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Early Metabolic Derangements in Daughters of Women with Polycystic Ovary Syndrome

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Context: Polycystic ovary syndrome (PCOS) is a familial endocrine-metabolic dysfunction, increasingly recognized in adolescent girls with hyperandrogenism. However, it is difficult to establish whether the metabolic abnormalities described in PCOS are present before the onset of hyperandrogenism. In children, a strong association of adiponectin levels with metabolic parameters of insulin resistance has been described.

Objective: The objective of the study was to evaluate adiponectin serum concentrations and metabolic parameters in prepubertal and pubertal daughters of women with PCOS to identify girls with increased metabolic risk.

Design: Fifty-three prepubertal and 22 pubertal (Tanner stages II–V) daughters of PCOS women (PCOSd) and 32 prepubertal and 17 pubertal daughters of control women (Cd) were studied. In both groups, an oral glucose tolerance test was performed with measurement of glucose and insulin. Adiponectin, leptin, C-reactive protein, SHBG, sex steroids, and lipids were determined in the fasting sample.

Results: Both groups had similar chronological ages, body mass index SD score, and Tanner stage distribution. In the prepubertal girls, 2-h insulin was higher ($P = 0.023$) and adiponectin levels were lower ($P = 0.004$) in the PCOSd group, compared with the Cd group. In the pubertal girls, triglycerides ($P = 0.03$), 2-h insulin ($P = 0.01$), and serum testosterone concentrations were higher ($P = 0.012$) and SHBG lower ($P = 0.009$) in PCOSd, compared with Cd, but adiponectin levels were similar in both groups.

Conclusions: Some of the metabolic features of PCOS are present in daughters of PCOS women before the onset of hyperandrogenism. Adiponectin appears to be one of the early markers of metabolic derangement in these girls. **(*J Clin Endocrinol Metab* 92: 4637–4642, 2007)**

POLYCYSTIC OVARY SYNDROME (PCOS) is a familial endocrine-metabolic disorder characterized by chronic anovulation and hyperandrogenism. Most women with PCOS also have peripheral insulin resistance, which plays a key role in the pathogenesis of the syndrome (1–3). In addition, women with PCOS also exhibit β-cell dysfunction and are at increased risk for impaired glucose tolerance and type 2 diabetes (4–6).

PCOS clinical signs often emerge during the peripubertal years, with premature pubarche being the earliest manifestation for some girls. In most girls, however, PCOS usually manifests after adolescence with weight gain (7), clinical hyperandrogenism, oligoamenorrhea, and insulin resistance (8–12). Nevertheless, the clinical features that are used to diagnose PCOS in adult women are difficult to apply during adolescence (13).

It has been proposed that the metabolic abnormalities described in this syndrome are present before the onset of hyperandrogenism. However, these studies were usually performed in girls with premature pubarche (14, 15). Therefore, a biochemical marker that could identify girls at increased metabolic risk before the onset of hyperandrogenism would be particularly helpful.

Adiponectin is a 29-kDa adipocyte-derived protein that is involved in the regulation of insulin action and glucose metabolism (16, 17). Serum adiponectin levels are inversely correlated with body mass index (BMI) and also with insulin resistance independent of BMI (18, 19). In adult women with PCOS, adiponectin concentrations change according to variations in fat mass and are apparently independent of insulin resistance (20). In children, a strong association of adiponectin levels with metabolic parameters of insulin resistance has been described (21). Moreover, in obese children and adolescents, adiponectin has been proposed as a good predictor of the metabolic syndrome and thus of higher cardiovascular risk (22).

Phenotypic and family aggregation studies in different populations have shown a high incidence of affected female relatives for PCOS patients, suggesting a genetic component in the etiology of PCOS (23–29). Therefore, we assessed adiponectin serum concentrations and metabolic parameters in prepubertal and pubertal daughters of women with PCOS, to attempt to identify girls with increased metabolic risk.

Subjects and Methods

Subjects

We studied 53 prepubertal girls (4–9 yr old) and 22 pubertal girls (Tanner stages II–V; 10–15 yr old) born to PCOS mothers [PCOS daugh-

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Abbreviations: BMI, Body mass index; Cd, daughters of control women; CRP, C-reactive protein; FAI, free androgen index; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment for insulin resistance; LDL-C, low-density lipoprotein cholesterol; PCOS, polycystic ovary syndrome; PCOSd, daughters of PCOS women; SDS, SD score; WHR, waist-to-hip ratio.

ters (PCOSd)]. As a control group, we included 32 prepubertal girls and 17 pubertal girls born to mothers with regular menses and without hyperandrogenism [Control daughters (Cd)].

PCOS mothers were recruited from patients attending the Unit of Endocrinology and Reproductive Medicine, University of Chile. This group of PCOS mothers is part of an unselected group of patients that has attended our clinic because they were diagnosed with PCOS. Diagnosis of PCOS was made according to the National Institutes of Health consensus criteria (30). PCOS mothers were evaluated before pregnancy, and they exhibited chronic oligomenorrhea or amenorrhea, hirsutism, serum testosterone concentration greater than 0.6 ng/ml and/or free androgen index (FAI) greater than 5.0, and androstenedione concentration greater than 3.0 ng/ml. In addition, PCOS women showed the characteristic ovarian morphology of polycystic ovaries on ultrasound, based on the criteria described by Adams *et al.* (31). PCOS mothers were normoglycemic, with different degrees of hyperinsulinemia, which were evaluated by an oral glucose tolerance test. All patients had an elevated waist to hip ratio (WHR), greater than 0.85. We excluded patients with hyperprolactinemia, androgen-secreting neoplasms, Cushing's syndrome, and late onset 21-hydroxylase deficiency as well as thyroid disease.

All PCOS daughters were born at term from singleton pregnancies. The prevalence of gestational diabetes for PCOS mothers, according to the World Health Organization criteria (32), was 30.2%, and the incidence of pregnancy-induced hypertension was 9.3%. In addition, 61% of PCOS patients were primiparous.

As control mothers, we selected 49 women of similar socioeconomic level as the PCOS patients, with a history of singleton pregnancies, regular 28- to 32-d menstrual cycles, absence of hirsutism and other manifestations of hyperandrogenism, and no history of infertility or pregnancy complications. Control mothers were comparable in age with PCOS mothers. However, PCOS mothers had a higher BMI than control mothers at the moment that the girls were evaluated [prepubertal: 27.2 (22.9–32.4) kg/m^2 *vs.* 29.3 (21.6–41.1) kg/m^2, $P = 0.04$; pubertal: 26.3 (23.6–31.2) kg/m^2 *vs.* 31.6 (21.5–41.1) kg/m^2, $P = 0.008$].

There were no siblings included in the groups of girls studied.

The protocol was approved by the institutional review boards of the San Juan de Dios and San Borja Arriarán Hospitals and the University of Chile. All parents signed informed consents before entering the study.

Study protocol

Girls were admitted with their mothers to the pediatric unit of our Clinical Research Center at approximately 0830 h. We performed a complete physical examination on each girl, including anthropometric measurements [weight, height, waist, hip, BMI, and BMI SD score (SDS) calculated by the Growth Analyzer Program using the U.S. BMI growth charts for age], and pubertal development was assessed according to the criteria of Tanner by the same observer (E.C.). Prepubertal and pubertal girls with a history of early puberty and precocious pubarche were not included in the study.

In both groups of girls, we performed an oral glucose tolerance test (1.75 g/kg, up to a maximum of 75 g glucose in 250 ml water) after a 12-h overnight fast. Blood samples were drawn at baseline and after 120 min. Serum glucose and insulin were determined in each sample. Circulating concentrations of adiponectin, leptin, C-reactive protein (CRP), SHBG, and serum lipids were determined in the fasting sample. Serum concentrations of testosterone, androstenedione, and estradiol were also determined. Postmenarchal girls were studied during the early follicular phase of the menstrual cycle (d 3–7). In the premenarchal girls, the study was performed whenever feasible.

Assays

Serum adiponectin was assayed by RIA (Linco Research Inc., St. Charles, MO) with a sensitivity of 1.0 ng/ml and intra- and interassay coefficients of variation of 1.8 and 9.0%, respectively. Leptin concentrations were measured by RIA (Linco) with a sensitivity of 0.5 ng/ml and intra- and interassay coefficients of variation of 3.9 and 4.7%, respectively. CRP concentrations were determined by an ultrasensitive immunoturbidimetric assay (CRP Latex HS; Roche Diagnostics, Mannheim, Germany), with a sensitivity of 0.03 mg/liter and intra- and interassay coefficients of variation of 1.3 and 5.7%, respectively. Serum insulin was assayed by RIA (Diagnostic Systems Laboratories, Inc., Webster, TX). The intra- and interassay coefficients of variation were 5 and 8%, respectively. SHBG was determined by RIA (Diagnostic Products Corp., Los Angeles, CA), with intra- and interassay coefficients of variation of 3.8 and 7.9%, respectively. Serum testosterone and androstenedione were assayed by RIA (Diagnostic System Laboratories); estradiol was determined by electrochemiluminescence (Roche, Basel, Switzerland). Assay sensitivities were 0.1 ng/ml, 0.1 ng/ml, and 5.0 pg/ml, respectively. Intra- and interassay coefficients of variation were 7.0 and 11.0% for testosterone; 3.7 and 4.9% for androstenedione; and 2.7 and 5.0% for estradiol.

Serum glucose was determined by the glucose oxidase method (Photometric Instrument 4010; Roche). The intraassay coefficient of variation of this method was less than 2.0%. The lipid profile was determined by standard colorimetric assays (Photometric Instrument 4010; Roche). Estimation of serum low-density lipoprotein cholesterol (LDL-C) concentration was calculated by Friedewald's formula: LDL-C = total cholesterol − high-density lipoprotein cholesterol (HDL-C) − (triglycerides/5).

Data analysis

The measurements derived from the oral glucose tolerance test included the following: 1) serum fasting glucose, serum fasting insulin, and homeostatic model assessment for insulin resistance (HOMA-IR) (33); 2) serum 2-h glucose and 2-h insulin; 3) serum lipid profile, total cholesterol, triglycerides, LDL-C, and HDL-C; 4) serum fasting adiponectin, leptin, SHBG, and CRP concentrations; and 5) serum steroid concentrations (testosterone, androstenedione, and estradiol).

Statistical evaluation

Data are expressed as median and range. Normal distribution was assessed by Kolmogorov-Smirnov test. Differences among study groups were assessed with the Student *t* test when data were normally distributed or Mann-Whitney test when not normally distributed. Categorical data were analyzed using χ^2 or Fisher's exact test. In the case of adiponectin concentration comparisons between prepubertal and pubertal

TABLE 1. Clinical characteristics of Cd and PCOSd

	Prepubertal		Pubertal	
	Cd (n = 32)	PCOSd (n = 53)	Cd (n = 17)	PCOSd (n = 22)
Age (yr)	6.0 (4.0–9.0)	6.0 (4.0–9.0)	12.4 (10.0–17.0)	12.5 (10.0–16.0)
Weight (kg)	23.3 (14.8–42.0)	22.5 (15.5–54.5)	44.0 (33.0–68.5)	55.7 (30.5–94.0)
Height (cm)	116.4 (101.0–150.0)	113.0 (98.0–143.0)	150.0 (138.0–162.0)	153.0 (131.0–167.0)
Weight SDS	0.9 (−0.7–3.0)	0.9 (−0.4–3.0)	0.7 (−0.2–2.0)	1.3 (−0.3–2.6)
BMI (kg/m^2)	17.4 (14.0–23.0)	17.1 (14.0–26.7)	21.3 (16.1–26.7)	23.4 (17.0–33.7)
BMI SDS	1.0 (−1.2–2.7)	1.0 (−1.1–2.7)	1.1 (−0.3–1.8)	1.4 (−0.3–2.3)
WC (cm)	56.8 (45.0–74.0)	55.0 (47.0–85.0)	72.0 (60.0–88.0)	72.0 (57.0–98.0)
WHR	0.5 (0.4–0.6)	0.5 (0.4–0.6)	0.5 (0.4–0.6)	0.5 (0.4–0.6)
Birth weight (kg)	3.3 (1.7–4.4)	3.3 (2.2–4.5)	3.3 (2.6–4.0)	3.2 (2.7–4.0)

Values are median and range.
WC, Waist circumference.

PCOS and control girls, an ANOVA test after a Tukey test was performed. Spearman correlations analysis was used to evaluate the relationship among the variables of interest. Statistical analysis was performed with STATA 7.0 package (STATA Corp., College Station, TX). $P < 0.05$ was considered to be statistically significant.

Results

Both groups of prepubertal and pubertal girls were comparable in age, BMI, BMI SDS, and waist circumference (Table 1). The distribution of Tanner stage scores for breast development was also similar between pubertal girls of both groups (Tanner II: Cd = 4 *vs.* PCOSd = 4; Tanner III: Cd = 5 *vs.* PCOSd = 4; Tanner IV: Cd = 2 *vs.* PCOSd = 5; and Tanner V: Cd = 6 *vs.* PCOSd = 9; $P = 0.711$). In addition, 81.8% of the pubertal PCOS daughters and 82.4% of the control girls were postmenarchal.

The adiponectin serum concentrations were significantly lower in the PCOSd group, compared with the Cd group during the prepubertal period [16.6 (2.7–30.4) *vs.* 21.8 (9.9–28.1) μg/ml, $P = 0.004$]. However, during the pubertal period, adiponectin levels were similar in both groups (Fig. 1A). In addition, in the Cd group, a decrease in adiponectin levels was observed between the prepubertal and pubertal periods ($P = 0.001$), which was not demonstrated in the PCOSd group ($P = 0.846$).

Table 2 shows the metabolic characteristics of prepubertal and pubertal control daughters and PCOS daughters. During the prepubertal period, fasting glucose, insulin, lipids, and HOMA-IR were not significantly different between both groups. Two-hour glucose was not significantly different between groups. However, 2-h insulin was significantly higher [28.7 (8.1–194.0) *vs.* 18.5 (5.0–66.7) μIU/ml, $P = 0.023$] in the PCOSd group, compared with the Cd group (Fig. 1B).

During the pubertal period, fasting glucose and insulin as well as HOMA-IR were similar between both groups. Triglyceride concentrations were significantly higher [138.0 (88.0–193.0) *vs.* 113.5 (60.0–174.0) mg/dl, $P = 0.03$] in the PCOSd group, compared with the Cd group. Two-hour glucose was similar in both groups. However, 2-h insulin was significantly higher [71.1 (5.8–128.6) *vs.* 42.4 (5.0–98.1) μIU/ml, $P = 0.012$] in PCOSd, compared with Cd (Fig. 1B).

Leptin serum concentration was similar in PCOSd and Cd during the prepubertal [10.5 (1.9–27.6) and 9.3 (1.7–30.4) ng/ml] and pubertal periods [22.0 (9.5–71.1) and 18.1 (7.0–55.3) ng/ml]. Similar results were observed for CRP [prepubertal period: 0.6 (0.03–12.2) and 0.7 (0.03–12.6) mg/dl; pubertal period: 0.1 (0.03–7.6) and 0.4 (0.03–10.3) mg/dl].

Serum steroid and SHBG concentrations in control and PCOS daughters are shown in Table 3. During the prepubertal period, steroid concentrations were not significantly different between both groups. However, during the pubertal period, testosterone concentrations were significantly higher [0.8 (0.3–2.1) ng/ml *vs.* 0.5 (0.2–0.6) ng/ml, $P = 0.0001$) (Fig. 1C); and SHBG significantly lower [13.8 (6.1–84.2) *vs.* 48.6 (10.2–118.7) nmol/l, $P = 0.009$] in the PCOSd group, compared with the Cd group. Therefore, the FAI was significantly higher in the PCOSd group. Moreover, using a cutoff value for serum testosterone greater than the mean plus 2 SD of the control group value (0.66 ng/ml), we observed that 63.0% of the pubertal girls showed high testosterone levels.

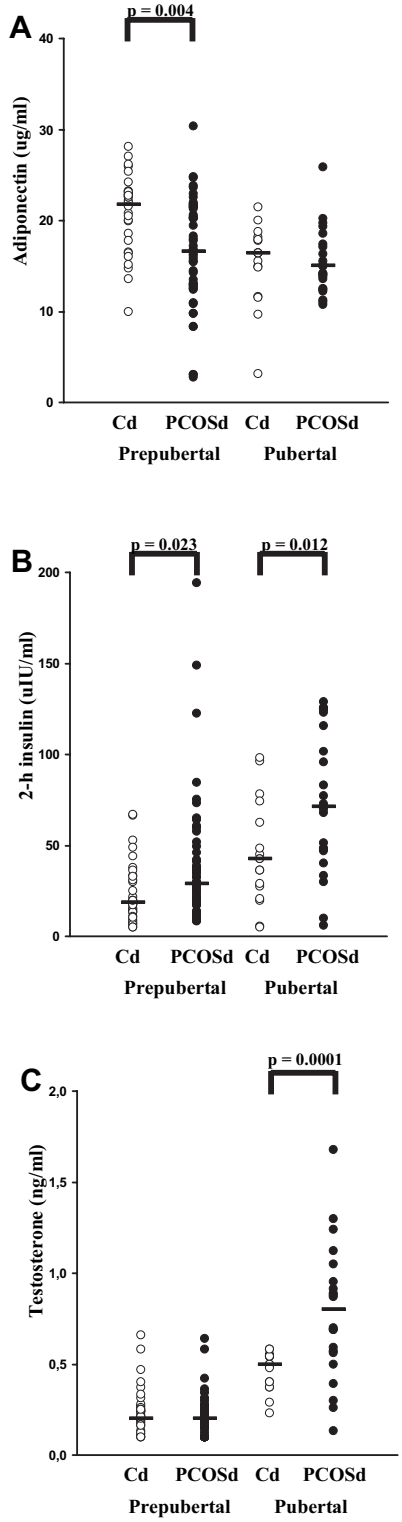

FIG. 1. Serum adiponectin (A), 2-h insulin (B), and testosterone (C) concentrations in Cd and PCOSd during the prepubertal and pubertal periods. *Open circles*, Cd; *shaded circles*, PCOSd. The *bars* indicate the median value.

In a Spearman regression analysis, serum adiponectin was

TABLE 2. Metabolic parameters of Cd and PCOSd

	Prepubertal		Pubertal	
	Cd (n = 32)	PCOSd (n = 53)	Cd (n = 17)	PCOSd (n = 22)
Fasting				
Glucose (mg/dl)	80.0 (59.0–103.0)	84.0 (55.0–101.0)	84.1 (71.0–101.0)	76.1 (60.0–101.2)
Insulin (μIU/ml)	7.7 (2.2–21.1)	6.8 (3.0–25.0)	11.2 (5.0–28.8)	12.1 (5.0–37.1)
HOMA-IR	1.6 (0.4–4.5)	1.3 (0.5–6.1)	2.2 (0.9–7.1)	2.2 (0.8–9.5)
Triglycerides (mg/dl)	92.5 (58.0–248.0)	105.0 (58.0–281.0)	113.5 (60.0–174.0)	138.0 (88.0–193.0)[a]
Cholesterol (mg/dl)	172.0 (116.0–202.0)	162.0 (125.0–228.0)	155.0 (121.0–200.0)	163.5 (122.0–210.0)
HDL-C (mg/dl)	38.1 (24.7–55.7)	42.5 (27.1–79.3)	42.6 (29.0–57.9)	41.5 (31.7–61.6)
LDL-C (mg/dl)	108.3 (62.7–143.1)	99.9 (60.5–159.7)	86.5 (71.0–127.9)	96.4 (36.9–137.1)
2 h				
Glucose (mg/dl)	95.0 (65.0–133.0)	98.5 (57.0–139.0)	91.9 (42.0–124.0)	92.2 (49.4–182.0)
Insulin (μIU/ml)	18.5 (5.0–66.7)	28.7 (8.1–194.0)[a]	42.4 (5.0–98.1)	71.1 (5.8–128.6)[a]

Values are median and range.
[a] $P < 0.05$ between Cd and PCOSd.

inversely correlated with 2-h insulin in the prepubertal PCOSd group (r = −0.450, $P = 0.047$). Other variables such as leptin and CRP were correlated with BMI (r = 0.445, $P = 0.006$; r = 0.369, $P = 0.012$, respectively) and waist circumference (r = 0.601, $P = 0.001$; r = 0.321, $P = 0.030$, respectively).

In PCOS pubertal daughters, leptin and CRP were correlated with BMI (r = 0.712, $P = 0.001$; r = 0.605, $P = 0.006$, respectively) and waist circumference (r = 0.716, $P = 0.001$; r = 0.539, $P = 0.017$, respectively).

Discussion

In this study we evaluated adiponectin serum concentrations and metabolic parameters in prepubertal and pubertal daughters of PCOS women. In addition, we determined serum sex steroid concentrations in these girls. Prepubertal PCOS daughters showed significantly lower concentrations of adiponectin and higher levels of poststimulated insulin, compared with control daughters. Pubertal PCOS daughters exhibited higher levels of testosterone, triglycerides, and poststimulated insulin and lower levels of SHBG, compared with controls. These findings suggest that some metabolic abnormalities may be observed in daughters of PCOS patients during childhood, well before the onset of hyperandrogenism.

The present study demonstrates for the first time that normal-weight prepubertal daughters of PCOS women exhibit significantly lower adiponectin concentrations, compared with daughters of normal women. This is a novel finding, which suggests that adiponectin concentrations could serve as an early marker of metabolic derangement in these girls. Interestingly, except for higher poststimulated insulin levels, no other abnormal metabolic parameters were observed. Although previous work has suggested that the reduction of adiponectin is mainly related to fat mass, our data indicate that prepubertal daughters of women with PCOS have lower adiponectin levels than would be expected on the basis of their BMI. It has been suggested that patients with increased visceral fat have lower adiponectin concentrations (34). Therefore, the lower adiponectin levels observed in these girls may be related to more abundant visceral fat. In this study, however, we evaluated exclusively WHR and did not perform direct measurements of fat or lean body mass. The waist to hip ratio was similar in daughters of PCOS women and controls and did not correlate with adiponectin concentrations.

Our data also demonstrate that the decrease in adiponectin concentrations was associated with increased poststimulated insulin levels, suggesting a possible relationship with insulin resistance. Several studies in rodents and adult humans suggest a protective role for adiponectin against the development of insulin resistance and dyslipidemia (35, 36). Studies in Pima Indian, Hispanic, and Asian-American children have demonstrated that plasma adiponectin levels correlate inversely with fasting insulin (37, 38). In addition, in Pima Indians hypoadiponectinemia precedes the decline in insulin sensitivity, independently of changes in body fat (39). Therefore, we propose that in our prepubertal daughters of PCOS patients, hypoadiponectinemia is more related to insulin resistance than to body fat.

In pubertal daughters of PCOS women, other metabolic abnormalities were apparent. Unexpectedly, however, adi-

TABLE 3. Serum steroid concentrations in Cd and PCOSd

	Prepubertal		Pubertal	
	Cd (n = 32)	PCOSd (n = 53)	Cd (n = 17)	PCOSd (n = 22)
Testosterone (ng/ml)	0.2 (0.1–0.6)	0.2 (0.1–0.6)	0.5 (0.2–0.6)	0.8 (0.3–2.1)[a]
Androstenedione (ng/ml)	0.4 (0.1–1.5)	0.3 (0.1–0.9)	0.9 (0.4–3.3)	0.9 (0.3–3.9)
SHBG (nmol/liter)	66.2 (15.2–147.5)	77.9 (9.5–167.0)	48.6 (10.2–118.7)	13.8 (6.1–84.2)[a]
Estradiol (pg/ml)	5.0 (5.0–32.6)	5.0 (5.0–12.8)	37.2 (5.0–104.7)	33.1 (6.1–64.2)
FAI	1.2 (0.3–4.2)	0.8 (0.2–15.3)	2.7 (0.7–5.0)	17.0 (0.8–39.0)[a]

Values are median and range.
[a] $P < 0.05$ between Cd and PCOSd.

ponectin serum concentrations were not lower than those observed in pubertal control girls. Adiponectin has been measured in other studies in children (37, 38, 40, 41); according to the study by Butte *et al.* (21) in Hispanic children, age, sex, and excess weight status exert independent effects on the expression of serum adiponectin. However, in our study both groups of pubertal girls were comparable in these aspects.

In a study of Hispanic and Asian-American children aged 12–14 yr, adiponectin values were lower in boys than girls (38), suggesting a sexual dimorphism in the expression of this adipocytokine, which is probably related to their sexual hormone milieu. Moreover, in adult women with PCOS, adiponectin levels are lower than those observed in normal women, presumably because of their higher testosterone levels (42). In this study, we observed higher testosterone levels in daughters of PCOS women compared with control daughters, so lower adiponectin levels in the PCOS pubertal group might be expected. It has been demonstrated that adiponectin levels decrease in normal girls during puberty (43), and in accordance with these findings, we observed that our prepubertal control girls exhibited higher adiponectin concentrations than our pubertal control girls. In the PCOS daughters, however, adiponectin concentrations were low during childhood and remained low during puberty, reaching levels similar to those observed in pubertal control girls. This observation suggests that the dynamics of adiponectin changes during puberty is different in control and PCOS girls. Interestingly, the decrease in adiponectin concentrations in PCOS daughters was present before the onset of hyperandrogenism.

We should point out that although there is a subgroup of girls within the PCOS daughters who exhibit lower adiponectin concentrations, associated with higher 2-h insulin and testosterone concentrations, we cannot establish with certainty whether some of these girls will develop PCOS. Further longitudinal studies that are being carried out by our group are necessary to answer this question.

In previous studies it has been suggested that fasting plasma glucose, fasting insulin, and HOMA-IR index are poor predictors of insulin resistance and glucose intolerance in young women (44, 45), which is in agreement with our results in prepubertal and pubertal girls. Recently low SHBG concentrations have been proposed as a surrogate marker for insulin resistance in men, postmenopausal women, and anovulatory women with PCOS (46–48). Moreover, according to the study by Blum *et al.* (49), SHBG concentrations more accurately reflect changes in insulin resistance than the HOMA-IR index. This is in agreement with our results in pubertal daughters of PCOS women, who exhibited normal HOMA-IR indexes despite low SHBG concentrations.

Other metabolic variables measured in our study, such as leptin and CRP, were similar in both groups, probably because total body fat mass and central fat distribution, reflected indirectly by the BMI and the WHR, were comparable.

Finally, an interesting point is that at least 30% of PCOS daughters came from pregnancies that were complicated by gestational diabetes, whereas all the control pregnancies were uncomplicated by design. In a previous study, we established that gestational diabetes was significantly higher in pregnant PCOS than normal pregnant women (50). Moreover, we proposed that low adiponectin and high insulin levels were implicated in the pathogenesis of gestational diabetes in these patients. Therefore, PCOS mothers with gestational diabetes may offer an altered intrauterine milieu to their daughters during fetal life that could be involved in the metabolic derangements observed in these girls during postnatal life.

In conclusion, our results suggest that some of the metabolic features of PCOS are present in daughters of PCOS women during childhood, well before the onset of hyperandrogenism. We have shown that adiponectin may be an early marker of metabolic derangement in these girls, which at this time appears to be independent of body weight.

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