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Adiponectin and resistin concentrations after glucose load in adolescents with polycystic ovary syndrome

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Abstract

Our aims were to evaluate the serum adiponectin and resistin levels at fasting and after glucose load and their interaction with risk of cardiovascular disease (CVD) in adolescents with polycystic ovary syndrome (PCOS). Twenty-two adolescents with PCOS and 16 healthy controls were included in the study. Oral glucose tolerance test (OGTT) was performed in all adolescents. Fasting lipids was measured. Insulin, glucose, adiponectin, and resistin levels were measured at 0 and 120 min of OGTT. Homeostasis model assessment of insulin resistance (HOMA-IR), quantitative insulin-sensitivity check index (QUICKI), fasting glucose-to-insulin ratio (FGIR), and the whole -body insulin sensitivity index (ISI) were calculated. Fasting adiponectin was correlated with ISI ($r = 0.729$, $p < 0.0001$), FGIR ($r = 0.696$, $p < 0.0001$), QUICKI ($r = 0.592$, $p = 0.004$) and HDL-C ($r = 0.516$, $p = 0.028$), systolic blood pressure ($r = -0.732$, $p < 0.0001$), body mass index ($r = -0.738$, $p < 0.0001$), waist circumference ($r = -0.706$, $p < 0.0001$), and HOMA-IR ($r = -0.595$, $p = 0.003$). No correlation was found between resistin and insulin resistance indexes. Obese adolescents with PCOS have increased CVD risk such as dyslipidemia, hypertension, and insulin resistance than normo-weight PCOS. Hypoadiponectinaemia could be increase risks levels in obese girls with PCOS.

Keywords: *Adiponectin, resistin, adolescent, insulin resistance, polycystic ovary syndrome, cardiovascular risk factors*

Introduction

Polycystic ovary syndrome (PCOS) is the most common reproductive disorder in women associated with hyperandrogenism and chronic anovulation which causes menstrual abnormalities. PCOS is often clinically recognizable in the perimenarcheal period, and similarities between the physiological changes of puberty and the pathological features of PCOS have been noted, such as the hyperpulsatile gonadotropin secretion, increased ovarian and adrenal steroidogenesis, menstrual irregularity, hyperinsulinemia, and insulin resistance that develop in both conditions [1–4]. The menstrual cycle after menarche is usually anovulatory with menstrual irregularities such as oligomenorrhea or secondary amenorrhea with increased serum androgen levels as a normal phenomenon during puberty [2,5,6]. Moreover, multifollicular ovaries could be found in healthy adolescent girls. Thus, diagnosis of PCOS in adolescents is less straightforward than in adults. However, clinical findings of hyperandrogenemia accompanied by menstrual irregularities and other findings of PCOS such as increased LH/FSH ratio, enlarged/polycystic appearance of the ovaries and hyperinsulinemia/insulin resistance in adolescents need to be investigated.

Insulin resistance was proposed as an underlying factor in the etiology of PCOS, usually associated with increased cardiovascular disease (CVD) risk factors including impaired glucose tolerance (IGT), type 2 diabetes mellitus, obesity, dyslipidemia, and hypertension [7]. This may suggest that women with PCOS are subject to an increased risk of CVD [8].

Adiponectin has recently been identified as an adipocyte-specific protein and plays a physiological role in the control of insulin sensitivity and in the regulation of energy balance. Recently, hypoadiponectinaemia has been reported in women with PCOS

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which correlates with the degree of obesity [9–12]. PCOS-related hyperandrogenemia may modulate serum adiponectin level and this hyperandrogenemia enhances the susceptibility of PCOS women to insulin resistance syndrome and its long-term complications [13,14].

Resistin is a protein and its predominant source is macrophages located mainly in intra-abdominal adipose tissue in humans. Several studies have found that it is related with obesity, type 2 diabetes, insulin sensitivity [15,16] but this is not confirmed by other reports [17]. Also, results obtained from studies in children showed did not show a relationship between resistin and insulin resistance [18,19]. The expression of resistin can be up-regulated by dehydroepiandrosterone [20], suggesting that resistin and androgen synthesis may be linked. The studies that investigated serum resistin levels in obese and overweight women with PCOS have contradictory results: serum resistin levels were found to be either increased [21,22] or similar [23].

Although studies of adipocytokines in PCOS in the adult population have provided new data to us, the topic of serum adiponectin and resistin levels in PCOS has not been as extensively investigated in the adolescent population.

The aims of the present study were as follows: (1) to determine serum concentrations of adiponectin and resistin at fasting and after glucose load in obese and N-W adolescents with PCOS in comparison with age- and body mass index (BMI)- matched girls without PCOS, (2) to investigate their interactions with each other and their relationship with risk factors for CVD such as insulin resistances, dyslipidemia, and hypertension.

Methods

Subjects

Twenty-two adolescent girls with PCOS (mean age 15.2 ± 1.1) and age-matched 16 healthy adolescent girls (mean age 15.1 ± 1.1) were included in the study. Girls with PCOS were separated into two groups: 10 were obese [BMI 26–41 (34.2 ± 5)], weight-matched with obese controls [BMI 25–36 (29.7 ± 4)], and 12 were normo-weight (N-W) [BMI 17.8–23.2 (20.1 ± 1)], weight-matched with N-W controls [BMI 18.3–22.2 (20.1 ± 1.4)].

PCOS was diagnosed by having two of the following three: (1) oligo- or anovulation, (2) clinical and/or biochemical signs of hyperandrogenism, (3) polycystic ovaries, after the exclusion of related disorders [24].

All girls were at least 2 year post menarche at the time of evaluation for PCOS based on symptoms that also included oligomenorrhea or amenorrhea ($\leq$6 menses/years), weight gain, hirsutism, and acne. Biochemical hyperandrogenemia was defined as serum total testosterone level above the 60 ng/dl [25].

Girls with hormonal disease such as Cushing's syndrome, late-onset 21-hydroxylase deficiency, thyroid dysfunction, type 2 diabetes, hyperprolactinaemia or androgen-secreting tumors, and who had taken hormonal medication were excluded from the study.

The control groups were composed of (1) N-W volunteers and (2) obese patients who were referred to the pediatric endocrinology outpatient clinic for dietary treatment of obesity. All controls had normal cycles and no signs of hyperandrogenism, and none of them taken any medication.

Subjects who had a BMI higher than the 95th percentile of normal for their age and sex were classified as obese based on the standards of the Centers for Disease Control and Prevention. Waist circumference (WC) was measured midway between the lowest rib and the top of the iliac crest at the end of gentle expiration. Hip circumference (HC) was measured at the level of the thorachanter major where the widest part of the buttocks. Waist to hip ratio (WHR) was calculated. Pubertal staging of the subjects was performed according to Tanner-Marshall's methods. Ferriman-Gallway (F-G) hirsutism score was determined in all subjects, those having scores more than eight being considered as hirsute [26].

Blood pressures were measured three times using the mercury sphygmomanometer as a convenient method while the subjects were seated after at least 15 min of resting. The average of the last two blood measurements taken was used for analysis. Children with a systolic blood pressure (SBP) and/or diastolic blood pressure higher than the 95th percentile of normal for their age and sex were classified as hypertensive [27].

All participants underwent transabdominal pelvic ultrasonographic examination with a conventional full-bladder by the same physician. Both ovarian volumes were calculated as: width $\times$ length $\times$ height $\times$ 0.523 [28].

Protocol of the study

Serum samples were obtained from adolescents during the interval from the 2nd to the 5th days of their menstrual cycle. Levels of FSH, LH, estradiol (E2), progesterone, 17-OH progesterone, free and total testosterone, dehydroepiandrosterone-sulfate (DHEA-S), cortisol, prolactin (PRL), T4, and TSH were measured. Girls with 17-OH progesterone level higher than 2 ng/ml underwent ACTH stimulating test to exclude nonclassic congenital adrenal hyperplasia. The LH/FSH ratio was calculated.

After overnight fasting, oral glucose tolerance test (OGTT) was performed for all adolescents within the same time interval (09.00–12.00 am). Fasting serum samples were obtained at 0 min of OGTT for total cholesterol (TC), triglyceride (TG), and high density lipoprotein [HDL -C]. The venous blood glucose and insulin levels were measured at 0, 30, 60, 90, and 120 min of OGTT. Delta insulin values were obtained as 0 min values minus the 120 min values.

Blood samples for adiponectin, and resistin were obtained after fasting and at 120 min of OGTT. Blood samples were immediately centrifuged and stored at -80°C until analysis.

Assays and calculations

Serum glucose was measured by the enzymatic-spectrophotometric glucose oxidize method (Roche Diagnostics, Mannheim, Germany). Insulin was measured using the commercial kit of DPC (Diagnostic Products Corporation, CA) with immune chemiluminescence assay (ICMA). Lipid parameters were determined by enzymatic methods using commercial kits. Total T4 (μg/dl), free T4 (ng/dl), and TSH (μIU/ml) were analyzed with commercial kits (Roche Diagnostic GmbH, Mannheim, Germany) by ICMA with the E170 Hitachi analyzer (Tokyo, Japan). PRL (ng/ml), E2 (pg/ml), LH (mIU/ml), FSH (mIU/ml), and total testosterone (ng/dl) were measured by ICMA with the Architect analyzer (Architect Reagent Kit, IL). 17-OH-progesterone (μg/dl) and free testosterone (pg/ml) were analyzed with Diagnostic Systems Laboratories (DSL, Lot. No 06087, and 03167, respectively) kit using radioimmunoassay. Cortisol (μg/dl), ACTH (pg/ml), and DHEAS (μg/dl) were measured by ICMA with the Immulite 2500 analyzer (DPC).

Serum resistin concentrations were measured by using a sandwich enzyme-linked immunosorbent assay (ELISA), according to the manufacturer's instructions (Linco Research, St Charls, Missouri, Cat. No. EZHR 95-K). The sensitivity was 0.16 ng/ml. Serum adiponectin concentrations were measured by using an ELISA, according to the manufacturer's instructions (Linco Research, St Charles, Missouri, Cat. No. EZHADP-61K). When using a 20 μl sample size, the sensitivity was 0.78 ng/ml.

Low density lipoprotein (LDL-C) concentration was calculated [29]. TC/HDL-C was calculated as atherogenic index [30].

Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated by the product of the fasting plasma insulin levels (in μIU/ml) and the fasting plasma glucose level (in mmol/L), divided by 22.5 [31]. Fasting glucose-to-insulin ratio (FGIR) was calculated by dividing fasting plasma glucose (mg/dl) by fasting serum insulin (μU/ml) levels [32]. Quantitative insulin-sensitivity check index (QUICKI) was determined by the formula: 1/[Log fasting insulin (μU/ml) + Log fasting glucose (mg/dl)] [33]. The insulin sensitivity index (ISI) was calculated as follows: $\text{ISI} = 10{,}000/\sqrt{(\text{fasting glucose} \times \text{fasting insulin})\ (\text{mean glucose during OGTT} \times \text{mean insulin during OGTT})}$ [34]. Thus, different indexes of insulin sensitivity were compared in the PCOS group. Delta adiponectin and resistin values were obtained as 0 min values minus the 120 min values.

Ethics

The local ethic committee approved the study. The purpose of the study was explained to all subjects before participation and written informed consents were obtained from the parents of patients and control children.

Statistical analysis

The analysis was performed using SPSS 10 Statistical Software Package (SPSS, Chicago, IL, USA). Axiological data, SBP, DBP, serum lipids, atherogenic indexes, insulin resistance indexes, and hormonal results were expressed as the mean $\pm$ SD unless otherwise stated. Normality of the data was tested with the 'Kolmogorov–Smirnov test'. Differences between the parameters of PCOS and controls were investigated by 'Mann–Whitney *U* test'. The General linear model followed by repeated measures was used to test the significance of the differences in fasting and at 120 min of OGTT resistin and adiponectin at groups and subgroup levels. Pearson correlation was used for the analysis of intercorrelations among the parameters investigated. A $p < 0.05$ was considered statistically significant.

Results

Baseline characteristics

Anthropometric and clinical findings of PCOS and control groups are given in Table I. The level of pubic hair and breast development was Tanner stage IV in two girls with PCOS, and Tanner V in the rest. F-G scores of girls with PCOS were higher than those of the controls, as expected. Seventeen girls with PCOS (77.2%) had hirsutism and both PCOS groups had similar F-G scores. Mean F-G score in the both control groups were lower than both PCOS groups. Three impaired glucose tolerant obese girls with PCOS were detected during OGTT. Eighteen girls with PCOS (81.8%) had oligomenorrhea. None of them had amenorrhea. Seven obese girls with PCOS (70%) had acanthosis nigricans. Three of the obese controls (33.3%) had acanthosis nigricans.

Table I. Clinical and ultrasonographic characteristics of the adolescents with polycystic ovary syndrome and the controls.

Parameters	Total PCOS ($n=22$)	Obese PCOS ($n=10$)	N-W PCOS ($n=12$)	Total controls ($n=16$)	Obese controls ($n=7$)	N-W controls ($n=9$)
Chronologic age, year	15.2 ± 1	14.7 ± 0.9	15.7 ± 1	15.1 ± 1	15.1 ± 1	15.1 ± 0.8
Weight, kg	68.9 ± 21	89.3 ± 15*,†	51.9 ± 4‡	61.1 ± 14	74.4 ± 11	51.6 ± 4
Height, cm	161 ± 5	161 ± 7	160 ± 3	159 ± 6	158 ± 6	160 ± 5
BMI, kg/m^2	26.5 ± 8	34.2 ± 5*,†	20.1 ± 1‡	24.3 ± 5	29.7 ± 4	20.1 ± 1
WC, cm	80.9 ± 16	96.4 ± 10*,§,†	68 ± 3‡	74.2 ± 11	84.7 ± 7	66.1 ± 5
HC, cm	101 ± 11	111 ± 9*,†	93.4 ± 3‡	98.8 ± 7	104 ± 8	94.8 ± 4
WHR	0.79 ± 0.1	0.86 ± 0.1*,†	0.72 ± 0.03¶,**	0.74 ± 0.08	0.81 ± 0.07	0.69 ± 0.03
SBP, mmHg	120 ± 15	129 ± 17††,‡‡	112 ± 9**	117 ± 11	125 ± 12	111 ± 7
DBP, mmHg	75 ± 9	78 ± 10	73 ± 7**	76 ± 9	85 ± 5	70 ± 7
Hirsutism score (F-G)	11 ± 7§§	11 ± 9†	11 ± 6¶¶	0.7 ± 1.8	1.7 ± 3	0 ± 0
Hirsutism; %	77.2	70	83	0	0	0
Oligomenorrhea, %	40.9	40	41.6	0	0	0
Right ovarian volume, ml	11.4 ± 7§§	10.2 ± 3***,†	12.4 ± 5¶¶,‡	4.8 ± 1	5.1 ± 1	4.6 ± 1
Left ovarian volume, ml	8.3 ± 3§§	8.9 ± 2***,†	7.7 ± 3¶	5.1 ± 1	5.1 ± 1	5.1 ± 1

F-G, Ferriman-Gallwey score.
§§, $p < 0.0001$ total PCOS *vs.* total controls; *, $p < 0.0001$ obese PCOS *vs.* N-W PCOS; ††, $p < 0.05$ obese PCOS *vs.* N-W PCOS; ***, $p < 0.0001$ obese PCOS *vs.* obese controls; §, $p < 0.05$ obese PCOS *vs.* obese controls; ¶¶, $p < 0.0001$ N-W PCOS *vs.* N-W controls; ¶, $p < 0.05$ N-W PCOS *vs.* N-W controls; †, $p < 0.0001$ obese PCOS *vs.* N-W controls; ‡‡, $p < 0.05$ obese PCOS *vs.* N-W controls; ‡, $p < 0.0001$ N-W PCOS *vs.* obese controls; **, $p < 0.05$ N-W PCOS *vs.* obese controls.

Pelvic ultrasonography

Eleven girls with PCOS (five of them in the obese group, seven of them in the N-W group) had polycystic ovaries. Six to ten subcapsular follicles and the stromal hyperplasia were detected in 12 girls with PCOS by ultrasonographic examination. Ovarian volumes for both groups with PCOS were significantly larger than the controls. There was no significant difference between ovarian volumes of obese and N-W PCOS groups. Both ovarian volumes of the obese PCOS group were larger than the obese controls, and similarly both ovarian volumes of the N-W PCOS group were larger than the N-W controls. Ovarian volumes of both control groups were similar (Table I).

Gonadotrophins and sex steroids

The basal serum hormone concentrations in adolescents with PCOS and the controls are shown in Table II. Mean plasma LH concentrations, free testosterone concentrations, 17-OH progesterone concentrations, DHEAS concentrations, and LH to FSH ratio were all significantly higher in the PCOS group. No significant differences were found in all hormonal measurements in both control groups.

Serum lipids

Although there were no significant differences in serum LDL-C, TC, and TG levels between the obese and N-W PCOS groups, fasting serum TG and LDL-C levels of the obese PCOS group were higher than those of the obese and N-W controls (Table II). However, there were no significant differences between TG and HDL-C levels of the obese groups with and without PCOS.

Insulin resistance indexes

Table II shows that, although fasting insulin levels were higher in PCOS patients than in the controls, the difference was not statistically significant. The values of the results obtained for three girls with PCOS having IGT were excluded and insulin resistance indexes (HOMA-IR, QUICKI, FGIR, and ISI) recalculated. There were no differences between fasting glucose, HOMA-IR, QUICKI and FGIR of the PCOS group and the controls. ISI, QUICKI and FGIR values of the obese PCOS patients lower than N-W PCOS group and the controls (Table II). Nevertheless, after an oral glucose challenge, 2 h insulin levels increased more in the obese PCOS patients than in the N-W PCOS patients.

Resistin and adiponectin

There was no difference in serum adiponectin and resistin concentrations of PCOS and control groups even after adjusting for BMI.

Serum resistin concentrations, after fasting resistin and at 120 min of OGTT, of the PCOS group were similar to those of the controls (Table II). During OGTT, serum resistin concentrations of the PCOS group and the controls did not change.

Serum adiponectin concentrations, after fasting and at 120 min of OGTT, of the obese PCOS group were lower than those of the N-W PCOS group

Table II. Resistin, adiponectin, serum lipids, glucose and insulin-related parameters, measures of insulin sensitivity in study groups.

Parameters	Total PCOS ($n=22$)	Obese PCOS ($n=10$)	N-W PCOS ($n=12$)	Total controls ($n=16$)	Obese controls ($n=7$)	N-W controls ($n=9$)
LH, mIU/ml	16.7 ± 15*	$17.9 \pm 18^{\dagger,\ddagger}$	$15.8 \pm 12^{\S,\P}$	3.2 ± 1.7	3.5 ± 1.8	3 ± 1.7
FSH, mIU/ml	5.6 ± 2.7	5.4 ± 3	5.7 ± 2	4.1 ± 1.8	4.5 ± 2	3.8 ± 1
LH/FSH	2.8 ± 1*	$3 \pm 1.9^{\dagger,\ddagger}$	$2.7 \pm 1^{\S,\P}$	0.9 ± 0.5	0.8 ± 0.4	0.9 ± 0.6
Estradiol, pg/ml	97 ± 89	95 ± 105	99 ± 81	70 ± 36	55 ± 28	81 ± 38
Testosterone, ng/dl	75.4 ± 40	86.4 ± 54	61.3 ± 23**	63 ± 36	75.1 ± 44	54 ± 29
fTestosterone, pg/ml	$2.4 \pm 1.7^{\dagger\dagger}$	$3.6 \pm 2.3^{\dagger}$	$1.8 \pm 0.7^{\ddagger\ddagger}$	1.6 ± 0.7	1.1 ± 0.7	1.8 ± 0.8
17-OH progesterone, ng/ml	$3.4 \pm 1.8^{\dagger\dagger}$	$4 \pm 1.7^{\ddagger}$	3 ± 1.9	2.1 ± 1.4	2.2 ± 1.4	2 ± 1.5
DHEA-S, μg/dl	$198 \pm 108^{\dagger\dagger}$	212 ± 142	$187 \pm 74^{\ddagger\ddagger}$	102 ± 60	117 ± 33	93 ± 73
HDL (C), mg/dl	44 ± 10	$40 \pm 8^{\ddagger}$	47 ± 12	47 ± 13	41 ± 10	52 ± 13
LDL (C), mg/dl	$90 \pm 31^{\dagger\dagger}$	97 ± 43**,‡	84 ± 14	67 ± 21	66 ± 25	67 ± 18
TC, mg/dl	$158 \pm 31^{\dagger\dagger}$	165 ± 41**,‡	151 ± 13	131 ± 27	127 ± 35	134 ± 21
TG, mg/dl	113 ± 61	$130 \pm 72^{\ddagger}$	94 ± 43	84 ± 31	99 ± 33	71 ± 25
TC/HDL-C	$3.7 \pm 1.1^{\dagger\dagger}$	$4.1 \pm 1.2^{\P}$	3.3 ± 0.8	2.8 ± 0.6	3.1 ± 0.6	2.6 ± 0.5
$Glucose_0$, mg/dl	82 ± 9	$81 \pm 11^{\dagger,\ddagger}$	83 ± 7	83 ± 5	84 ± 6	83 ± 5
$Glucose_{120}$, mg/dl	108 ± 73	157 ± 82	67 ± 28	68 ± 47	93 ± 61	48 ± 18
$Insulin_0$, μ IU/ml	21 ± 17	33 ± 19	12 ± 3	12 ± 6	16.3 ± 6	9.6 ± 4
$Insulin_{120}$, μ IU/ml	106 ± 4	$115 \pm 26^{\dagger,\P}$	98 ± 14	96 ± 21	98 ± 29	94 ± 15
Delta insulin, μIU/ml	86 ± 60	$124 \pm 68^{\S,\ddagger}$	55 ± 28	56 ± 43	77 ± 59	39 ± 15
HOMA-IR	4.2 ± 3	$6.5 \pm 3^{\dagger\dagger,**}$	2.3 ± 0.7	2.5 ± 1	3.3 ± 1	2 ± 0.8
FGIR	5.6 ± 3	$3.1 \pm 1^{\dagger,**,\ddagger}$	7.8 ± 3	8.8 ± 5	6.3 ± 3	10.8 ± 6
QUICKI	0.319 ± 0.02	$0.297 \pm 0.02^{\dagger,\ddagger}$	0.336 ± 0.01	0.340 ± 0.03	0.324 ± 0.02	0.352 ± 0.03
ISI	$3.11 \pm 1.5^{\dagger\dagger}$	$1.72 \pm 0.7^{\dagger,\ddagger,\P}$	$4.27 \pm 0.9^{\S\S}$	5.17 ± 3.27	3.52 ± 2.1	6.45 ± 3.5
$Resistin_0$, ng/ml	18.6 ± 5	19.1 ± 7	18 ± 4	23.9 ± 10	19.5 ± 7	27.7 ± 12
$Resistin_{120}$, ng/ml	18.5 ± 6	21.4 ± 6	16.1 ± 4	22.6 ± 8	19.3 ± 6	24.4 ± 10
$Adiponectin_0$, ng/ml	17.1 ± 6	$11.6 \pm 4^{\dagger,\P}$	$21.6 \pm 4^{\P\P}$	18 ± 5	15.3 ± 4	20.1 ± 6
$Adiponectin_{120}$,ng/ml	13.6 ± 5	$10.4 \pm 4^{\S,\P}$	16.4 ± 4	16.2 ± 7	14.5 ± 6	17.5 ± 8
Delta Adiponectin	3.41 ± 4	$1.25 \pm 2^{\S}$	5.22 ± 4	1.8 ± 4	0.77 ± 4	2.60 ± 4

*, $p < 0.0001$ total PCOS vs. total controls; ††, $p < 0.05$ total PCOS vs. total controls; †, $p < 0.0001$ obese PCOS vs. N-W PCOS, §, $p < 0.05$ obese PCOS vs. N-W PCOS; **, $p < 0.05$ obese PCOS vs. obese controls, ‡, $p < 0.0001$ obese PCOS vs. N-W controls; ¶, $p < 0.05$ obese PCOS vs. N-W controls, ‡‡, $p < 0.0001$ N-W PCOS vs. N-W controls; ¶¶, $p < 0.05$ N-W PCOS vs. obese controls; §§, 0 0.05 N-W PCOS vs. N-W controls.

($p < 0.05$). Acute glucose load caused a significant decrease in adiponectin concentrations in N-W girls with or without PCOS in comparison with obese peers (Table II).

Although statistically significant change in delta adiponectin was greater in the PCOS group than for the control group ($F = 17.330$, $p < 0.0001$), delta resistin was similar in the PCOS and control groups. We also found a significant difference in delta adiponectin between the obese and normal-weight (N-W) PCOS groups ($F = 6.489$, $p = 0.011$) (Figure 1).

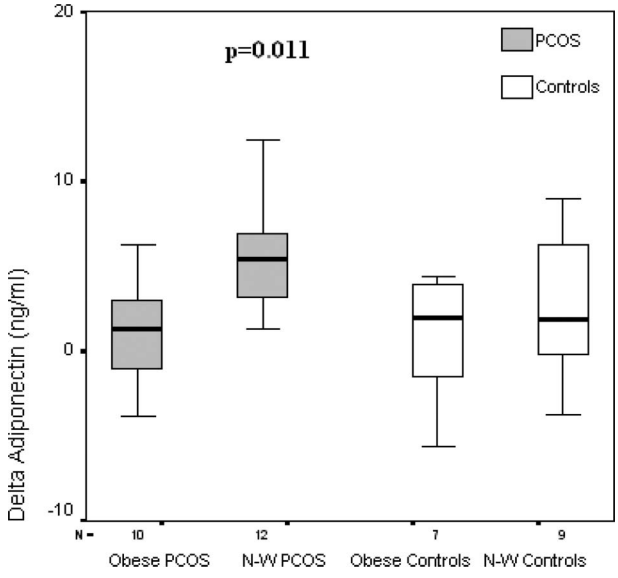

Figure 1. Box-plot graph of the changing in serum adiponectin (delta adiponectin) level at fasting and 120 min of OGTT in study groups.

Correlations between variables

The correlation between in clinical and laboratory findings and serum levels of adiponectin and resistin in the PCOS group was given in Table III. There was no correlation between gonadotrophins, sex steroids, adiponectin, and resistin in the PCOS group.

SBP and BMI showed positive correlation ($r = 0.684$, $p < 0.0001$) in PCOS group. WHR and BMI were negatively correlated with both adiponectin levels in PCOS group.

Serum HDL-C showed statistically significant positive correlation with fasting (Figure 2) and at 120 min of OGTT adiponectin and inverse correlation with resistin in the PCOS group (Table III).

Table III. Correlations between in adipocytokines and clinical and laboratory findings of the adolescents with polycystic ovary syndrome.

	Resistin 0 min		Resistin 120 min		Adiponectin 0 min		Adiponectin 120 min	
Parameters	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*
BMI		NS	0.518	0.014	−0.738	<0.0001	−0.560	0.007
WC		NS	0.481	0.023	−0.706	<0.0001	−0.626	0.002
HC		NS		NS	−0.727	<0.0001	−0.532	0.011
WHR		NS	0.563	0.006	−0.647	0.001	−0.543	0.009
SBP		NS		NS	−0.711	<0.0001	−0.762	<0.0001
HDL-C		NS	−0.713	0.001	0.516	0.028	0.556	0.017
LDL-C		NS		NS		NS	−0.494	0.037
TC/HDL-C		NS	0.481	0.023	−0.529	0.024	−0.678	0.002
I_0		NS		NS	−0.652	0.001	−0.587	0.004
I_{120}	−0.429	0.047	NS	NS	NS			
Delta insulin		NS		NS	−0.533	0.011	−0.573	0.05

BMI, body mass index; WC, waist circumference; HC, hip circumference; WHR, waist to hip ratio; SBP, systolic blood pressure; LOV, left ovarian volume; I_0, fasting insulin; I_{120}, insulin at 120 min of OGTT.

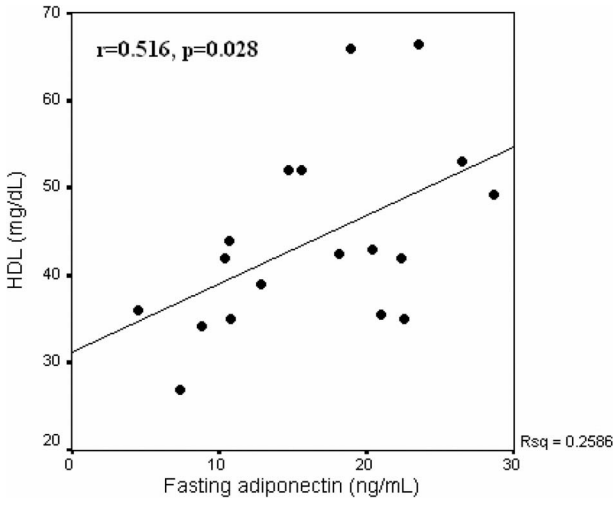

Figure 2. Positive correlation between in HDL-C and fasting adiponectin in PCOS group.

This significant correlation between HDL-C and fasting adiponectin ($r = 0.516$, $p = 0.028$) and resistin 120 min of OGTT ($r = -0.713$, $p = 0.001$) was found particularly in the obese PCOS group. Moreover, atherogenic indices were negatively correlated with fasting adiponectin and adiponectin at 120 min of OGTT.

Fasting adiponectin showed significant correlation between insulin resistance indexes in the PCOS group (Figure 3) and these correlations became stronger after adjusting for BMI. Resistin had no correlation with all insulin resistance indexes. However, the correlations between both resistin concentrations and the parameters of insulin resistance remained significant when adjusted for BMI [Fasting insulin ($r = 0.761$, $p < 0.0001$), QUICKI ($r = -0.824$, $p < 0.0001$), HOMA-IR ($r = 0.809$, $p < 0.0001$), FGIR ($r = -0.692$, $p < 0.0001$), and WBISI ($r = -0.846$, $p < 0.0001$)]. Resistin at 120 min of OGTT was negatively correlated with fasting adiponectin ($r = -0.583$, $p = 0.004$) and adiponectin at 120 min ($r = -0.783$, $p < 0.0001$).

Statistical significant negative correlations were found between delta insulin and both adiponectin levels in PCOS group.

Discussion

The studies investigating adipocytokines in PCOS are usually carried out within the adult population. Since there are an insufficient number of studies on adolescent girls with PCOS, it was necessary to compare our results with similar studies of adults with PCOS. In the present study, we found no differences between the serum adiponectin and resistin concentrations of girls with PCOS and that of controls at fasting and after glucose load. However, fasting adiponectin concentrations of the obese PCOS group were lower than those of N-W PCOS group. Delta adiponectin was also lower in the obese PCOS group than in the N-W PCOS group. These findings are in accordance with previous studies in women with PCOS [9,10,14].

A significant inverse correlation was found between BMI and fasting adiponectin in the PCOS group in our study. Since obese women with and without PCOS have decreased adiponectin concentrations as compared with N-W PCOS and healthy women [35], adiponectin concentration is inversely regulated by obesity. Also, in the present study, significant negative correlation between adiponectin at120 min of OGTT and BMI was observed. Statistical significant negative correlations were found between delta insulin and both adiponectin levels in the PCOS group. Moreover, delta adiponectin was lower than the obese PCOS than N-W PCOS. Taken together, increased insulin might be responsible in faster decrease in adiponectin concentrations of N-W PCOS group after acute glucose load. This result also may explain why obese patients

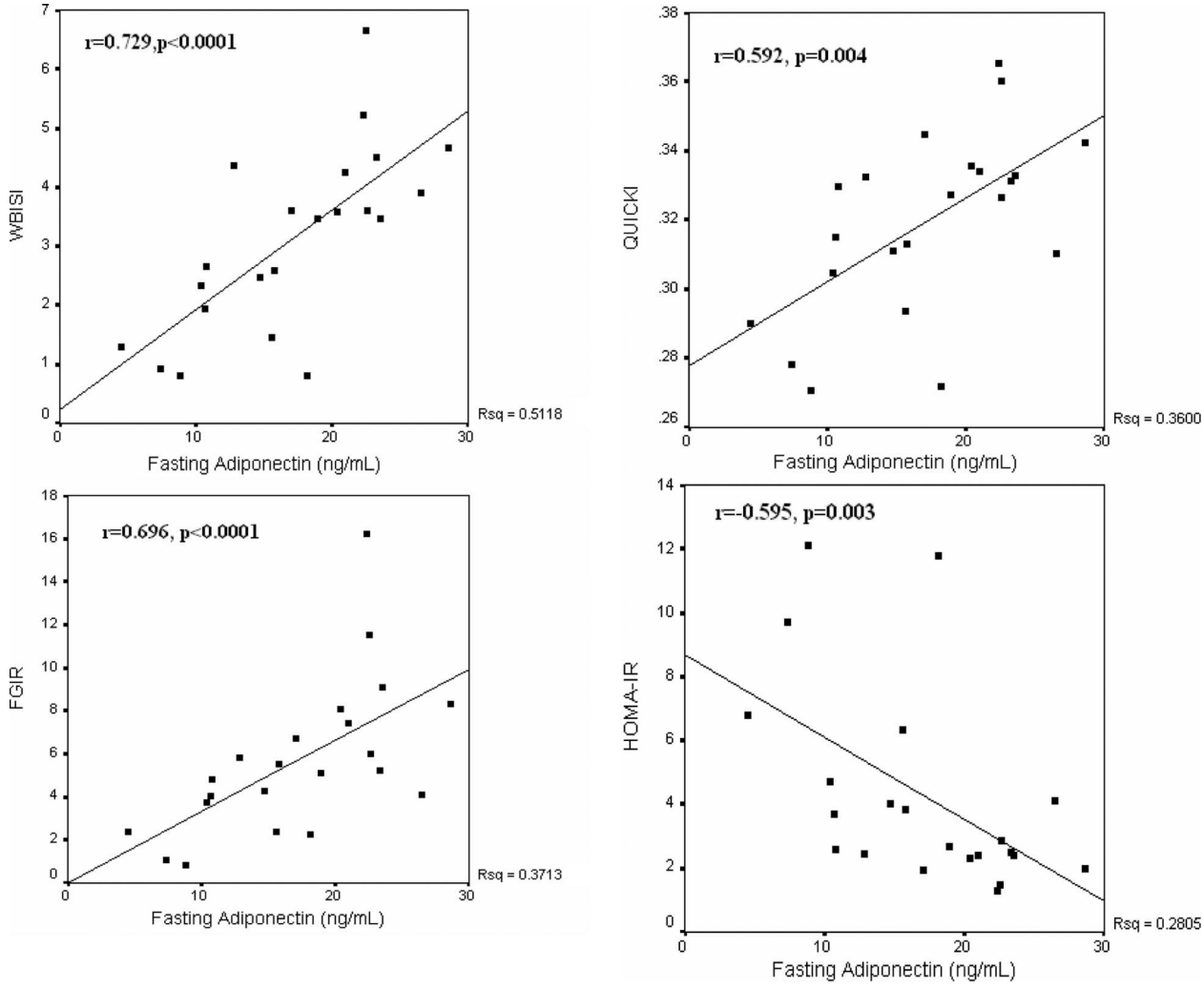

Figure 3. Correlation between adiponectin and insulin sensitivity indexes in PCOS group.

with continuous hyperglycemic status are more insulin resistant and they have hypoadiponectinaemia and increased cardiovascular risk.

Currently, only a few studies on serum adiponectin concentrations during OGTT in children and in women with PCOS have been published [35,36]. Böttner et al. [36], shown that adiponectin levels did not have significant alterations after glucose load in obese children and they concluded that the serum adiponectin concentrations are not affected by acute glucose challenge. Panidis et al. [9] found decreased fasting adiponectin concentrations in obese women with and without PCOS than in N-W counterparts. They also observed that differences between serum adiponectin concentrations at fasting and at 120 min of OGTT were not significant in patients with and without PCOS, while the rate of decrease in adiponectin concentrations during OGTT was lower in subjects with N-W than obese counterparts. In contrary, Lewandowski et al. [37] found significant increase in adiponectin concentrations at 120 min of OGTT in obese women with PCOS but the study included neither N-W nor obese control groups.

Our data showed significant correlations between adiponectin and ISIs. Fasting insulin and HOMA-IR showed inverse correlations with adiponectin while QUICKI, FGIR, and WBISI showed positive correlations with it in our patients with PCOS. These results are in accordance with previously published data obtained from studies in obese children [19] and women with PCOS [10,14]. It has been shown that adiponectin is negatively correlated with LDL-C and positively correlated with HDL-C in the adult population [38]. Ibanez and de Zegher [39], also found a striking parallelism between body composition and adiponectin in patients with PCOS and the authors suggest that the characteristic adiposity of the patients is tightly linked to their adipocytokines-lipid balance.

The early appearance of atherosclerosis in PCOS is likely to be the consequence of hyperinsulinemia and insulin resistance. In the present study, girls with PCOS had higher insulin levels and greater insulin resistance indexes than the controls. Moreover, CVD risk criteria such as BMI, WC, and SBP showed positive correlation with HOMA-IR, and inverse

correlation with ISI, FGIR and QUICKI while HDL-C was positively correlated with adiponectin in patients with PCOS. Recently, Shroff et al. [40] showed that although no differences in adiponectin concentration between obese women with and without PCOS, young obese women with PCOS have early coronary atherosclerosis compared with the obese controls.

In the adolescents with and without PCOS studied here, there was no significant change in serum resistin concentrations after fasting and after acute glucose load. This result suggests that resistin concentrations might be increased with chronic hyperglycemia such as diabetes. Reinehr et al. [18] evaluated resistin concentrations in obese and lean children and they found increased resistin concentrations in girls in comparison with the boys and no relation between resistin concentrations and pubertal status and ISIs. Similarly in our study, no correlation was found between fasting resistin and anthropometric measurements, ISIs, serum lipids, and atherogenic indexes.

We suggest that resistin concentrations of girls with PCOS show positive correlation with insulin resistance independent of BMI because statistically significant correlations were found between resistin and ISIs in our PCOS group after adjusting for BMI. Silswal et al. [41] shown that resistin leads to increased release of pro-inflammatory cytokines that cause insulin resistance. Since obese girls with PCOS have increased WC, increased TG and LDL-C and decreased HDL-C compared with obese and N-W controls, our results suggest that obese adolescents with PCOS may have an increased CVD risk.

In summary, although there were no significant differences in adiponectin concentrations between the PCOS and control groups, we found lower adiponectin concentrations in the obese PCOS group than the other study groups at fasting and after glucose load, while similar resistin concentrations revealed. We determined significant correlations between adiponectin and cardiovascular risk criteria such as hypertension, dyslipidemia, insulin resistance, and higher WC in girls with PCOS.

Atherosclerosis is a very slow process and usually seen after the fifth decade. Our patients were very young and selected group. The number of subject in each of our subgroups was small. Considering the limitations of the study, our results should not be generalized to an overall population. Further studies, and especially studies of larger groups, are needed before these preliminary results can be confirmed.

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