CLINICAL STUDY

Lower insulin sensitivity differentiates hirsute from non-hirsute Sicilian women with polycystic ovary syndrome

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Abstract

Objective: It is well known that hyperandrogenism and insulin-resistance with or without compensatory hyperinsulinism are closely associated, but the Rotterdam Consensus has concluded that principally obese women with polycystic ovary syndrome (PCOS) should be evaluated for the metabolic syndrome. Our aim was to study insulin sensitivity in PCOS women with hirsutism regardless of obesity.

Methods: Clinical characteristics, sex hormones and fasting- and after OGTT-glycemia and insulinemia, homeostatic model of insulin resistance (HOMA IR), and Matsuda index of insulin sensitivity were analyzed in 130 women with PCOS. Hirsutism has been evaluated through the Ferriman–Gallwey (FG) map scoring system.

Results: PCOS women with hirsutism (57.7% of participants) showed significant higher values of total testosterone levels ($P=0.016$), free testosterone ($P=0.027$), DHEA sulfate ($P=0.017$), and $\Delta 4$ androstenedione ($P=0.018$). They had similar body mass index (BMI) ($P=0.073$) and were significantly less insulin sensitive ($P=0.002$) than those without hirsutism (42.3% of participants). In women with PCOS and hirsutism, there was a significant correlation between FG score and insulin-sensitivity indexes (HOMA IR, $\rho=0.33$, $P=0.005$; Matsuda index, $\rho=-0.34$, $P=0.003$) but not with the androgen levels. Moreover, women with hirsutism showed a significantly greater insulin ($P=0.019$), C-peptide ($P=0.002$), and glucose ($P=0.024$) areas under the curve (auc2h).

Conclusions: Our study suggests that the increased responsiveness of the pilo-sebaceous unit to androgens seems to be influenced by insulin sensitivity and that insulin resistance should be assessed in all hirsute women with PCOS regardless of their BMI, as insulin resistance was found in hirsute women irrespective of whether they were overweight or obese.

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Introduction

Polycystic ovary syndrome (PCOS) is the most common hormonal reproductive alteration in women of child-bearing age, estimated in population-based studies with a prevalence of 5–10% (1–3). PCOS is characterized by hyperandrogenism, insulin resistance with or without compensatory hyperinsulinism (4), oligo-amenorrhea, hirsutism, acne, seborrhea, obesity, impaired glucose tolerance or type 2 diabetes, dyslipidemia, and infertility. The Rotterdam Consensus Conference (RCC) (5) proposed that the syndrome can be diagnosed after the exclusion of other medical conditions that cause irregular menstrual cycles and androgen excess (non-classical congenital adrenal hyperplasia, Cushing's syndrome, hyperprolactinemia, hypothyroidism, virilizing adrenal or ovarian neoplasm), and the determination that at least two of the following are present: oligoovulation or anovulation, elevated levels of circulating androgens and/or clinical

hyperandrogenism, and polycystic ovaries as defined by ultrasonography. Furthermore, PCOS diagnosis requires the careful evaluation of associated metabolic disturbances, which may be responsible for several long-term complications, i.e. an increased risk of developing diabetes, dyslipidemia, cardiovascular disease, stroke, and endometrial carcinoma (6–9).

Considering the heterogeneity of PCOS, the Rotterdam Consensus has concluded that only obese women with PCOS should be screened for the metabolic syndrome. However, hyperinsulinemia and insulin resistance may play a major role in the development of most cases of PCOS, as hyperinsulinemia and insulin resistance precede hyperandrogenism (10, 11) and both lean and obese women with PCOS show insulin resistance, albeit with different severity (12, 13). Moreover, insulin-sensitizing agents, such as metformin or thiazolidinediones, slightly improve hyperandrogenic symptoms (14). Insulin acts synergistically with

luteinizing hormone (LH) to enhance the androgen production of theca cells and inhibits hepatic synthesis of sex hormone binding globulin (SHBG), in turn increasing free bioavailable testosterone levels (15). In addition, specific biochemical defects allow the hyperandrogenism to become evident when insulin resistance occurs; a dysfunction in serine phosphorylation may be responsible for P450c17 enhancement inducing the 17,20 lyase activity and subsequent androgen production. Likewise, increased serine phosphorylation of the insulin receptor impairs its tyrosine kinase activity and causes a reduction in insulin sensitivity (16). Our aim was to evaluate insulin sensitivity in PCOS women with or without hirsutism. The present study confirms the importance of evaluating insulin sensitivity together with biochemical hyperandrogenism mainly in PCOS women with hirsutism regardless of their body mass index (BMI).

Materials and methods

Subjects

The Institutional Review Board at the Faculty of Medicine of the University of Palermo approved the study. We retrospectively studied a group of 130 consecutive (2003–2005) women with PCOS in reproductive age (age range 16–42 years, mean age = 24.56 ± 5.2 years), with mean BMI values of 30.13 Kg/m^2 (s.d. = 6.96; range 18–50). All patients had been followed in our Outpatient Clinic. The diagnosis of PCOS was made on the basis of at least two of the following criteria, in agreement with the Rotterdam Consensus (5):

- (i) clinically evident hyperandrogenism (hirsutism, evaluated with Ferriman–Gallwey (FG) score (17) and/or acne/seborrhea) and/or biochemical hyperandrogenism;
- (ii) oligomenorrhea (irregular cycles > 34 days);
- (iii) PCO (polycystic ovaries as defined by ultrasonography).

Amenorrhoeic women (absence of vaginal bleeding > 6 months) were excluded from the study because of their small number and various progesterone bleeding induction schemes, potentially interfering with hormonal pattern. Patients were asked about a family history of oligo-amenorrhea, hirsutism, and acne and for the modality of menarche. Weight, BMI, waist circumference and blood pressure were also evaluated. We also used the FG map scoring system, estimated from two observers, which has 11 domains depicting portions of the body. Hirsutism was defined as FG score > 8 (17). Patients were tested for follicle-stimulating hormone (FSH), LH, 17- β -estradiol, 17-OH-progesterone, basal prolactin (PRL), total and free testosterone, DHEA sulfate (DHEAS), Androstenedione, total cholesterol, high density

lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, and triglycerides during the follicular phase (7th day). On the same day, we performed an oral glucose tolerance test (OGTT; 75 g glucose) and measured glycemia, insulinemia, C-peptide at 0, 30, 60, 90, and 120 min. Progesterone levels were assessed again during the luteal phase (21st day). Biochemical hyperandrogenism was diagnosed when androgen levels were as follows: total testosterone > 2.08 nmol/l, free testosterone > 6.94 pmol/l, DHEAS > 11.69 $\mu\text{mol/l}$, and androstenedione > 6.98 nmol/l (calculated on the basis of the 95th percentile upper limits of basal serum androgen normality in a control group of 30 healthy eumenorrhoeic women without hirsutism and family history of PCOS).

Trans-vaginal ovary ultrasounds were performed on the 10th day from the beginning of the last period. Assessment of the pelvis was performed by transvaginal ultrasound using a 7.5 MHz vaginal probe transducer (General Electric LOGIQ 400 MD). Both ovaries were measured in the sagittal, transverse, and coronal plane. Ovaries were classified as polycystic based on the presence of 12 or more follicles in each ovary measuring 2–8 mm in diameter, and/or increased ovarian volume (> 10 ml) (5). The women treated with clomiphene citrate, oral contraceptives, anti-androgens, or drugs to control their appetite during the 6 months before the first visit were excluded from the study. Patients, who showed high PRL levels (> 25 $\mu\text{g/l}$) on the 7th day were screened on the following day for PRL pulse assay and excluded from the study if PRL was > 25 $\mu\text{g/l}$ in at least two samples. We also excluded patients with 17-OH-Pg levels > 6.05 nmol/l who, after 250 μg Synacthen, showed 17-OH-Pg > 30.26 nmol/l at 60 min. Patients with DHEAS > 16.32 $\mu\text{mol/l}$ were screened with a TC scan and excluded when adrenal hyperplasia or adenoma or virilizing androgen-secreting neoplasms were present. Cushing's syndrome was excluded when clinical and hormonal evaluation suggested its presence (phenotype, increased 24 h free urinary cortisol, high cortisol levels after 1 mg of overnight dexamethasone). Clinical and biochemical euthyroidism had been previously assessed in all patients.

Assays

All hormones were measured in our laboratory using commercial kits. These included ELISA (DRG Diagnostics, DRG Instruments GmbH, Germany) for FSH (mUI/ml), LH (mUI/ml), 17- β -estradiol (pg/ml), 17-OH-Pg (ng/ml), progesterone (ng/ml), PRL (ng/ml), total testosterone (ng/ml), free testosterone (pg/ml); the inter- and intra-run precision had a coefficient of variation (CV) of 3.9 and 6.2% respectively; correlation with RIA and conventional equilibrium dialysis method was performed on 16 males and 19 females: coefficient of regression $r = 0.97$; Pantec, Torino, Italy), androstenedione (ng/ml; Arnika, Milan,

Italy), insulin (mUI/l; the intra- and interassay CVs were ≤ 4 and $\leq 3.6\%$ respectively) and C-peptide ($\mu\text{U/l}$); chemiluminescence assays were used for DHEAS ($\mu\text{g/dl}$). Blood glucose levels (mg/dl) were measured by the colorimetric method (Glucocard, Menarini Diagnostics, Italy). Total cholesterol, HDL, and triglycerides were measured in our central laboratory using standard assays. LDL cholesterol levels were calculated with Friedewald's formula. The conversion factors for the International System (SI) are: glucose (mg/dl vs mmol/l : 0.0555), insulin (mUI/l vs pmol/l: 6.0), total cholesterol (mg/dl vs mmol/l : 0.0258), total testosterone (ng/ml vs nmol/l : 3.467), free testosterone (pg/ml vs pmol/l : 3.47), DHEAS ($\mu\text{g/dl}$ vs $\mu\text{mol/l}$: 0.0272), androstenedione (ng/ml vs nmol/l : 3.492), 17- β -estradiol (pg/ml vs pmol/l : 3.671), 17-OH-Pg (ng/ml vs nmol/l : 3.026), progesterone (ng/ml vs nmol/l : 3.180), PRL (ng/ml vs $\mu\text{g/l}$: 1), FSH (mUI/ml vs IU/l: 1), and LH (mUI/ml vs IU/l: 1).

Insulin sensitivity was estimated using basal insulin and glucose values to calculate homeostatic model of insulin resistance (HOMA IR) (18) ($\text{glycemia (mmol/l)} \times \text{insulinemia (}\mu\text{U/ml)} / 22.5$). The Matsuda index of insulin sensitivity (19) was calculated on the basis of glucose and insulin values during the OGTT ($10\,000 / \text{glucose (mg/dl)} \times \text{insulin (}\mu\text{U/ml)} \times \text{glucose mean} \times \text{insulin mean}$). These parameters are considered equivalent to the gold standard euglycemic hyperinsulinemic clamp (20). The area under the insulin and C-peptide curves during OGTT and area under the curve (AUC) glucose/AUC insulin ratio were also calculated.

Statistical analysis

We used the SPSS 11 software, Windows Edition (SPSS, Chicago, IL, USA), for all our statistical analysis. Continuous variables with normal distribution (age, BMI) were analyzed as mean values $\pm$ s.d. and ranges; continuous variables without normal distribution were analyzed as median values and interquartile range. Rates and proportions were calculated for categorical data. As continuous variables were without normal distribution, we used non-parametric tests and differences were analyzed by Mann-Whitney *U*-test. Correlations among FG score, circulating androgens and insulin sensitivity indexes, in the subgroup of hirsute women, were determined by using the Spearman's test, the non-parametric equivalent for Pearson's test. $P < 0.05$ was considered statistically significant. For categorical variables, differences were analyzed by means of the χ^2 -test and Fisher's exact test when appropriate.

Results

We studied a group of 130 women, aged from 16 to 42 years (24.56 ± 5.2 s.d.), with a BMI value of

$30.13 \text{ Kg/m}^2 \pm 6.9$ s.d. Seventy-five women (57.7%) were hirsute, 65 (50%) had acne/seborrhea, 69 (53%) had oligomenorrhea, 57 (43.84%) had increased total testosterone, 80 (61.53%) had increased free testosterone, 17 (13%) had increased DHEAS, 80 (61.53%) had increased $\Delta 4$ -androstenedione, and 92 (70.76%) had PCO. Patients were divided into two subgroups depending on the presence/absence of hirsutism (FG score > 8 ; Tables 1 and 2) and their biochemical and clinical characteristics were analyzed. We found that women with hirsutism had BMI comparable to those without hirsutism (31.19 ± 7.36 vs $28.70 \pm 6.16 \text{ Kg/m}^2$; $P = 0.073$; Table 1, Fig. 1). In addition, total and free testosterone, DHEAS, and $\Delta 4$ -androstenedione levels were higher in hirsute women, but other sex hormones were comparable in the two groups (Table 1). Analyzing insulin sensitivity by HOMA IR and the Matsuda index, we found that patients without hirsutism had significantly higher insulin sensitivity than those with hirsutism (Table 2). Moreover, the insulin, C-peptide, and glycemic AUC2h during OGTT were notably higher in the hirsute women (Table 2). Finally, reduced HDL cholesterol (1.23 vs 1.72 mmol/l , median values; $P < 0.001$) and increased triglycerides levels (0.91 vs 0.74 mmol/l , median values; $P = 0.022$) were observed in hirsute compared with non-hirsute women. No other statistical differences were observed for clinical and biochemical data. Moreover, there was a linear correlation among the different parameters in relation to the FG score in the subgroup with hirsutism (HOMA IR, Matsuda index, OGTT insulin AUC2h, and AUCglucose/AUCinsulin ratio; Table 3; Fig. 2). There was no correlation with androgen levels. Furthermore, a correlation between waist circumference and FG score was found in hirsute women ($\rho = 0.283$; $P = 0.018$), differently from those without hirsutism ($\rho = -0.115$; $P = 0.457$).

Applying the current criteria for the diagnosis of the metabolic syndrome (21) in both groups of women affected by PCOS, we found that the metabolic syndrome was present in only 25.33% of hirsute women and in 14.54% of women without hirsutism ($P = \text{NS}$, Table 4). In addition, only 12% of PCOS women had fasting glucose $\geq 5.6 \text{ mmol/l}$ or manifest type 2 diabetes, again with no different prevalence in the two groups. The group with hirsutism had lower HDL cholesterol levels than the non-hirsute one ($P < 0.001$; Tables 2 and 4). Triglycerides levels were significantly lower in women without hirsutism (Table 2), but when we classified women with < 1.7 and $> 1.7 \text{ mmol/l}$ value (21) no significant difference was detected (Table 4).

Dividing the whole cohort of patients into women with oligomenorrhea (69/130) and in women with regular menses (61/130), we found that oligomenorrhic women had significantly lower progesterone levels during the luteal phase (21st day) (3.18 ($1.59\text{--}8.90$) nmol/l vs 9.54 ($3.81\text{--}25.44$) nmol/l ; median/interquartile range; $P < 0.001$). No other statistical

Table 1 Clinical and hormonal parameters in women with and without hirsutism.

	Women with hirsutism (<i>n</i> =75)		Women without hirsutism (<i>n</i> =55)		<i>P</i> value
	Mean±s.d.	Range	Mean±s.d.	Range	
<i>Clinical characteristics</i>					
Age	24.72±5.83	16–42	24.35±4.28	18–32	0.975
BMI	31.19±7.36	18–50	28.70±6.16	18–42	0.073
	Median	Interquartile range	Median	Interquartile range	
Menarche age	12	11–13	11.84±1.53	10–15	0.616
Systolic blood pressure	110	110–120	115	110–120	0.571
Diastolic blood pressure	70	70–80	70	70–80	0.481
Waist (cm)	88	78–100	88	80–100	0.868
FG score	18.5	12.75–22	7	5–7	0.000*
Family history	Subjects (%) 21 (28)		Subjects (%) 15 (27)		0.927
<i>Diagnostic criteria according to Rotterdam Consensus</i>					
	Subjects (%)		Subjects (%)		
Acne/seborrhea	38 (50.66)		27 (49.09)		0.859
Oligomenorrhea	39 (52)		30 (54.54)		0.611
PCO	51 (68)		41 (74.54)		0.418
<i>Biochemical hyperandrogenism</i>					
Increased total testosterone	35 (46.66)		22 (40)		0.449
Increased free testosterone	52 (69.33)		28 (50.90)		0.033*
Increased DHEAS	10 (13.33)		7 (12.72)		0.919
Increased Δ4androstenedione	48 (64)		32 (58.18)		0.501
<i>Hormonal pattern</i>					
	Median	Interquartile range	Median	Interquartile range	
FSH (IU/l)	6.72	5.09–9	7.10	6.4–7.9	0.677
LH (IU/l)	7.9	4.05–13	8.2	5.7–11	0.836
LH/FSH	1.18	0.64–1.6	1.07	0.82–1.5	0.849
17-β-estradiol (pmol/l)	135.82	99.11–187.03	144.63	102.78–201.90	0.179
17-OH-Pg (nmol/l)	4.23	2.54–6.35	3.63	2.57–6.65	0.653
Progesterone (nmol/l)	4.45	2.48–19.84	4.45	1.84–13.67	0.451
Basal PRL (μg/l)	9.5	6.96–15.6	11.4	7.5–13.9	0.382
Total testosterone (nmol/l)	1.97	1.45–2.77	1.45	0.55–2.60	0.016*
Free testosterone (pmol/l)	9.23	5.72–13.35	6.94	3.81–9.02	0.027*
DHEAS (μmol/l)	7.43	5.29–9.94	5.64	3.91–8.01	0.017*
Δ4androstenedione (nmol/l)	8.03	5.93–10.47	6.98	5.93–8.38	0.018*

BMI, body mass index; FG, Ferrimen–Gallwey; PCO, polycystic ovaries; FSH, follicle-stimulating hormone; LH, luteinizing hormone; 17-OH-Pg, 17-OH-progesterone; PRL, prolactin. *Significant values when $P < 0.05$.

differences were observed for clinical, hormonal, and metabolic variables (data not shown).

Discussion

The presence of insulin resistance and compensatory hyperinsulinemia in mainly obese women with PCOS is considered a key factor in the development of hyperandrogenism (22). Nevertheless, the diagnosis of PCOS is still difficult, especially considering the heterogeneity of clinical phenotypes and laboratory findings. It would be helpful to develop improved diagnostic criteria based on

a particular clinical phenotype, i.e. hirsutism, oligomenorrhea or obesity. In our study, we confirm the complexity of this syndrome by studying a sample of affected women from Sicily, in whom we evaluated different biochemical and metabolic patterns in relation to the presence or absence of hirsutism. Acne/seborrhea, menstrual cycle, and PCO did not differ in PCOS women with or without hirsutism. The reduced insulin sensitivity in hirsute women *per se* suggests that, in these women, decreased insulin sensitivity plays a significant role, as also indicated by our analysis: we found a high correlation between FG score and all the insulin sensitivity indexes in hirsute women, while this

Table 2 Metabolic parameters in women with and without hirsutism.

	Women with hirsutism (n=75)		Women without hirsutism (n=55)		
	Median	Interquartile range	Median	Interquartile range	
Total Cholesterol (mmol/l)	4.66	4.04–5.41	4.97	4.02–5.76	0.703
HDL Cholesterol (mmol/l)	1.23	1.08–1.36	1.72	1.23–2.08	<0.001*
LDL Cholesterol (mmol/l)	2.83	2.36–3.84	2.96	1.87–3.60	0.262
Triglycerides (mmol/l)	0.91	0.73–1.26	0.74	0.47–1.19	0.022*
Fasting glucose (mmol/l)	4.66	4.32–5.32	4.82	4.49–5.14	0.356
Fasting insulin (pmol/l)	108.6	67.2–169.8	72.3	46.62–105.6	0.002*
Fasting C-peptide (μU/l)	2.1	0.8–4.27	1.2	0.9–3.6	0.568
Glucose 120 min (mmol/l)	5.88	4.77–6.93	4.82	4.03–5.99	0.007*
Insulin 120 min (pmol/l)	454.8	254.7–930.42	450.6	156–666	0.109
C-peptide 120 min (μU/l)	8.9	6.6–11.6	7.5	4.8–9.4	0.005*
HOMA IR	4.08	2.30–6.51	2.49	1.56–3.77	0.002*
Matsuda index	2.6	1.82–4.8	3.68	2.51–6.03	0.002*
AUC2h glycemia	768.39	644.74–863.30	687.64	593.57–780.05	0.024*
AUC2h IRI	61 242	39 402–112 680	48 960	29 430–68 778	0.019*
AUC2h plasmatic C-peptide	984	732–1442	785	637–1016	0.002*
AUC2hgl/AUC2hIRI ratio	0.012	0.0075–0.017	0.014	0.0095–0.024	0.057

HDL, high density lipoprotein; LDL, low density lipoprotein; HOMA IR, homeostatic model assessment of insulin resistance; AUC, area under curve; IRI, insulin resistance index. *Significant values when $P < 0.05$.

relation was not observed between FG and circulating androgens. In our study, a higher FG score is associated with decreased insulin sensitivity. With regards to BMI, it is noteworthy that in our cohort we also found hirsute women with insulin resistance and normal weight. This suggests that the responsiveness of the pilo-sebaceous unit to androgen levels could be affected by decreased insulin sensitivity. In addition, the effect of insulin and the insulin-like growth factor (IGF) system has been accurately investigated *in vitro* (23), and some authors (24) have shown that insulin/IGF plays a role in stimulating hair follicle growth acting together with androgens. Other authors suggest that also idiopathic hirsutism is associated with insulin resistance and an increased prevalence of impaired glucose tolerance (25). However, it still remains unclear if the correlation we found between insulin sensitivity and FG score is due to

insulin resistance or compensatory hyperinsulinism (26). In fact, it is extremely difficult to evaluate the effect of insulin resistance/hyperinsulinism on the response to androgens of the pilo-sebaceous unit by the measure of the activity of 5- α -reductase. Circulating dihydroxytestosterone is not related to intracellular hormone levels, and its evaluation through the metabolite 3- α -androstenedione glucuronide is strongly influenced by the liver component, which is higher than the cutaneous one. In addition, it still remains to be established whether our Sicilian PCOS women are more susceptible to develop the metabolic syndrome for their genetic predisposition or environmental factors and this may influence their hirsutism prevalence. In this light, it is to be noted that our cohort of patients is constituted by women in reproductive age and possibly they will develop metabolic syndrome after menopause.

Figure 1 Class of obesity in polycystic ovary syndrome (PCOS) women with or without hirsutism. Patients with PCOS divided on the basis of body mass index are equally distributed in relation to presence or absence of hirsutism.

Table 3 Correlation between insulin sensitivity indexes, androgen levels, and Ferriman–Gallwey (FG) score in the subgroup of hirsute women.

	Sperman ρ coefficient	P value
HOMA IR	0.330	0.005*
Matsuda index	−0.344	0.003*
AUCglyc/AUCins	−0.235	0.047*
AUC glycemia	−0.002	0.984
AUC insulinemia	0.249	0.034*
AUC c-peptide	0.108	0.366
Testosterone	−0.281	0.053
Free testosterone	0.158	0.183
DHEAS	−0.033	0.782
$\Delta 4$ Androstenedione	0.079	0.506

AUC, area under curve. *Significant values when $P < 0.05$.

Our findings lead us to hypothesize that the metabolic abnormalities could have an impact after the menopause in PCOS women (27). Diabetes mellitus, hyperlipidemia, and hyperinsulinemia could potentially affect health in this era of life in the hirsute PCOS women. In our study, the prevalence of fasting glycemia ≥ 5.6 mmol/l or manifest type 2 diabetes (21) was around 15%, not different with respect to other PCOS women cohorts.

In conclusion, the evaluation of insulin sensitivity by fasting/after OGTT insulinemia is as useful as the screening for circulating androgens in PCOS women

Figure 2 Correlation between Ferriman–Gallwey (FG) score and insulin sensitivity indexes (HOMA IR, Matsuda) in the subgroup of hirsute women.

Table 4 Metabolic syndrome according to the new International Diabetes Federation (IDF) definition in women with and without hirsutism.

	Subjects (%)		
	Women with hirsutism (n=75)	Women without hirsutism (n=55)	P value
Metabolic syndrome	19 (25.33)	8 (14.54)	0.134
Waist circumference ≥ 80 cm	51 (68)	37 (67.27)	0.119
$T_g \geq 1.7$ mmol/l or specific treatment	7 (9.33)	6 (10.9)	0.767
HDL cholesterol ≤ 1.29 mmol/l or specific treatment	47 (62.66)	15 (27.27)	$<0.001^*$
Systolic BP ≥ 130 mmHg or diastolic BP ≥ 85 mmHg or specific treatment	6 (8)	9 (16.36)	0.140
Fasting glucose ≥ 5.6 mmol/l or previously diagnosed type 2 diabetes	12 (16)	8 (14.54)	0.820

T_g , triglycerides; HDL, high density lipoprotein; BP, blood pressure. *Significant values when $P < 0.05$.

with hirsutism. In this light, it is noteworthy that recent work suggested that more practical fasting measures of insulin sensitivity by the HOMA model equate well with measures requiring a 2 h glucose tolerance test (28) and that fasting blood tests for glucose and insulin may be sufficient to determine insulin sensitivity in the clinic context. It is to be noted that a certain controversy still persists regarding the application of mathematical indices in different insulin-resistant populations as they cannot be considered *a priori* equivalent to the euglycemic clamp technique (29). In addition, our findings seem to confirm that evaluation of the hypothalamic–pituitary–ovary axis should be performed in PCOS women with oligomenorrhea, with special attention to progesterone levels in the luteal phase.

Our data suggest that in the Sicilian population the evaluation of insulin sensitivity indexes in hirsute women with normal levels of circulating androgens could help to diagnose PCOS, which is important given the high prevalence of metabolic syndrome in women with this condition.

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