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CLINICAL ARTICLE

Clinical and metabolic features of polycystic ovary syndrome

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KEYWORDS
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Abstract

Objective: To explore the clinical and metabolic features of Chinese women with polycystic ovary syndrome (PCOS). *Methods:* The clinical data of 273 Chinese women diagnosed as having PCOS were retrospectively studied. *Results:* Of these women 34.8% had hirsutism, 45.1% had acne, 94.1% had some menstrual abnormality, and 96.7% had typical appearances of polycystic ovaries on ultrasonographic examination. The prevalence of overweight women was 30.4%, and the prevalence of insulin resistance was 12.8% using the glucose to insulin ratio (GIR) and 21.6% using the homesostasis model assessment (HOMA). Body mass index was significantly correlated with fasting insulin level (r=0.50), GIR (r=0.37) and HOMA (r=0.53). *Conclusion:* Menstrual abnormality and polycystic ovaries were the main clinical manifestations in this cohort of Chinese women with PCOS. The prevalence of hyperandrogenism, obesity, and insulin resistance was lower in this cohort than in women from other races with the same condition. Ethnic differences needs to be considered when studying the clinical and metabolic features of women with PCOS.

1. Introduction

Polycystic ovary syndrome (PCOS) is characterized by chronic anovulation and hyperandrogenism, and is considered to be the most common endocrinopathy among women of reproductive age (4%–6%) [1]. The prevalence of PCOS varies with ethnicity or race. It was reported to be 6.6% in the southeastern United States [2], 6.8% in Greece [3], 6.5% in Spain [4], 13% among Mexican American women [5], and 52% among the female South Asian immigrants of Britain [6]. Insulin resistance, which may be between 50% and 70% among women with PCOS [7], is now recognized as a major risk factor for the development of metabolic syndrome in these women.

Studies have shown ethnic variation in the clinical and metabolic features of women with PCOS. Norman et al. [8] reported a stronger insulin response to a glucose load in Asian Indian women with PCOS than in their white European counterparts; Wijeyaratne et al. [9] reported a higher prevalence of oligomenorrhea, hirsutism, acne, and acanthosis nigricans in South Asian women than in white women, along with higher fasting insulin concentrations and lower insulin sensitivity;

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Table 1 Clinical data of Chinese PCOS women [a]

Characteristic	All patients (n=273)	Overweight (n=83)	Normal weight (n=190)	P value
Age, y	24.83±5.31	25.65±6.52	24.47±4.65	0.09
Age at menarche, y	13.41±1.76	13.25±1.83	13.48±1.72	0.02
Age at onset, y	17.25±4.91	18.29±5.79	16.79±4.41	0.31
BMI [b]	22.25±4.32	27.51±3.35	19.95±2.11	0.000
Menstrual cycle				
Regular	5.90	3.61	6.84	0.18
Irregular	94.10	96.39	93.16	
Oligomenorrheic	66.30	63.86	67.37	
Amenorrheic	17.20	24.10	14.21	
Inordinate	10.60	8.43	11.58	
Hyperandrogenism				
Hirsutism and/or acne	55.70	54.22	56.32	0.75
Hirsutism	34.80	38.55	33.16	0.39
Acne	45.10	44.58	45.26	0.92
Elevated T level	14.70	16.87	13.68	0.49
PCOS on ultrasonography	96.70	90.36	99.47	0.000
Insulin resistance				
HOMA	21.60	47.00	10.50	0.000
GIR	12.80	29.80	5.80	0.000

Abbreviations: BMI, body mass index; GIR, glucose to insulin ratio; HOMA, homesostasis model assessment; PCOS, polycystic ovary syndrome; T, testosterone.
[a] Values are given as mean±SD or percentage unless otherwise indicated.
[b] Calculated as weight in kilograms divided by the square of height in meters.

and Kauffman et al. [10] reported a higher prevalence of insulin resistance in Mexican American women with PCOS than in white women with the same condition. Thus, the impact of ethnicity on clinical and metabolic features of PCOS needs to be considered.

Most data about the clinical features of women with PCOS are available from American and European studies, and there has been scant reporting about the clinical features of Chinese women with PCOS beside the study by Lam et al. with 90 Chinese women from Hong Kong [11]. The aim of this study was to explore the clinical and metabolic features of Chinese women with PCOS. Differences between overweight women and women of normal weight were analyzed.

2. Methods

2.1. Patients

The records of 273 women diagnosed as having PCOS at the gynecological outpatient department of the Second Affiliated Hospital of Sun Yat-Sen University were retrospectively studied. Of these patients, 51 were adolescents (≤19 years) whose condition was diagnosed 2 years after menarche. The

Table 2 Laboratory values for Chinese women with PCOS [a]

Variable	All patients (n=273)	Overweight (n=83)	Normal weight (n=190)	P value
PRL, μg/L	21.88±83.33	14.70±9.22	17.80±15.44	0.09
FSH, U/L	5.39±1.92	4.97±1.61	5.58±2.01	0.02
LH, U/L	11.69±7.10	9.32±5.33	12.72±7.53	0.000
LH/FSH ratio	2.27±1.40	1.97±1.06	2.40±1.50	0.02
E2, ng/L	82.89±68.58	69.30±41.26	88.69±76.71	0.03
T, nmol/L	2.47±1.29	2.52±1.36	2.44±1.26	0.62
FIN, mU/L	12.09±9.81	18.90±12.14	9.11±6.72	0.000
FPG, mmol/L	5.10±1.12	5.38±1.31	4.97±1.01	0.005
HOMA	2.76±2.35	4.44±2.96	2.03±1.54	0.000
GIR	11.72±7.92	7.83±7.16	13.42±7.65	0.000

Abbreviations: FSH, follicle-stimulating hormone; GIR, glucose to insulin ratio; LH, luteinizing hormone; E2, 17β-estradiol; FIN, fasting insulin; FPG, fasting plasma glucose; HOMA, homesostasis model assessment; PCOS, polycystic ovary syndrome; T, testosterone.
[a] Values are given as mean±SD unless otherwise indicated.

study was approved by the institutional review board for clinical research.

Based on the revised criteria published in 2003 by the European Society of Human Reproduction and Embryology and the American Society for Reproductive Medicine [12,13], the diagnosis of PCOS was made in the presence of (1) oligomenorrhea and/or anovulation; (2) clinical and/or biochemical signs of hyperandrogenism; and (3) polycystic ovaries (presence in each ovary of 12 or more follicles measuring 2 to 9 mm in diameter and/or increased ovarian volume (> 10 mL), with the exclusion of other conditions such as congenital adrenal hyperplasia, androgen-secreting tumors, or Cushing's syndrome. Any medications known to affect sex hormone or carbohydrate metabolism were discontinued at least 3 months before the study. All women were euthyroid.

2.2. Protocol

A standardized form was used to take medical history and a physical examination was performed, with emphasis on menstrual dating and regularity, hirsutism, acne, medications taken, and gynecological and family history. Menstrual cycles were defined as (1) regular menses, i.e., a cycle with an intermenstrual interval of 21 to 35 days; (2) oligomenorrhea, i.e., an intermenstrual interval of 36 days or longer; (3) amenorrhea, i.e., an intermenstrual interval of 6 months or longer; and (4) inordinate menses, i.e., an irregular cycle with an intermenstrual; interval of 20 to 40 days and menses lasting from 5 to 15 days [2].

A fasting blood sample was obtained in the morning between the third and fifth day of either spontaneous or progestin-induced withdrawal bleeding. Levels of prolactin, luteinizing hormone, follicle stimulating hormone, estradiol, total testosterone, and fasting insulin (FIN) were measured by chemiluminescence using the ACS180·SE autoanalyzer (Bayer Diagnostics, Fernwald, Germany). Fasting plasma glucose was measured by a glucose oxidase assay (Tosoh Corp., Tokyo, Japan). Transvaginal or transanal ultrasonographic evaluation was performed in all patients using the Shimadzu SDM-450 real-time device (Shimadzu Corp., Kyoto, Japan).

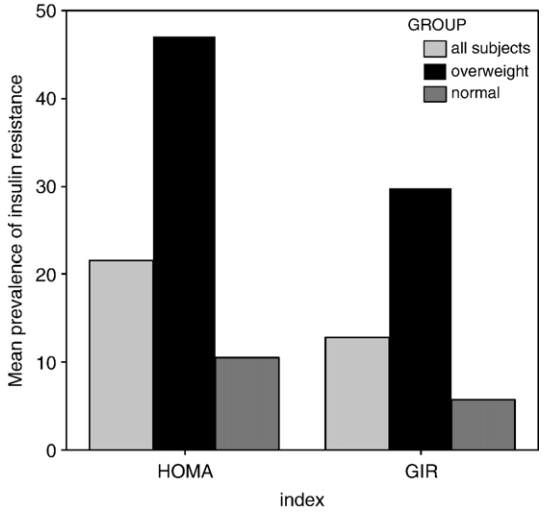

Figure 1 The prevalence of insulin resistance in all subjects, overweight and normal-weight patients. HOMA, Homeostasis model assessment; GIR, fasting glucose to insulin ratio.

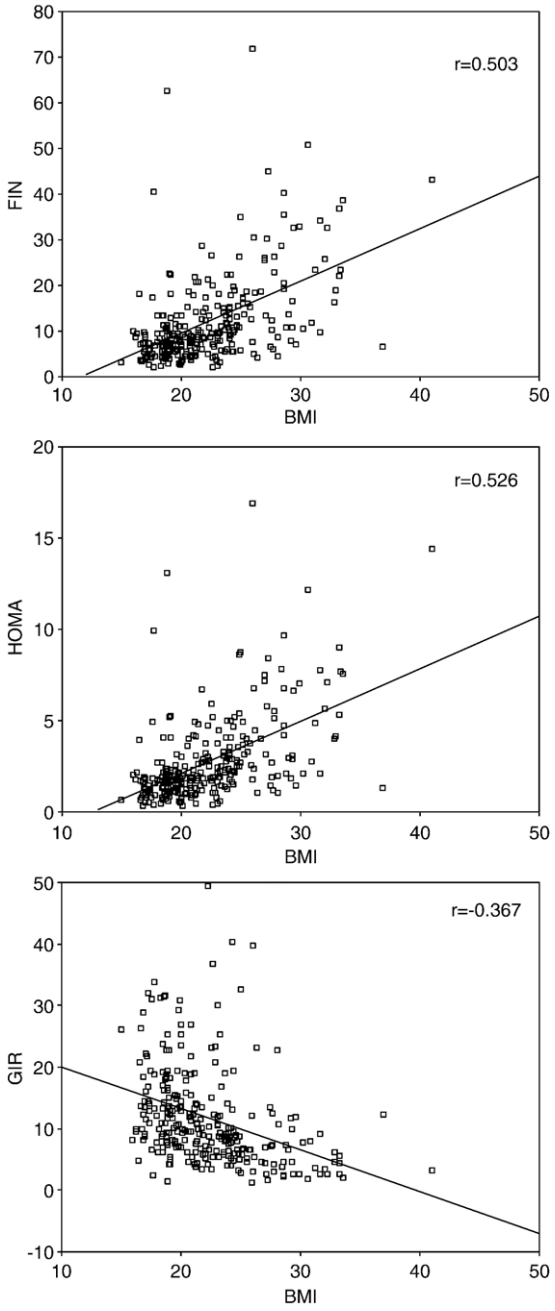

Figure 2 Relationships between BMI and FIN, GIR and HOMA ($P < 0.001$). Analysis by linear regression and Pearson correlation coefficient was shown.

Body mass index was calculated as weight in kilograms divided by the square of height in meters. The patients were classified based on the criteria of International Life Science Association of China as being overweight (BMI <24) or of normal weight (BMI <24) [14]. Biochemical hyperandrogenemia was defined as a serum level of total testosterone higher than 3.47 nmol/L.

Insulin sensitivity was calculated by 2 methods [7], the fasting glucose to insulin ratio (GIR, calculated with glucose

expressed as milligrams per deciliter and insulin expressed as microunits per milliliter) and the homeostasis model assessment (HOMA). The latter was calculated according to the following formula:

Fasting insulin×fasting glucose/22.5

Insulin resistance was defined as a GIR of 4.5 or less or a HOMA of 3.8 or higher.

2.3. Statistical analysis

Continuous data were compared between the 2 groups using analysis of variance and categorical data were compared using the χ^2 test. Partial correlations were used to compare correlations between BMI and levels of testosterone and FIN and well as HOMA and GIR. The statistical analyses were performed using the Statistical Package for Social Sciences, version 10.0 (SPSS Inc., Chicago, Ill, USA). Values are reported as mean ± SD; was attributed to $P<0.05$ (2-tailed) considered statistically significant.

3. Results

A total of 273 Chinese patients with PCOS were studied, including 51 adolescents (18.7%). Of the 222 adult patients, 33 (14.9%) had a history of pregnancy (abortion, ectopic pregnancy, and/or premature or full-term delivery). The clinical and laboratory features are summarized in Tables 1 and 2. Although the serum testosterone level of adolescent girls (2.42 ± 1.05 nmol/L) was approximately that of women (2.48 ± 1.35 nmol/L), the prevalence of both acne (58.8% vs. 41.9%; $P=0.03$) and hirsutism (52.90% vs. 30.60%; $P=0.003$) was significantly higher in adolescent girls than in women. No other differences were found between women and adolescent girls except age (data not shown).

Of the 273 patients with PCOS studied, 82 (30.4%) were overweight (BMI ≥24). Based on World Health Organization Asian criteria [15], the prevalence of obesity (BMI ≥25) was 21.3%. Only 5.5% of the women had a BMI higher than 30. The results of the comparisons between patients with PCOS who were overweight and of normal weight are presented in Tables 1 and 2. No differences were found in the prevalence of hyperandrogenism and serum testosterone levels. Overweight patients had a higher FIN level, a higher HOMA, and a lower GIR. The prevalence of insulin resistance was significantly higher among overweight women ($P=0.000$) (Fig. 1).

Significant relationships were found by partial correlation analysis between BMI and FIN level ($r=0.50$; $P<0.001$), BMI and HOMA ($r=0.53$; $P<0.001$), BMI and GIR ($r=0.37$; $P<0.001$) (Fig. 2). There was no significant relationship between BMI and serum levels of testosterone ($r=0.03$; $P=0.62$).

4. Discussion

Reports are scant about the clinical features of Chinese women with PCOS. Whereas Lam et al. [11] conducted their study with 90 Chinese women from Hong Kong, the present study was based on a greater sample of 222 women and 51 adolescent girls who were all from the southern China Han population. And although the Liang and Jing's summary included 380 Chinese women with PCOS [16], the women were from various parts of China and had been diagnosed according to different criteria, which probably weakened the study's reliability.

Although Legro et al. found no racial differences among the phenotypes of 626 infertile women with PCOS, the authors reported that Asian women tended to have a milder phenotype [17]. The proportion of Asian women in their study (2.7%) may be too low to offer strong evidence, however. In the present study almost all women (94.1%) presented with menstrual disturbances and the typical ultrasonographic appearance of polycystic ovaries (96.7%); moreover, 45.1% had acne and 34.8% had hirsutism. The prevalence of hirsutism was about 30% in both the study by Lam et al. and the present study, and Liang et al. found the prevalence of hirsutism to be 30.77% among Chinese women with PCOS and 69% among their white counterparts [16]. Legro et al. [7] showed levels of total testosterone to be significantly lower in Asian (50.5 ± 19.7 ng/dL) than in white (62.7 ± 29.4 ng/dL) and African–American (65.6 ± 27.2 ng/dL) women. Thus, the low prevalence of hirsutism in Asian women with PCOS is probably due to an ethnic difference. The prevalence of acne was higher in the present study (45.1%) than in the study by Lam and colleagues (26.7%). The reason might be partly due to the inclusion of adolescents in the present study, as the prevalence of acne was significantly higher in the adolescents than in the adults (58.8% vs. 41.9%).

An epidemiological survey of women with PCOS has shown BMI to differ with ethnicity. Carmina et al. [18] found that American women with PCOS had a significantly higher BMI than their Italian counterparts, and Lo et al. [19] found the prevalence of obesity (BMI ≥30) to be 67.5% among white, 80.3% among black, 45.1% among Asian, and 73.8% among Hispanic women with PCOS, and 68.9% among women from other races [19]. These findings show the prevalence of obesity to be the lowest among Asian women. Considering that Asians have a lower mean BMI than populations from other races, WHO has redefined a BMI of 25 or higher as class 1 obesity for Asian Indians [15]. With this criterion, the prevalence of obesity in the present study was 21.3%. BMI (26.6 ± 7.1) and prevalence of obesity (51.1%) are significantly higher among Hong Kong women [11]. The reason might be that the culture of Hong Kong is more similar to that of Europe. Only 5.5% of the cohort had a BMI higher than 30 in the present study, and the prevalence of obesity (21.3%) was significantly lower than that found by Lo et al. [19] for Asian women (45.1%). The Asian women in that study had all immigrated to Northern California or were descended from immigrants, and their living habits may have been different from Asian living in Asia.

Normal insulin sensitivity varies widely and is influenced by age, ethnicity, and obesity. Reaven et al. [20,21] emphasized that powerful ethnic differences exist with regard to glucose disposal, and Whincup et al. [22] demonstrated that in Britain insulin resistance was greater among Asian than among white children. This variation makes it difficult to evaluate insulin resistance in different populations by one certain standard. Reaven [20] and WHO [23] consider the insulin sensitivity index (SI) of the lowest 25% of a

general population to be insulin-resistant. The European Group for the Study of Insulin Resistance defined insulin resistance as the SI of the lowest 10% of a nonobese, nondiabetic, normotensive white population [24]. Legro et al. used the SI of the lowest 10% of an obese population without PCOS to define insulin resistance [25]. In the present study, insulin resistance was defined as a GIR of 4.5 or less or a HOMA of 3.8 or higher [7]. The prevalence of insulin resistance in this cohort (12.8% with GIR and 21.6% with HOMA) was significantly lower than in American, Italian or Mexican female populations (70%) [7], and in Chinese women from Hong Kong (40.7%) [11] as well. This is probably related to the lower prevalence of obesity and insulin resistance in Chinese populations as well as the definition of insulin resistance. The cut-off values used in the present study may be too high for a Chinese cohort and consequently the prevalence of insulin resistance was underestimated. A previous study suggested threshold values of 10.7 for GIR and 2.14 for HOMA to be used in Chinese women with PCOS [26].

As an important metabolic feature of PCOS, insulin resistance is present in both obese and nonobese women with PCOS [1]. Legro et al. [7] reported a higher prevalence of insulin resistance in obese (64%) than in nonobese (20%) women with PCOS. Results of euglycemic hyperinsulinemic clamps have showed obese women with PCOS to have a higher insulin resistance [5,27–32]. In this study, the prevalence of insulin resistance was significantly higher in overweight patients than in patients of normal weight. Moreover, indexes of insulin resistance such as FIN level, HOMA, and GIR were all significantly correlated to BMI. The results showed that obesity would worsen the severity of insulin resistance even though the prevalence of insulin resistance was relatively low in this Chinese cohort.

In conclusion, menstrual abnormalities and polycystic ovaries were the main clinical manifestations in this cohort of Chinese women who had PCOS. The prevalence of hyperandrogenism (including hirsutism, acne, and biochemical hyperandrogenemia), obesity, and insulin resistance was lower in this cohort than in women from other races. Obesity may worsen the severity of insulin resistance, but ethnic differences needs to be considered when studying the clinical and metabolic features of women with PCOS.

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