Endocrine and glycolipid metabolism characteristics of diminished ovarian reserve in Chinese women with polycystic ovary syndrome

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Abstract

Objective: This study was performed to evaluate the endocrine and glycolipid metabolism characteristics of diminished ovarian reserve (DOR) in Chinese patients with polycystic ovary syndrome (PCOS).

Methods: In total, 1179 patients with PCOS and 70 healthy women who presented to the Department of Gynecological Endocrinology in Ren Ji Hospital from June 2015 and June 2019 were enrolled in this study. Parameters of endocrine and glycolipid metabolism were measured. The differences in indices among the control group, simple PCOS group, and PCOS with DOR group were analyzed.

Results: The prevalence of DOR in Chinese women with PCOS was 20.8%. The body mass index and waist/hip ratio were significantly higher in the simple PCOS group than in the PCOS with DOR group. There were significant differences in the concentrations of luteinizing hormone, follicle-stimulating hormone, estradiol, testosterone, and androstenedione among the three groups. The fasting serum insulin concentration and homeostatic model assessment of insulin resistance were significantly higher in the simple PCOS group than in the PCOS with DOR group.

Conclusions: The endocrine and glycolipid metabolism characteristics were different between the simple PCOS group and PCOS with DOR group.

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Background

Polycystic ovary syndrome (PCOS) is the most common gynecological endocrine disturbance and affects 5% to 15% women of reproductive age.[1] Compelling evidence suggests that patients with PCOS have a higher risk of metabolic disorders, such as insulin resistance (IR), type 2 diabetes mellitus, and lipid abnormalities. IR is clinically defined as the need for an increased amount of insulin to perform normal glucose uptake and utilization. Li et al.[2] reported that IR occurred in 56.3% of Chinese Han women with PCOS. The homeostatic model assessment of IR (HOMA-IR) is widely used to measure IR among patients with PCOS.

Diminished ovarian reserve (DOR), a challenging condition in the field of reproductive medicine, is characterized by impaired ovarian function and poor fertility outcomes. Many factors may give rise to DOR, including genetic abnormalities, iatrogenic causes, and autoimmune and metabolic disorders. The diagnostic standard of DOR is based on a serum follicle-stimulating hormone (FSH) concentration of >10 to <25 IU/L in women aged <40 years. The other criteria are an FSH/luteinizing hormone (LH) ratio of >3, basal estradiol (E2) concentration of >80 pg/mL, or antral follicle count (AFC) of <4.[3]

Patients with PCOS typically have higher LH concentrations than those without PCOS. However, some patients with PCOS may also have DOR with a high FSH or basal E2 concentration. These patients might have metabolic conditions different from those of patients with simple PCOS. In this study, we explored the differences in endocrine and glycolipid metabolism between patients with PCOS and DOR and patients with simple PCOS.

Materials and methods

Patients

The study was based on routine clinical practice and conducted in the Department of Gynecological Endocrinology in Ren Ji Hospital. The ethics committee of Ren Ji Hospital approved this research (2015-087K). Written informed consent was obtained from each participant. Patients with PCOS who had received no pretreatment from June 2015 to June 2019 were included in this study. PCOS was diagnosed according to the 2003 Rotterdam criteria,[4] which define PCOS by at least two of the following three features: anovulation, hyperandrogenism, and polycystic ovary morphology. The study also included a control group of healthy women with regular menses. The exclusion criteria for all women were a history of Cushing's syndrome, androgen-secreting tumors, or adrenal hyperplasia. The diagnostic criteria for PCOS with DOR were as follows: PCOS complicated by a basal FSH concentration of >10 to <25 IU/L, an FSH/LH ratio of >3, a basal E2 concentration of >80 pg/mL, or an AFC of ≤4.[3]

Laboratory assessment

Weight and height were measured with an RGZ-120 electronic scale (Jiangsu Suhong Medical Device Co., Ltd., Jiangsu, China). The waist and hip circumferences were measured, and the body mass index (BMI) and waist–hip ratio (WHR) were calculated. The formula used to calculate the BMI was weight (kg) / height (m)^2. The AFC was evaluated by transvaginal ultrasound. Blood samples were collected from all patients and tested in the clinical laboratory of Ren Ji Hospital. The concentrations of reproductive hormones, including LH, FSH, E2, prolactin, thyroid-stimulating hormone, total testosterone, and androstenedione, were measured using an IMMULITE 2000 (Diagnostic Products Corporation, Siemens Healthineers, Erlangen, Germany). The concentrations of metabolic parameters, including fasting plasma glucose, insulin, total cholesterol (TC), triglycerides (TG), and low-density lipoprotein (LDL) cholesterol, were measured using a Roche cobas 8000-c702 analyzer (Roche Diagnostics, Basel, Switzerland).

The equation used to compute the HOMA-IR was HOMA-IR = fasting insulin (mIU/L) × fasting glucose (mmol/L) / 22.5.[5]

Statistical analysis

All data are presented as mean ± standard deviation. Statistical analyses were performed using SPSS for Windows, version 21.0 (IBM Corp., Armonk, NY, USA). One-way analysis of variance was used to compare three or four independent groups according to quantitative data, and the least significant difference test was used for the post hoc analysis. A P value of <0.05 was considered statistically significant.

Results

Among 1179 patients with PCOS, 245 had DOR. Therefore, the prevalence of DOR among all patients with PCOS was 20.8%. The control group comprised 70 healthy women. The main clinical characteristics and endocrine parameters of the three groups are shown in Table 1. There was

Table 1. Clinical features and endocrine parameters among the three groups.

	Control (A) (n = 70)	Simple PCOS (B) (n = 934)	PCOS with DOR (C) (n = 245)	P (A vs. B)	P2 (A vs. C)	P (B vs. C)	P value
Age, years	25.56 ± 6.03	25.78 ± 4.98	25.79 ± 4.90	0.724	0.738	0.980	0.937
Height, cm	1.63 ± 0.05	1.62 ± 0.05	1.62 ± 0.05	0.642	0.560	0.771	0.843
Weight, kg	55.69 ± 7.31	62.59 ± 13.58	58.33 ± 12.56	<0.001*	0.117	<0.001*	<0.001*
BMI, kg/m^2	21.00 ± 3.35	23.74 ± 4.81	22.31 ± 4.60	<0.001*	0.062	<0.001*	<0.001*
Waist/hip ratio	0.82 ± 0.06	0.84 ± 0.07	0.83 ± 0.06	0.003*	0.288	0.005*	0.001*
LH, IU/L	6.60 ± 2.00	10.31 ± 6.60	16.22 ± 13.50	<0.001*	<0.001*	<0.001*	<0.001*
FSH, IU/L	5.90 ± 1.46	6.52 ± 1.42	9.28 ± 3.93	0.014*	<0.001*	<0.001*	<0.001*
E2, pmol/L	167.49 ± 39.90	175.70 ± 62.49	487.68 ± 298.20	0.643	<0.001*	<0.001*	<0.001*
Prolactin, μg/L	13.10 ± 6.27	13.24 ± 11.17	13.23 ± 7.43	0.909	0.923	0.989	0.994
T, nmol/L	1.92 ± 0.59	2.28 ± 0.85	2.44 ± 0.82	0.001*	<0.001*	0.006*	<0.001*
AD, ng/mL	2.72 ± 0.90	3.22 ± 1.22	3.31 ± 1.33	<0.001*	<0.001*	0.270	0.002*
TSH, mIU/L	1.83 ± 0.52	2.28 ± 2.14	2.19 ± 1.58	0.065	0.170	0.553	0.171

Data are presented as mean ± standard deviation.
*Statistically significant ($P < 0.05$).
PCOS, polycystic ovary syndrome; DOR, diminished ovarian reserve; BMI, body mass index; LH, luteinizing hormone; FSH, follicle-stimulating hormone; E2, estradiol; T, testosterone; AD, androstenedione; TSH, thyroid-stimulating hormone.

no difference in age, height, prolactin concentration, or thyroid-stimulating hormone concentration among the three groups. Weight ($P < 0.001$), BMI ($P < 0.001$), and WHR ($P = 0.005$) were all significantly higher in the simple PCOS group than in the PCOS with DOR group. However, there were no differences in these three indices between the control group and the PCOS with DOR group. The concentrations of LH ($P < 0.001$), testosterone ($P = 0.006$), and E2 ($P < 0.001$) were significantly lower in the simple PCOS group than in the PCOS with DOR group; however, the androstenedione concentration was not significantly different between the two groups.

Table 2 shows a comparison of metabolic parameters among the three groups. With respect to IR, the fasting plasma insulin concentration ($P = 0.005$) and HOMA-IR ($P = 0.006$) were significantly higher in the simple PCOS group than in the PCOS with DOR group. The TG concentration was significantly higher in the simple PCOS group than in the PCOS with DOR group ($P < 0.001$), whereas the TC and LDL cholesterol concentrations were similar between these two groups.

Discussion

Patients with one of the following features are classified as having DOR: basal FSH concentration of >10 to <25 IU/L, FSH/LH ratio of >3, basal E2 concentration of >80 pg/mL, or AFC of ≤ 4.[3] Women with PCOS usually have a higher LH concentration or LH/FSH ratio than those without PCOS. In addition, an increased AFC on ultrasonography is a cardinal feature for the diagnosis of polycystic ovaries, which in turn is a criterion used to diagnose PCOS. However, some patients with PCOS have a high FSH concentration, FSH/LH ratio, or basal E2 concentration but a low AFC. There seems to be a contradiction between these patients with PCOS complicated by DOR and patients with simple PCOS. Therefore, we explored various characteristics between these patients.

In the present study, we found that the prevalence of DOR in Chinese patients with PCOS was 20.8%, which is higher than that in a previous study performed by Jin et al.[3] The diagnostic criteria for PCOS with DOR in the study by Jin et al.[3] was an elevated FSH concentration of >40 IU/L on two occasions >4 weeks apart. We used an

Table 2. Metabolic parameters among the three groups.

	Control (A) (n = 70)	Simple PCOS (B) (n = 934)	PCOS with DOR (C) (n = 245)	P (A vs. B)	P (A vs. C)	P (B vs. C)	P value
Fasting plasma glucose, mmol/L	4.92 ± 0.39	5.20 ± 0.78	5.13 ± 0.58	0.002*	0.029*	0.200	0.005*
Fasting plasma insulin, mg/dL	4.83 ± 1.66	9.02 ± 7.51	7.59 ± 6.14	<0.001*	0.004*	0.005*	<0.001*
HOMA-IR	1.05 ± 0.38	2.16 ± 2.05	1.79 ± 1.63	<0.001*	0.005*	0.006*	<0.001*
TC, mmol/L	4.36 ± 0.71	4.60 ± 0.88	4.67 ± 0.83	0.009*	0.003*	0.245	0.011*
TG, mmol/L	1.07 ± 0.40	1.18 ± 0.80	0.97 ± 0.56	0.209	0.377	<0.001*	<0.001*
LDL cholesterol, mmol/L	2.37 ± 0.46	2.69 ± 0.79	2.67 ± 0.76	0.001*	0.003*	0.760	0.002*

Data are presented as mean ± standard deviation.
*Statistically significant ($P < 0.05$).
PCOS, polycystic ovary syndrome; DOR, diminished ovarian reserve; HOMA-IR, homeostatic model assessment of insulin resistance; TC, total cholesterol; TG, triglycerides; LDL, low-density lipoprotein.

FSH concentration of >25 IU/L as a diagnostic criterion for PCOS with DOR according to the guideline development group recommendation.[6]

Kulkarni et al.[7] observed associations of an increasingly affluent diet and high BMI with the incidence of PCOS. Weight management is a first-line treatment for women with PCOS.[8] However, we observed no difference in the BMI or WHR between the PCOS with DOR group and the control group in the present study. Further research on lifestyle intervention outcomes in women with PCOS with different levels of ovarian reserve is necessary.

A previous study showed that the HOMA-IR, TG concentration, and LDL cholesterol concentration were higher and that the high-density lipoprotein cholesterol and anti-Mullerian hormone (AMH) concentrations were lower in patients with DOR than in controls.[9] However, the cardiovascular disease risk markers, such as HOMA-IR, LDL cholesterol, TC, and TG, remain unknown in patients with PCOS with DOR. In the present study, the fasting plasma insulin concentration and HOMA-IR were significantly lower in the PCOS with DOR group than in the simple PCOS group but higher than those in the control group. The TC and LDL cholesterol concentrations were higher in the simple PCOS group and PCOS with DOR group than in the control group, but they were not significantly different between the simple PCOS group and the PCOS with DOR group. The TG concentration was significantly lower in the PCOS with DOR group than in the simple PCOS group.

Measurement of AMH, which is expressed by the antral follicles, is regarded as a useful tool for the diagnosis of PCOS. Both the AMH concentration and the LH/FSH ratio are significantly correlated with the AFC in patients with PCOS.[10] Women with PCOS have high AMH concentrations, whereas those with DOR have low AMH concentrations. Because of the varying sensitivity and specificity, the AMH has yet to be adopted as part of the diagnostic criteria for PCOS.[11,12] Additionally, there are several cutoff values of the AMH concentration ranging from 1.1 to 2.0 ng/mL in patients with DOR.[13,14] Because of its limitation in the diagnosis of PCOS and its high cost of measurement, AMH was not evaluated in the present study. A next step could be to compare the response to ovulation induction drugs between patients with PCOS complicated by DOR and patients with simple PCOS.

Conclusions

In this study, we compared the metabolic characteristics between patients with simple PCOS and patients with PCOS with DOR. The hormone concentrations, BMI, and HOMA-IR were significantly higher in the simple PCOS group than in the PCOS with DOR group. These findings were obtained from a single-center study; thus, large-scale multicenter studies are needed to confirm our results.

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