6 and 2.00 were defined as overweight.[15]

SBP and DBP of each patient in the study group were measured twice (within 10–20-min intervals) after a 20-min rest, using the same sphygmomanometer with a cuff that covers two-thirds of the left arm, by the same person each time, and the average of these two values was recorded.

Laboratory analyses

Blood samples of the participants were obtained for fasting blood sugar, total blood cholesterol, triglyceride, low-density lipoprotein (LDL) cholesterol, very low-density lipoprotein (VLDL) cholesterol, high-density lipoprotein (HDL) cholesterol, insulin, C-peptide and adiponectin and resistin values while the participants were in an 8–12-h fasting state. The serum samples, which were separated from the same blood samples to be used for measurements of adiponectin and resistin levels, were stored at −80°C. Glucose, total blood cholesterol, triglyceride, VLDL, LDL and HDL were analyzed with an Abbott Aeroset device (Abbott Laboratories, Abbott Park, Illinois, USA) using aeroset glucose, triglyceride, aeroset cholesterol and direct HDL kits. VLDL and LDL were calculated using the following formulas: VLDL = triglyceride/5 and LDL = cholester-cholesterol − (triglyceride/5) (Friedwald formula). The values were expressed in milligrams per deciliter. C-peptide was analyzed with an Immulite 2000 device (Flanders, New Jersey, USA) using Immulite 2000 C-peptide insulin kits according to the immunoassay method. Insulin was measured in micro-international units per milliliter and C-peptide in nanograms per milliliter. HOMA-IR (homeostasis model assessment of insulin resistance) was calculated according to the formula: HOMA-IR = [fasting blood sugar (milligrams per deciliter)/18] × [fasting blood insulin (micro-international units per milliliter)/22.5].[16] Those with a HOMA-IR value over 2.5 were defined as insulin resistant.[17] Every 5-ml of blood sample taken for adiponectin and resistin was left for coagulation, then centrifuged and the resulting serum was divided into two separate tubes and stored at −80°C for further analysis. Each sample was studied by double-checking according to the ELISA method (BioVendor; adiponectin: RD 191023100, resistin: RD 191016100).

Echocardiographic measurements

Two-dimensional M-mode, pulsed-wave (PW) Doppler and tissue Doppler echocardiography analyses were performed in all the study and control groups. Left ventricular wall (LVW) thickness, left ventricular mass, stroke volume, cardiac output and systolic and diastolic functions of the left ventricle were measured using an M-mode, two-dimensional color-coded echocardiography device (Vivid pro-7, GE, Vingmed Ultrasound, Horten, Norway). Mitral diastolic inflow velocity profile was assessed by using PW Doppler sample at the four-chamber view after proper sampling position of PW Doppler. The peak mitral E velocity (milliseconds), the peak velocity of mitral A (milliseconds), the E/A ratio (%) and deceleration time (milliseconds) were measured. Isovolumic relaxation time (IVRT) was measured as the interval between the cessation of the systolic flow and onset of the mitral inflow at the apical five-chamber view by using PW Doppler.

In the tissue Doppler echocardiography analysis, IVRT, isovolumic contraction time (IVCT), early mitral diastolic inflow velocity (E'), late mitral diastolic inflow velocity (A') and ejection time were measured by measuring myocardial velocities at the mitral lateral annulus with apical four-chamber view. Myocardial performance index (MPI) was calculated by the formula: MPI = IVRT + IVCT/ejection time.

Diastolic and systolic aortic root diameters were measured at 3 cm above the aortic valve by the use of M-mode echocardiography, and arterial pressure was measured simultaneously. Aortic stiffness index (β) was calculated by the formula: β = (SBP/DBP)/[(SD − diasto-diastolic diameter)/diastolic diameter].

Statistical analysis

Statistical evaluation was done by using SPSS for Windows 13.0 (California State University, USA). Categorical data were defined by number and percentage, whereas

Table 1 Demographic and clinic data of the obese and overweight groups

	Obese ($n=71$), mean + SD	Overweight ($n=24$), mean + SD	Control ($n=40$), mean + SD	*P*0	*P*1	*P*2	*P*3
Age (years)	12.1 ± 2.6	12.0 ± 1.93	11.1 ± 2.39	0.112	0.962	0.05	0.135
Sex (male/female)	44/27	6/18	21/19	0.007	0.002	0.331	0.031
Weight (kg)	67.7 ± 16.9	60.5 ± 12.7	35.9 ± 10.7	0.0001	0.042	0.0001	0.0001
Height (cm)	150.7 ± 12.1	145.9 ± 32.0	141.4 ± 14.0	0.033	0.259	0.01	0.331
BMI SDS	2.58 ± 0.41	1.68 ± 0.2	−0.03 ± 0.8	0.0001	0.0001	0.0001	0.0001
SBP (mmHg)	112.6 ± 12.7	114.1 ± 14.0	111.4 ± 8.7	0.675	0.610	0.592	0.381
DBP (mmHg)	70.2 ± 9.4	68.2 ± 9.3	67.5 ± 8.4	0.285	0.358	0.132	0.751

*P*0, among obese, overweight and control groups; *P*1, between the obese and overweight groups; *P*2, between the obese and control groups; and *P*3, between the overweight and control groups. BMI SDS, BMI SD score.

measurable (quantitative) data by the arithmetic mean (X) ± SD. After normality testing with Shapiro–Wilk test, one-way analysis of variance, unpaired *t*-test, Pearson's correlation analysis and multiple regression analysis were applied for variables that showed normal distribution, whereas Mann–Whitney *U*-test was applied for the data that did not show normal distribution and χ^2-test was applied for the categorical data. A *P* value less than 0.05 was set as statistically significant.

Results

In the study, 71 obese, 24 overweight and 40 normal weight healthy children were included. In Table 1, clinical and anthropometric qualities are shown; in Table 2, biochemical qualities are demonstrated; and in Table 3, echocardiographic qualities of the groups are demonstrated.

Cholesterol and LDL values of the obese and overweight groups were higher than those of the control group ($P<0.01$). In the obese group, triglyceride and VLDL levels were higher than those in the control and overweight groups ($P<0.001$), whereas HDL levels were lower ($P<0.05$). HOMA-IR, fasting insulin and fasting C-peptide values were higher in the obese and overweight groups than those in the control group ($P<0.001$). Adiponectin level in the obese and overweight groups were lower than those in the control group ($P<0.001$). Resistin level was lower in the obese and overweight groups than in the control group ($P<0.05$).

The measurements of the left ventricular systolic and diastolic functions are shown in Table 3. When compared with the control group, the LVW thickness and left ventricle mass values were increased in the overweight and obese groups, and this increase was statistically significant. There were statistically significant variations detected in the overweight and obese groups regarding mitral *E*, mitral *A*, deceleration time and IVRT when scanned with conventional Doppler ($P<0.05$); however, no statistically significant difference was observed concerning *E*/*A* ratio ($P>0.05$) (Table 3).

Mitral *E* and mitral *A* were statistically significantly shorter in the obese group than in the control group ($P<0.01$). In the obese group, deceleration time was significantly longer compared with that of the control group ($P<0.05$). IVRT was significantly shorter in the obese and overweight groups than in the control group ($P<0.01$ and <0.05, respectively).

In the evaluation of diastolic functions with tissue Doppler echocardiography, no statistically significant differences were detected among the groups for E', A', IVCT or IVRT ($P>0.05$). A' level in the overweight group was significantly increased in comparison with that of the control group ($P<0.05$). E/E' was a statistically significantly shorter in the obese group than in the control group ($P<0.01$) (Table 3). For aortic stiffness index (ASI) and Tei index, there were no statistically significant differences among the groups ($P>0.05$) (Table 3).

Table 2 Biochemical data of the obese, overweight and control groups

	Obese, mean + SD	Overweight, mean + SD	Control, mean + SD	*P*0	*P*1	*P*2	*P*3
Cholesterol (mg/dl)	($n=71$) 177.5 ± 34.7	($n=24$) 166.4 ± 23.6	($n=38$) 139.0 ± 25.9	0.0001	0.128	0.0001	0.001
TG (mg/dl)	($n=71$) 144.6 ± 73.8	($n=24$) 115.8 ± 61.2	($n=38$) 87.8 ± 31.0	0.0001	0.052	0.0001	0.087
HDL (mg/dl)	($n=70$) 40.6 ± 8.2	($n=24$) 43.5 ± 8.2	($n=38$) 44.5 ± 8.6	0.055	0.147	0.023	0.654
VLDL (mg/dl)	($n=70$) 28.4 ± 13.2	($n=23$) 23.4 ± 11.2	($n=38$) 18.8 ± 8.0	0.0001	0.073	0.0001	0.139
LDL (mg/dl)	($n=69$) 108.5 ± 29.6	($n=24$) 99.6 ± 22.2	($n=38$) 73.9 ± 22.4	0.0001	0.159	0.0001	0.0001
HOMA-IR	($n=70$) 4.1 ± 2.3	($n=23$) 3.7 ± 1.9	($n=38$) 1.1 ± 0.5	0.0001	0.388	0.0001	0.0001
Fasting glucose (mg/dl)	($n=70$) 90.6 ± 11.5	($n=23$) 93.3 ± 6.7	($n=38$) 90.9 ± 5.3	0.485	0.239	0.901	0.328
Fasting insulin (μIU/ml)	($n=70$) 18.4 ± 10.4	($n=23$) 16.5 ± 8.6	($n=38$) 5.1 ± 2.2	0.0001	0.352	0.0001	0.0001
Fasting C-peptide (ng/ml)	($n=37$) 3.6 ± 2.1	($n=11$) 3.6 ± 2.4	($n=38$) 1.4 ± 0.5	0.001	0.978	0.0001	0.0001
Adiponectin (μg/ml)	8.4 ± 3.6	8.5 ± 3.3	12.7 ± 4.5	0.0001	0.922	0.0001	0.0001
Resistin (ng/ml)	5.9 ± 4.1	5.5 ± 3.2	8.2 ± 5.6	0.028	0.739	0.016	0.036

*P*0, among obese, overweight and control groups; *P*1, between obese and overweight groups; *P*2, between obese and control groups; and *P*3, between overweight and control groups. HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance; LDL, low-density lipoprotein; TG, triglyceride; VLDL, very low-density lipoprotein.

Table 3 Echocardiographic measurements of overweight, obese and control groups

	Obese ($n=71$), mean ± SD	Overweight ($n=24$), mean ± SD	Control ($n=40$), mean ± SD	*P*0	*P*1	*P*2	*P*3
Left ventricular diameters							
IVSD (mm)	7.7 ± 1.6	7.7 ± 1.6	6.6 ± 0.9	0.0001	0.867	0.0001	0.003
IVSS (mm)	12.0 ± 2.1	11.8 ± 2.3	10.9 ± 1.48	0.02	0.772	0.006	0.064
LVWDd (mm)	7.1 ± 1.6	6.5 ± 1.2	5.6 ± 1.2	0.0001	0.07	0.0001	0.019
LVWDs (mm)	11.2 ± 1.8	11.6 ± 1.8	9.7 ± 1.6	0.0001	0.356	0.0001	0.0001
LVEDd/m^2 (mm/m^2)	26.6 ± 4.7	27.4 ± 2.8	36.2 ± 5.2	0.0001	0.451	0.0001	0.0001
LVEDs/m^2 (mm/m^2)	16.4 ± 3.8	17.0 ± 2.2	22.2 ± 3.9	0.0001	0.433	0.0001	0.0001
Ao (mm)	26.3 ± 3.5	25.3 ± 2.5	22.6 ± 3.2	0.0001	0.202	0.0001	0.002
LA (mm)	32.9 ± 3.9	31.8 ± 4.1	26.5 ± 4.2	0.0001	0.290	0.0001	0.0001
LV mass(g)	124 ± 44.4	119.5 ± 34.9	82.2 ± 26.2	0.0001	0.621	0.0001	0.0001
ASI	9.7 ± 4.6	10.3 ± 4.6	8.4 ± 3.4	0.174	0.540	0.133	0.088
Systolic functions							
EF (%)	68.5 ± 7.8	67.9 ± 6.2	69.2 ± 6.6	0.789	0.712	0.659	0.499
IF (%)	39.3 ± 6.8	37.8 ± 5.1	38.7 ± 5.4	0.602	0.321	0.648	0.577
Diastolic functions							
Mitral *E* (ms)	0.9 ± 0.1	1 ± 0.1	1 ± 0.1	0.016	0.063	0.008	0.720
Mitral *A* (ms)	0.5 ± 0.1	0.6 ± 0.09	0.6 ± 0.1	0.008	0.284	0.002	0.151
E/A (%)	1.6 ± 0.4	1.6 ± 0.3	1.6 ± 0.7	0.960	0.929	0.775	0.891
IVRT (ms)	85.4 ± 28.9	86.2 ± 27.5	100 ± 20.0	0.017	0.905	0.006	0.045
DT (ms)	112.8 ± 23.8	101.7 ± 23.4	99.5 ± 31.1	0.023	0.075	0.011	0.740
Tissue Doppler measurements							
E′ (ms)	0.1 ± 0.07	0.1 ± 0.04	0.1 ± 0.04	0.645	0.899	0.398	0.445
A′ (ms)	0.08 ± 0.06	0.1 ± 0.1	0.07 ± 0.02	0.140	0.137	0.421	0.049
E/E′	5.5 ± 1.2	5.9 ± 1.4	6.6 ± 2.8	0.016	0.469	0.004	0.118
IVCT (ms)	67.8 ± 18.0	71.2 ± 15.1	70.0 ± 17.2	0.634	0.400	0.496	0.804
IVRT (ms)	78.2 ± 18.1	85.0 ± 23.1	78.2 ± 22.7	0.338	0.163	0.994	0.200
ET (ms)	263.0 ± 30.5	265.2 ± 28.8	243 ± 20.6	0.001	0.726	0.0001	0.003
Tei index	0.5 ± 0.1	0.5 ± 0.1	0.6 ± 0.1	0.350	0.549	0.151	0.579

*P*0, among obese, overweight and control groups; *P*1, between obese and overweight groups; *P*2, between obese and control groups; and *P*3, between overweight and control groups. Ao, aortic root diastolic diameter; Aorta DD, aorta diastolic diameter; Aorta SD, aorta systolic diameter; ASI, aortic stiffness index; CO, cardiac output; DT, deceleration time; EF, ejection fraction; ET, ejection time; IF, injection fraction; IVCT, isovolumic contraction time; IVRT, isovolumic relaxation time; IVSD, interventricular septum diastolic diameter; IVSS, interventricular septum systolic diameter; LA, left atrium systolic diameter; LVEDd, left ventricular end-diastolic diameter; LV mass, left ventricular mass; LVEDs, left ventricular end-systolic diameter; LVWDd, left ventricular wall diastolic diameter; LVWDs, left ventricular wall systolic diameter.

No significant correlations were determined between resistin level and mitral *E*, mitral *A*, deceleration time, IVRT, LVW diastolic diameter (LVWDd), interventricular septum diastolic diameter (IVSD), left ventricular end-diastolic diameter (LVEDd), ASI or Tei index in the obese, overweight and control groups. However, a positive correlation was observed between resistin level and left ventricle mass in the obese group ($r=0.326$, $P=0.013$), but no significant correlations were found between adiponectin and mitral *E*, mitral *A*, deceleration time, IVRT, left ventricular mass, LVWDd, IVSD, LVEDd, ASI or Tei index in the obese, overweight and control groups.

In the obese group, there were statistically significant correlations between left ventricular mass, LVWDd and HOMA-IR, whereas there was a negative correlation between mitral *E* and HOMA-IR. There were no correlations between mitral *E*, left ventricular mass, LVWDd and HOMA-IR in the overweight and control groups. There were no significant correlations between HOMA-IR and mitral *A*, deceleration time, IVRT, IVSD, LVEDd, ASI, Tei index in the obese, overweight and control groups, either.

The linear regression analysis showed resistin level as the only independent predictor of left ventricular mass in the obese children ($\beta=3.59$, $P=0.016$). Interventricular septum systolic diameter (IVSS) values were positively affected by resistin ($\beta=0.14$, $P=0.04$), and IVSD was positively affected by SBP ($\beta=0.059$, $P=0.038$).

Discussion

Obesity, in correlation with the risk factors such as impaired glucose tolerance, insulin resistance, dyslipidemia and hypertension, leads to metabolic syndrome, type 2 diabetes and cardiovascular diseases. These complications, quite prevalent among obese adults, now have started to occur among obese children. Hence, in the near future, it would not be a great surprise to see a dramatic change in the prevalence of glucose intolerance, type 2 diabetes mellitus, hypertension, dyslipidemia and ischemic heart disease among young adults.[17,18]

In our study, we observed changes in cardiac structure and diastolic functions and decreased serum adiponectin and resistin levels among the obese and overweight children. Moreover, it was determined that resistin, fasting insulin and HOMA-IR were associated with left ventricular mass. These findings suggested that resistin and insulin resistance might contribute to the cardiac changes by increasing left ventricular mass. Another finding was that decreased serum resistin levels may lead to cardiac hypertrophy in childhood obesity, and this effect was more striking than were DBP values.

Wong *et al.*[19] determined that left ventricular mass significantly increased in the obese and overweight groups. Likewise, in Bogalusa Heart Study,[20] it was revealed there was a strong relationship between left ventricular mass and childhood obesity. In the light of which it was suggested that childhood obesity played a major part in the development of left ventricular hypertrophy.[20] It was also reported in this study that ejection fraction was significantly decreased in obese patients. However, in many echocardiographic studies,[21–23] similar to our study, no difference in left ventricular systolic functions was detected. These results support the studies suggesting that left ventricular systolic functions are affected only in the individuals with severe obesity and only in a late period for that matter.[21,24] In addition, an increase in stroke volume in the obese, an indication of increased volume overload, was observed in the Strong Heart Study. Likewise, in our study, stroke volume was significantly increased in the obese and overweight groups compared to the control group.

Few studies are available about the effects of obesity on diastolic heart functions in obese children and adolescents.[25,26]

Harada *et al.*[27] observed variations in transmitral venous wave velocities, a sign of deterioration in the early diastolic load, in asymptomatic obese children, using the pulse-wave Doppler method. Mehta *et al.*[28] observed that there was a decrease in E' and an increase in A' in obese and overweight children, which signified an impairment of the relaxation of the myocardium. In our study, we detected a decrease in E' and an extension of deceleration time in the obese group compared with the control group. Pascual *et al.*[29] support the results of the study by Peterson *et al.*[30] Unlike in the literature, in our study we found a shortening of IVRT in the obese and overweight groups compared with the control group and a reduction in mitral A in the obese group compared with the control group, which might have been due to the relatively lower number of the participants in the control group than in the obese group. On the contrary, A' was significantly increased in the overweight group compared with the control group. Hence, it can be said that the increase in A' in the overweight group on the tissue Doppler echocardiogram and a reduction in mitral A and an extension of deceleration time in the obese group on the pulse wave echocardiogram indicate subclinical diastolic function impairment in obese and overweight children. Yet, both our study and the previous studies fail to fully elaborate the deteriorations of diastolic functions in obese and overweight children.

In many studies on obese and hypertensive individuals, the relationship between insulin resistance and left ventricular mass was researched and varying results were obtained. In some studies, this relationship was confirmed, whereas in other studies it was not.[31,32] In our study, it was found that left ventricular mass values were increased in the obese and overweight groups compared with the control group ($P < 0.01$). Moreover, the existence of diastolic anomalies such as relaxation anomalies was demonstrated in the obese and overweight individual by means of conventional echocardiography and tissue Doppler echocardiography. In the light of these evaluations, we believe that the rises in fasting insulin and HOMA-IR levels brought about cardiac modifications by raising left ventricular mass.

It is thought that serum adiponectin level is related to systemic insulin sensitivity, and that lowered serum adiponectin level plays a role in the pathogenesis of obesity.[33–37] In our study, parallel to the literature, adiponectin levels were found to be significantly low in the obese and overweight groups compared with the control group. Although in our research, adiponectin levels were significantly lower in the cases with insulin resistance than in the cases without insulin resistance, no significant correlations were found between adiponectin and HOMA-IR in the obese, overweight and control groups. Unlike in the study by Panagopoulou *et al.*[36] in which a negative correlation between adiponectin and triglyceride and LDL in obese children was detected, in our study we found a significant positive correlation between adiponectin and total cholesterol in the obese children. This finding suggests that the increased cholesterol in obesity in children might have an expanding effect on adiponectin by means of a positive feedback effect. In a study that focused on the relationship between plasma adiponectin levels and left ventricular diastolic function and left ventricular hypertrophy, a significant negative correlation was found between adiponectin level and BMI, IVRT and left ventricular mass; at the same time, a significant positive correlation between adiponectin level and E/A was observed, and a diastolic dysfunction in those with a low adiponectin level was shown.[38]

In another study with uncomplicated obese patients, which evaluated the correlation between adiponectin levels and left ventricular mass index, it was suggested that obesity led to left ventricular hypertrophy and adiponectin had a lowering effect on left ventricular mass index.[38] In our study, we did not find any relationship between adiponectin levels and left ventricular mass and LVW thickness or diastolic functions in the obese, overweight and control groups. As the studies about the relationship between adiponectin and cardiac functions mostly involve adults and as there are not any studies focusing on this correlation in children, the relationship between adiponectin and cardiac functions in childhood obesity remains unclear. Thus, we believe that studies on this subject will be useful.

Resistin, a hormone released from fat tissue, is thought to be related to obesity and insulin resistance. In the early studies on mice, it was found that resistin caused insulin

resistance.[11] So far, the studies in search of the relationship between obesity and resistin have yielded conflicting results.[11–14,39–47]

In our study, the resistin levels in the obese and overweight groups were significantly lower than those in the control group ($P < 0.05$). The studies that emphasized that resistin levels in the obese increased or did not change were mostly about resistin gene expression and were usually performed on adults. Gerber *et al.*[47] demonstrated in their study that resistin had different molecular isoforms present in human blood. The same isoform (dimeric) was evaluated in the studies by Azuma *et al.*[14] and Degawa-Yamauchi *et al.*,[39] who suggested that serum resistin levels increased in the obese; however, in the study by Gerber *et al.*,[47] they suggested that it did not change. We believe that the differences in the results of earlier studies and our study might have been due to the fact that the studies by Azuma *et al.*[14] and Degawa-Yamauchi *et al.*[39] were conducted on adults and ours was on children and that the individual differences in resistin levels were due to the demonstrated resistin gene polymorphisms. In addition, experimental studies[11] suggested that resistin is acting like an insulin antagonist. On the basis of this fact, we think that hyperinsulinemia, depending on insulin resistance in the obese and overweight children in our study, might have suppressed the resistin levels. Our study revealed that serum resistin levels were lower in obese and overweight children than in normal weight children. This finding supports the results of the studies by Way *et al.*[42] and Milan *et al.*[43] on mice. The studies about resistin level–obesity relationship on obese individuals, especially obese children, have remained limited and, thus, new studies are needed.

In our research, no significant correlations were found between serum resistin level and fasting insulin, HOMA-IR in the obese, overweight and control groups either ($P > 0.05$). In conclusion, no correlations were determined between serum resistin level and insulin resistance in the obese, overweight and normal weight children in our study. These findings support the findings of the studies by Degawa-Yamauchi *et al.*,[39] Lee *et al.*,[45] Nagaev and Smith,[13] Savage *et al.*[12] and Gerber *et al.*[47] who put forward that resistin did not have a significant effect on insulin resistance. Furthermore, despite a significant positive correlation between resistin, and triglyceride and VLDL ($r = 0.41$, $P = 0.001$ and $r = 0.44$, $P > 0.001$, respectively) and a significant negative correlation between resistin and HDL ($r = -0.26$, $P < 0.05$) in the obese group in our study, no significant correlations were found between serum resistin level and triglyceride, VLDL and HDL ($P > 0.05$) in the overweight group. However, significant negative correlations were found between resistin, and triglyceride and VLDL ($r = -0.41$, $P < 0.01$ and $r = -0.41$, $P < 0.05$, respectively) in the control group. These results suggest that in obese children, resistin might help the development of dyslipidemia via insulin resistance or some other unknown mechanisms, and it might have a protective effect against dyslipidemia in healthy children.

In a study about cardiac contractility and its role in hypertrophy, it was suggested that resistin was effective on direct cardiac hypertrophy by means of autocrine and paracrine mechanisms in the heart, and that high resistin levels in diabetic patients might contribute to the development of cardiac hypertrophy.[48]

To our knowledge, there are no studies that focus on the relationship between resistin and heart functions in humans. In our study, we detected a significant positive correlation between resistin levels and left ventricular mass and IVSS in obese children. In linear regression analyses, we found a statistically significant relationship between resistin levels and left ventricular mass and IVSS in the obese cases as well. This finding supports the results of the study by Kim *et al.*[48] on mice, which suggested that resistin might be influential in the development of cardiac hypertrophy. Kim *et al.* directly investigated the resistin expression in mouse hearts, whereas in our study we evaluated serum resistin levels in children.

In conclusion, cardiac changes such as increased LVW diameters, left ventricular mass and diastolic dysfunction occur in obese and overweight children, even in asymptomatic conditions. It was shown that, however, decreased adiponectin levels did not show any correlation with cardiac changes and serum resistin levels in the obese cases were related to left ventricular hypertrophy. Further, molecular experiments are required to clarify the resistin role. We think that more studies are needed to investigate the correlation between adiposity hormone levels and cardiac hypertrophy.

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