Epidemiologic investigation of polycystic ovarian syndrome (PCOS) in Han ethnic women of reproductive age in Liaoning Province, China

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Summary

Objective: To determine the incidence of polycystic ovary syndrome (PCOS) among Han women of reproductive age in Liaoning Province in Northeastern China, based on the Revised Rotterdam 2003 criteria. *Materials and Methods:* A retrospective cohort study was carried out on 1,600 women using questionnaires, physical examination, ultrasonography, and biochemical indices (aged = 19 to 45 years; n = 1,600). PCOS patients were identified using the Revised Rotterdam 2003 criteria. *Results:* A total of 132 Han women of reproductive age were diagnosed with PCOS, with a prevalence of 8.25%. The prevalence of menstrual dysfunction was as follows: 97 patients (73.48%) had abnormal menstruation, three (2.27%) had polymenorrhea, and 94 (71.21%) had oligomenorrhea. Up to 64 patients (48.48%) had androgen excess, 42 (31.82%) had biochemical evidence of androgen excess, and 34 (25.76%) had clinical androgen excess. Up to 34 patients (25.76%) were obese (body mass index [BMI] ≥ 25) and 19 (14.39%) had hirsutism (F-G scoring ≥ 6). A total of 127 patients (96.22%) were diagnosed with PCOS via ultrasonography, 67 of whom (50.76%) had a unilateral polycystic ovary and 60 (45.46%) had bilateral polycystic ovaries. *Conclusions:* The prevalence of PCOS in this study population was 8.25%, with an infertility rate of 27.8%. The classical manifestation of PCOS is PCO, abnormal menstruation, and obesity. The high-risk factors of PCOS include high free testosterone index, homeostasis model assessment-insulin resistance (HOMA-IR), increased serum testosterone and androstenedione, decreased sex hormone-binding globulin, long history of infertility, menarche later than 16 years old, and failure to have regular menstruation within two years.

Key words: PCOS; Physical examination; Distribution features; Physical examination.

Introduction

Polycystic ovary syndrome (PCOS) is a common complicated endocrine and metabolic disorder that affects five to ten percent of the population [1]. The diagnostic criteria for PCOS remain controversial because of the diversity and heterogeneity of its clinical features [2]. According to the Rotterdam criteria, the prevalence of PCOS in women seeking primary healthcare in Salvador, Brazil, was 8.5% [3]. In a community sample of an Iranian population, the prevalence of PCOS was 7.1% (95% CI: 5.4%–8.8%) using the National Institutes of Health (NIH) definition, 11.7% (95% CI: 9.5%–13.7%) based on the Androgen Excess Society (AES) criteria, and 14.6% (95% CI: 12.3%–16.9%) using the Rotterdam definition [4]. Different ethnic groups have different prevalence rates. The PCOS prevalence rates among Black and among Caucasian American women of reproductive age were 8.0% and 4.8%, respectively [5]. The prevalence of PCOS among Mexican women is approximately 6.0%, similar to that in other populations, but lower than the 12.8% among Mexican-American women [6]. The prevalence of PCOS among unselected women from Southern China is 2.2%, much lower than the average prevalence [7].

However, Southern China and Northeastern China differ greatly in climate, environment, and lifestyle. Thus, the prevalence of PCOS among Han ethnic women of reproductive age in Northeast China may differ from that in Southern China.

European Society of Human Reproduction and Embryology / American Society for Reproductive Medicine (ESHRE/ASRM) -sponsored PCOS Consensus Workshop in Rotterdam discussed and recommended the current criteria for PCOS [8]. These criteria emphasise the exclusion of other diseases that can cause androgen excess; thus, it is an exclusion criterion. Although the Rotterdam criteria was established based on ten years of research as a bridge for international science communication, further research should confirm whether it is suitable for Han ethnic women of reproductive age in China.

The etiology and pathogenesis of PCOS is still unclear. At present, PCOS is regarded as a consecutive process, beginning with prepuberty or earlier, during which adult clinical manifestations change with heredity and environment [9]. Up to 50 million of the five billion women of reproductive aged in China will have PCOS, with an incidence rate of five to ten percent. Thus, providing proper diagnosis and treatment, and preventing long-term complications are arduous tasks. Meanwhile, the diverse clinical manifestations and severe long-term complications of PCOS have gradually attracted attention [8,10-13]. Although

drugs effectively prevent type 2 diabetes, hypertension, hyperlipidemia, and cardiovascular events, support from evidence-based medicine is lacking [14]. Presently, changing lifestyles (changing dietary habits, exercise for weight reduction) is an easy, cheap, and efficient therapy [15]. Hence, it is the most efficient, safest, and cheapest management strategy for patients diagnosed with PCOS.

The clinical manifestations of PCOS differ according to race and to age [16-19]. Thus, we should focus on the features of PCOS among the Han population in China to understand PCOS, to diagnose and treat the disease correctly, as well as to prevent its long-term complications. A total of 1600 Han women of reproductive age who came from four sites in Liaoning Province were investigated via epidemiologic cluster layer sampling.

Materials and Methods

Participants

We surveyed women of reproductive age who were permanent residents in four different areas in Liaoning Province, Northern China, including the two cities Shenyang and Yingkou, and the two towns Benxi and Zhangwu.

This sampling frame was chosen because it was the most logistically feasible, maximising the representativeness of geographic position and economic level in presenting prevalence and enabling further research on PCOS. All the Han ethnic women aged 19 years to 45 years were investigated, and finally, 1,600 women participated the study. Suspected PCOS patients were screened using inclusion criteria, and the controls were filtered from the cohort according to 1:1. The PCOS patients were diagnosed according to the diagnostic criteria recommended by the 2003 Rotterdam ESHRE/ASRM. Nest cases control study of diagnosed PCOS patients and normal controls were carried out.

Questionnaire

A total of 1,600 Han women of reproductive age from Liaoning Province were investigated from May to December in 2008. The questionnaire included common status, menstruation history (menarche age, primary or secondary amenorrhoea, functionary uterus bleeding, oligo-menstruation), recent hormone or drug intake, disease and treatment history, birth status, diet and exercise habit, familial disease history (including diabetes, hypertension, cardiovascular events, seborrheic alopecia, and the menstruation history of first and second degree relatives), and childbearing history of married women (pregnancy-induced hypertension, gestational diabetes, preterm birth, and macrosomia).

Physical examination

Height and weight were measured (to calculate the body mass index, BMI), as well as abdominal circumference and waistline (to calculate waist to hip ratio, WHR). The subjects were examined for hair distribution (F-G hirsutism score) [20], acne, seborrheic alopecia, lactation, exophthalmos, swollen thyroid, and beast masses, as well for acanthosis nigricans. Blood pressure and pulse rate were recorded, and gynaecologic examinations (vulvae, vagina, cervix, body of uterus, appendix, and rectal examination for unmarried women) were performed.

Ultrasonography

Using an Ssc370 type ultrasound machine with 7.3 Hz, pelvic ultrasonography was performed per vagina for married women and per rectum for unmarried women. The size (length, width, thickness) and position of the uterus and endometrial thickness were measured. The sizes of both ovaries were measured, and the number of two to nine mm antral follicles (on longitudinal and coronal sections of the ovaries) was determined to obtain the mean value and describe special status.

Endocrine and biochemical indexes checking

The fasting blood glucose (FBG) of suspected PCOS patients and matched controls from the cohort were determined. Fasting venous blood samples were collected and sent to the Third Hospital of Beijing Medical University to determine fasting insulin (INS), triglyceride (TG), total cholesterol (TCH), high density lipoprotein (HDL), low density lipoprotein (LDL), thyroid stimulating hormone (TSH), testosterone (T), sex hormone-binding globulin (SHBG), androstenedione (A), as well as to calculate homeostasis model assessment of insulin resistance and the free testosterone index (FAI).

Intake, exclusion, and diagnostic criteria

Healthy Han ethnic women of reproductive age (19 to 45 years) in from Liaoning Province were included in the study. To minimise treatment bias, the authors excluded pregnant women or those suspected of pregnancy, lactating women, and those with endocrine diseases, as well as those on long-term oral contraceptives or subcutaneously injected contraceptive.

PCOS patients were diagnosed using ESHRE/ASRM of 2003 (8). Women who fulfilled any of the three criteria were considered suspected PCOS patients.

Normal women with signs of irregular menstruation, hirsutism, acne, and sebaceous flux were matched by ages (± 2) and BMI (± 2) in the cohort.

Statistical analysis

Descriptive statistics were generated to enable comparisons between groups. Continuous variables were checked for normality, and the means are presented with standard deviations, medians, or interquartile ranges, as appropriate. Distributions were compared using Student's t-test or Mann–Whitney U as appropriate. Categorical variables were compared using a Pearson's χ^2 test. Differences with p-values < 0.05 were considered significant. All statistical analyses were carried out using SPSS 15.0.0 for Windows.

Results

Common features of researched groups

The age, profession, education degree, average family income, married/unmarried ratio, number of pregnancies and deliveries, BMI, and obesity distribution of the three groups are shown in Tables 1 and 2.

Of the 1,600 respondents, 132 (8.25%) were diagnosed with PCOS using the diagnostic criteria proposed by ESHRE/ASRM in 2003.

Menstruation history

Up to 97 of the 132 (73.48%) diagnosed PCOS patients had abnormal menstruation. Among the 97 cases, three (2.27%) had polymenorrhea, 94 (71.21%) had oligomenorrhea, six (4.55%) had secondary oligomenorrhea; 61 cases (64.9%) had menstrual cycles lasting 35 days to 60 days, whereas 33 cases (35.1%) had menstrual cycles last-

Table 1. — *Common features of researched groups.*

Features	All	Suspected PCOS and controls	PCOS
Number	1,600	966	132
Age (year)	34.38 ± 5.07	33.17 ± 4.89	31.15 ± 4.89
Profession (%) cadre/teacher/office clerk/medical staff/ student/worker/farmer/business/others	13.6 / 19.1 / 31.6 / 2.8 / 0.2 / 14.1/3.3/9.1/6.4	10.6 / 16.0 / 33.7 / 3.7 / 0.3 / 14.0 / 3.8 / 9.7 / 8.1	10.6 / 15.9 / 34.1 / 4.5 / 2.3 / 12.1 / 4.5 / 12.1 / 3.8
Education degree (%) illiterate / elementary school / high school (polytechnic school) / junior college and higher	0 / 0.9 / 42.7 / 56.4	0 / 0.6 / 44.4 / 55.0	0 / 0 / 43.6 / 56.8
Average income of the family (%) < 700 yuan / 701-1,500 yuan / < 1,501-5,000 yuan / > 5,000 yuan	22.5 / 48.6 / 27.9 / 1.1	18.7 / 44.5 / 35.4 / 1.3	18.9 / 50.8 / 28.8 / 1.5
Married/unmarried ratio	1546 / 54	924 / 42	115 / 17
Pregnancy/delivery times	1.84 ± 1.12 / 0.92 ± 0.39	1.82 ± 1.14 / 0.88 ± 0.41	1.72 ± 1.09 / 0.82 ± 0.44
Menarche (age)	14.39 ± 1.51	14.18 ± 1.44	14.27 ± 1.64
BMI	22.73 ± 4.60	22.84 ± 3.29	23.27 ± 3.93
Obesity BMI ≥ 25	285	189	34

ing more than 60 days. The mean menarche age was 14.27 years ± 1.64 years old. The menarche ages of 20 cases were older than 16. In 42 cases (31.8%), regular menstruation began more than two years after menarche.

Androgen excess

The prevalence of androgen excess was 43.5%, among which biochemical androgen excess was 29.8%, whereas clinical androgen excess was 23.7%. Up to 19 cases (14.4%) exhibited hirsutism (F—G ≥ 6 score), 13 cases had acne (9.95%), eight (6.1%) had sebaceous flux, and two cases (1.5%) had acanthosis nigricans syndrome. Thus, the main manifestations of androgen excess among Han ethnic women of reproductive age in Liaoning Province were acne, hirsutism, sebaceous flux, and thick pores.

Hirsutism was mild in Liaoning province, with only 19 cases (14.39%) with F-G scores more than 6. Total score distribution was as follows: muffle 96 scores (37.20%), lower abdomen 52 score (20.16%), chest 43 score (16.67%), thigh 30 score (11.63%), upper abdomen 19 score (7.36%), mandible 15 score (5.81%), upper arm 1 score (0.39%), back 1 score (0.39%), and hip 1 score (0.39%). The main manifestations of hirsutism among Han women of reproductive age are thin hairs on the upper lip, thick hairs in middle of the lower abdomen, thick pubes extending to the crissum and groin, but seldom male distribution, long hair around the areola, and hairs inside the thigh, mainly near groin.

Polycystic ovaries

Polycystic ovaries are prominent among the PCOS patients. A total of 126 cases (96.2%) had polycystic ovaries, 68 of which were bilateral 58 (44.3%) were unilateral. The average number of follicles in the left ovary was 14.05 ± 5.51 and 15.23 ± 6.14 in the right ovary.

Table 2. — *Three groups divided according to age.*

Age (years)	19 - 25	26 - 35	36 - 45
Total number	65 (4.06%)	810 (50.63%)	725 (45.31%)
Suspected PCO and normal	50 (5.18%)	581 (60.14%)	335 (34.68%)
Diagnostic PCOS	16 (12.12%)	92 (69.70%)	24 (18.18%)

Obesity

BMI is often used to evaluate obesity. In 2000, the WHO Western Atlantic regional officials, the International Association for the Study of Obesity (IASO), and the International Obesity Task Force (IOTF) set the overweight and obesity cut-offs at BMIs of 23 kg/m² and 25 kg/m². Only 29 cases (21.96%) were overweight and 34 cases (25.75%) were obese. The patients were divided into an obesity group (34 cases, BMI ≥ 25) and a non-obesity group (98 cases). The triglyceride levels, free testosterone index, fasting insulin, constriction blood pressure, and hirsutism in the obesity group were higher than those in the non-obesity group. The levels of high-density lipoprotein and sex hormone-binding globulin were significantly lower than those in the non-obesity group ($p < 0.05$). The other biochemical indices, such as cholesterol, androstenedione, number of follicles, low density of lipoprotein, and diastole blood pressure, did not significantly differ between the two groups ($p > 0.05$). The incidence rates in the obesity group of silent lifestyle, abnormal menstruation, history of infertility, and interval from menarche to regularisation of menstrual cycle exceeding two years were higher than those in the non-obesity group, but the differences were not significant (the χ^2 values were 1.64, 0.869, 2.663, 0.625 respectively, $p > 0.05$, Table 3)

Age distribution features

The 132 diagnosed PCOS patients were divided into three groups in terms of age: 19 years to 25 years, 26 years

Table 3. — *Clinical and biochemical characteristics of 132 patients in obesity and non-obesity groups.*

Items	Obesity group	Non-obesity group	t value	p value
TG (mmol/l)	1.67 ± 1.23	1.09 ± 0.68	3.436	0.001*
HDL (mmol/l)	1.24 ± 0.36	1.44 ± 0.31	-3.130	0.002*
FAI	8.91 ± 8.07	4.92 ± 3.95	3.776	0.000*
SHBG (nmol/l)	33.90 ± 16.68	55.57 ± 22.19	-5.203	0.000*
INS (uIU/ml)	7.01 ± 4.21	4.54 ± 6.25	2.140	0.034*
F-G SCORE	3.00 ± 3.45	1.59 ± 2.29	2.689	0.008*
DBP (mmHg)	124.62 ± 25.13	111.04 ± 11.97	4.173	0.000*
FBG (mmol/l)	5.89 ± 1.28	5.37 ± 0.72	2.933	0.004*
HOMA-IR	1.88 ± 0.21	1.11 ± 0.16	2.952	0.004*
TCH (mmol/l)	4.75 ± 0.69	4.68 ± 0.38	0.463	0.644
A (nmol/l)	11.52 ± 4.13	11.80 ± 4.44	-0.323	0.747
LON (number)	14.94 ± 5.34	13.73 ± 5.59	1.098	0.274
RON (number)	16.35 ± 6.39	14.85 ± 6.03	1.235	0.219
LDL (mmol/l)	2.24 ± 0.59	2.19 ± 0.57	0.437	0.663
T (nmol/l)	2.28 ± 1.07	2.21 ± 1.06	0.325	0.745
SBP (mmHg)	84.59 ± 15.38	81.24 ± 74.07	0.261	0.795

TCH? A? LON? RON? T? SBP?

Table 4. — *Age distribution of 132 PCOS patients.*

Group (age)	Cases	Proportion (%)	Accumulative proportion (%)
20 - 25	16	12.1	12.1
26 - 35	92	69.7	81.8
36 - 44	24	18.2	100.0

to 35 years, and 36 years to 44 years. The 26 years to 35 years old group accounted for 69.7%, less than that in the 36 years old group, which occupies 81.8% (Table 4).

Fertility survey

Of the 132 PCOS patients, 17 were unmarried women and 115 were married women. Among the patients who had been pregnant, 32 took longer than one year to conceive, 17 took longer than one year, six took longer than two years, three took longer than three years, and two took longer than four years. Only 11 patients had histories of pregnancy, but with no live births, and four patients had at most four miscarriages. The control group included five unmarried women and 127 married women. Among those with histories of pregnancy, 15 took longer than one year to conceive, ten took longer than one year, and five took longer than two years. Three had histories of pregnancy, but with no live births and one a history of miscarriage. The clinical criterion for infertility, set by the WHO in 1995, is one year. The prevalence of infertility among the diagnosed PCOS patients was 27.83%, whereas that in control group was 11.81%.

Discussion

The prevalence of PCOS in Europe was five to ten percent [20]. The prevalence rates in Jinan City and in Yan Tai City were 6.46% and 7.2%, respectively, as reported by Chen *et al*. [21]. The prevalence of PCOS in this present epidemiologic search was 8.25%, which is consistent with that in Europe and slightly higher than those in Jinan City and Yan Tai City in China. The prevalence of PCOS is correlated with economic level. However, larger sample size is needed to confirm whether PCOS can be attributed to the difference in quality of life, nutrition, lifestyle, or pressure.

PCOS is a common complicated endocrine and metabolic disorder in women of reproductive age [22]. The symptoms improve with age [23]. PCOS is centralised around the age of 35 years, in accordance with the aforementioned fact [24]. The present study shows that the main clinical manifestation of PCOS in Liaoning Province is abnormal menstruation, with rate reaching 97%, whereas the androgen excess rate was only 23.7%. This result is different from those of a previous European research, wherein the abnormal menstruation rate was 80% and the androgen excess rate was 69% [9]. However, it is similar to the rate in Japan, wherein the abnormal menstruation rate was 92% and the androgen excess rate was 23% [25]. This difference may be because F-G scoring is unsuitable for Asians. Among the 132 matched controls, the correlations between body hair and sex hormone F-G scoring were 71.5%, 85.8%, 93.8%, 97.7%, 98.8%, and 100%, which correspond to scores 0, 1, 2, 3, 4, and 5, respectively. Thus, to determine the normal value from the skewed distribution, the authors set the critical value of F-G scoring to 3. The result is slightly higher than that of Zhao *et al*. [26], with a critical value of 2. These results show that hirsutism among Han women of reproductive age is slightly lower than that among women in occident countries, which may have resulted from racial differences. This result proves that racial difference affects the clinical manifestations of PCOS; thus, the diagnostic criteria should be established according to the different racial characteristics.

Furthermore, the incidence of obesity in this study differs from that in Europe. The obesity rate is 25.76%, which is clearly lower than the rate in Europe (50%–70%) [27], but similar to that in Japan (20%) [28]. However, the present rate is higher than in the study by Chen in 2004 (8.23%) [29]. The difference may be due to research time, caseload, and quality of life. Oligoovulation and non-ovulation are very common in PCOS; thus, many patients consult at the hospital for infertility [30]. Therefore, more attention should be given to treating infertility in the clinic. In this study, the infertility rate of PCOS in the unselected population was only 27.8%, which is lower than that of the normal group (11.82%). Therefore, infertile PCOS patients should initially be observed for endocrinal and metabolic disorders. Drugs to stimulate ovulation are unnecessary during the beginning of treatment.

Significantly more women in the PCOS group required more than two years to have regular menstruation than that

in the control group ($p < 0.05$). The authors defined menstrual delay as the occurrence of menarche later than 16 years. Significantly more women had menstrual delay in the PCOS group than that in the control group ($p < 0.05$). Thus, patients with delayed menarche and delayed regular menstruation, especially oligomenorrhea, have higher risk of PCOS. Therefore, patients who experience delayed menarche or long menstrual cycles, fail to establish regular menstrual cycles within two years after menarche, and those with complications that cause androgen excess, such as obesity and polycystic ovaries, should be examined for PCOS. These patients should be diagnosed earlier to receive the appropriate intervention.

The etiology of PCOS is still unclear. Recent studies have linked increased androgen and insulin resistance with PCOS [31, 32]. The study showed that free androgen index (FAI), homeostasis model assessment-insulin resistance (HOMA-IR), increased serum testosterone, and androstenedione, and decreased SHBG are high-risk factors for PCOS.

Conclusions

The prevalence of PCOS in Han women of reproductive age in Liaoning Province is 8.25%, with an infertility rate of 27.8%. The classical manifestation of PCOS among Han women in Liaoning Province is PCOs and abnormal menstruation, whereas obesity, acne, and hirsutism are minor indicators. In addition, androgen excess rate among PCOS patients is lower than that in other studies. FAI, HOMA-IR, increased serum testosterone and androstenedione, and decreased SHBG, long history of infertility, menstrual delay as menarche later than 16-years-old, and failure to have regular menstruation with two years after menarche are high-risk factors for PCOS.

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