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Defining polycystic ovary syndrome phenotype in Vietnamese women

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Abstract

Aim: This study aimed to evaluate the unique phenotype of the Vietnamese polycystic ovarian syndrome (PCOS) population.

Methods: In this multicenter cross-sectional descriptive study, a total of 901 reproductive-age women were recruited at three medical centers in Vietnam from June 2016 to May 2018. Group I included 479 patients with PCOS (Rotterdam 2003 consensus) and Group II included 422 non-PCOS women, consisted of women with regular menstrual cycle, collected at the same time of PCOS recruitment, without ovarian disease or ovarian failure. Main outcome measures were anthropomorphic, serum hormone, ultrasound and physical characteristics of PCOS.

Results: The Vietnamese PCOS population was lean, but with a higher weight and body mass index compared to controls. About 34.4% of PCOS subjects had hirsutism, primarily confined to the leg, arm and pubis. The PCOS population had higher serum luteinizing hormone (LH), LH : follicle stimulating hormone ratio, anti-Mullerian hormone and testosterone. The PCOS population had double the ovarian volume compared to controls. PCOS subjects had no increase in metabolic disease history and had on average optimal serum markers for low metabolic disease risk. Group D (O + polycystic ovary morphology [PCOM]) was the most prevalent phenotype noted in our Vietnamese PCOS cohort (67.6%). Modified Ferriman–Gallwey, levels of LH, testosterone and anti-Mullerian hormone were highest in Group A (O + H + PCOM) and lowest in Group D (O + PCOM).

Conclusion: The Vietnamese PCOS population is characterized by a lean body type, nonfacial hirsutism, anovulatory, enlarged ovaries and typical PCOS serum hormone markers, low risk factors for metabolic syndrome. Nonclassical phenotypes for PCOS were more frequent than the classic phenotype.

Key words: anovulation, hirsutism, PCOS, phenotype; Vietnam, Southeast Asian.

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Introduction

Polycystic ovarian syndrome (PCOS) affects the general health of 6–15% of women and is one of the most common endocrine and metabolic disorders.[1] In addition to ovulatory dysfunction, PCOS is related to metabolic disorders including obesity, glucose intolerance, dyslipidemia, hypertension, and a sevenfold increase in the risk of type 2 diabetes mellitus and cardiovascular disease.[2] In the United States, over 4.3 billion dollars is spent annually on the treatment of PCOS.[2] Most of what is known about PCOS is generated from data based predominantly on studying Caucasian women. Manifestations of PCOS are heterogeneous among different ethnicities, and have varying impacts on patients' fertility, medical health and overall well-being.[3] Knowledge of ethnic differences in clinical manifestations can assist providers in diagnosing and managing PCOS in specific populations.

Previous studies have compared PCOS phenotypes within and between ethnic groups in attempts to characterize these variations. Hispanic subjects have a higher incidence of metabolic syndrome, suggesting a potential use for ethnicity-specific cutoffs for insulin resistance.[4] Middle Eastern populations have higher rates of hirsutism but lower body mass index (BMI) and an improved cardiovascular risk profile.[4]

Limited data exist on PCOS phenotypes in specific Asian populations, especially from Vietnam. Studies among mixed ethnic groups in the United States have included small numbers of Asian subjects and lacked information regarding their geographic origins.[5] East Asians generally have lower rates of hirsutism and a higher prevalence of metabolic syndrome compared to Caucasian, Hispanic and African American patients.[6–10] Asia is a massive continent with ethnic heterogeneity, and therefore each group must be studied separately in order to have reliable information regarding phenotypic manifestations of PCOS. Studies of indigenous Sri Lankan, Chinese, Korean and Japanese PCOS patients have also reported a high prevalence of metabolic syndrome and risk factors for type 2 diabetes, but with varying rates of hyperandrogenism.[10–13] These populations have different baseline characteristics and the existing data cannot be assumed to extrapolate the phenotype of South East (SE) Asians.

The phenotype and long-term metabolic risk of the SE Asian PCOS population have not been well characterized. The objective of this study was to evaluate and characterize the endocrine profiles, anthropometrics and metabolic disorder characteristics in PCOS women in Vietnam which is one of the representatives of SE Asia.

Methods

Design

This was a prospective, cross-sectional, descriptive study to determine the PCOS phenotype of Vietnamese population.

Recruitment of subjects

Women in the study population were diagnosed with PCOS by Rotterdam criteria seeking care at three Assisted Reproduction Technology Centers in central Vietnam: Hue University Hospital, Hue Central Hospital and Danang Hospital for Women and Children. The study was from June 2016 to May 2018. A total of 901 women at 18–45 years of age were consecutively recruited at the beginning of the study. About 479 PCOS patients (study group) were compared to 422 non-PCOS controls during the same time. Diagnosis of PCOS was established based on Rotterdam 2003 consensus, with the presence of two of the three following criteria: (i) oligo- and/or anovulation, (ii) clinical and/or biochemical signs of hyperandrogenism or (iii) polycystic ovaries by ultrasound examination (minimum of 12 follicles with 2–9 mm diameters in each ovary and/or increasing ovarian volume with a minimum size of 10 mm^3). The control group included women of infertile couple due to other causes, such as male infertility, tubal factor or idiopathic. Inclusion criteria for the control group were women without PCOS, regular menstrual cycle every 21–35 days, no ovarian disease (ovarian cyst, tumor or endometrioma) and no history of ovarian surgery or ovarian failure. All subjects meeting control criteria during the time frame were included. The study was approved by the Hue University of Medicine and Pharmacy Ethics Committee, approval number was H2016/236. Informed written consent was obtained from all participants.

Variables assessed

Fertility, medical, family history and physical exam were performed on PCOS subjects and controls.

Baseline clinical evaluation included height, weight, BMI, waist and hip circumferences, transvaginal ultrasound and evaluation of hirsutism, acne, alopecia and

acanthosis nigricans. Waist and hip circumferences were measured in the standing position, around the abdomen at the levels of navel and pubic symphysis respectively. Body mass index was calculated based on weight and height in meters squared (kg/m^2) and patients were classified as overweight if BMI ≥23 kg/m^2 and obese if BMI ≥25 kg/m^2 according to World Health Organization (WHO) Asian criteria. Body mass index was also assessed by National Institutes of Health (NIH) classifications stratifying by <25, 25–29.9, 30–34.9, 35–39.9 and >40 kg/m^2. Evaluating hirsutism was done based on visually scoring hirsutism system using modified Ferriman–Gallwey (mFG) score. The densities of terminal hairs at nine different body sites (upper lip, chin, chest, upper and lower back, upper and lower abdomen, arm, forearm, thigh and lower leg) were scored from 0 (no hair) to 4 (similar to that of a well-virialized adult male), and total score was calculated.[14] The cutoff of mFG for Asian PCOS population at 5 was used to define clinical hirsutism. In day 2–4 of natural cycle or in day 2–4 of progesterone withdrawal in case of oligo or amenorrhea state, transvaginal ultrasound examination was performed by Aloka SSD 3500SX with vaginal probe 7 MHz and serum samples were collected for hormone assay. The sizes of the ovaries were measured in three dimensions and the total numbers of follicles 2–9 mm in diameter were counted. The ovarian volume was calculated by 3-dimensional on both sides. The uterus was measured in three dimensions: length, depth (in the sagittal view) and width (in the coronal or transverse view). The endometrium was analyzed for thickness and echogenicity. The thickest part of the endometrium was measured perpendicular to its longitudinal plane in the anteroposterior diameter from echogenic to echogenic border. Serum testing included anti-Mullerian hormone (AMH), day 3 estradiol, follicle stimulating hormone (FSH), and luteinizing hormone (LH), testosterone, prolactin, fasting lipid profile, fasting blood glucose, 2-h glucose tolerance testing (GTT) and HbA1C. Follicle stimulating hormone, LH, estradiol and prolactin were measured by immunoradiometric assay. Testosterone was measured by enzyme immunoassay, while AMH was determined by an Elecsys Roche System based on electrochemiluminescence technology. The median AMH yielded by the Elecsys assay was 6.81 ng/mL on women with PCOS; the sensitivity, specificity, positive predictive value, and negative predictive value for an AMH cutoff of 15.0 pmol/L (2.1 ng/mL) were 81.3%, 64.7%, 21.7% and 96.6% respectively (Roche study No. RD001727. 2016). Hyperandrogenemia was defined if total testosterone levels >0.88 ng/mL (NIH 1990).[15]

PCOS patients were classified into four phenotypes groups according to NIH extension of ESHRE/ASRM 2003, Group (A) Oligo + HA + PCO; Group (B) Oligo + HA; Group (C) HA + PCO and Group (D) Oligo + PCO.

Metabolic syndrome will be defined based on National Cholesterol Education Program – Adult Treatment Panel III criteria modified for Asian population[16] with at least three of the following five abnormal variables present: (i) waist circumference ≥80 cm, (ii)serum triglyceride ≥1.7 mmoL/L, (iii) serum high-density lipoprotein (HDL)-cholesterol <1.3 mmoL/L, (iv) blood pressure ≥130/85 mmHg or the use of antihypertensive and (v) fasting plasma glucose ≥5.6 mmoL/L.[16]

The reference intervals of lipid profile will be also established by the National Cholesterol Education Program – Adult Treatment Panel[16] and criteria for the diagnosis of diabetes and prediabetes are established by American Diabetes Association.[17]

Data analysis

Categorical data were assessed for normal distribution using Shapiro–Wilk test. Polycystic ovarian syndrome and control groups, four phenotype groups of PCOS were compared with Student's *t*-test or Mann–Whitney *U* where appropriate. Kruskal–Wallis test was used to compare four phenotypes of PCOS. Dichotomous variables were compared with two-tailed Chi square or Fischer exact test where appropriate. Age and weight were statistically different between the two groups; therefore, linear regression adjusting for age was utilized to compare anthropomorphic and endocrine variables. Linear regression adjusting for weight was utilized to compare lipid and glucose intolerance tests. $P < 0.05$ was considered statistically significant. Data analysis was performed with SPSS 24 software (IBM).

Results

Fertility and menstrual history

The prospective study enrolled a total of 901 subjects, including 479 PCOS subjects and 422 controls. The comparisons of fertility, and menstrual history between PCOS and control subjects are presented in Table 1. The PCOS group was younger at 28.9 versus

Table 1 Characteristics of infertility, menstrual cycles, history of metabolic diseases and hyperandrogenism in polycystic ovarian syndrome (PCOS) and control subjects

Variable	PCOS (n = 479)	Control (n = 422)	P value
Primary infertility	74.1%	64.5%	0.002
Mode of prior conception			0.04
Natural	86.6%	94.4%	
Intrauterine insemination	1.8%	2.3%	
In vitro fertilization	11.6%	3.3%	
Duration of infertility (years)	3.0 ± 2.2	4.4 ± 2.7	0.000
Menstrual cycles			
Oligomenorrhea or amenorrhea	55.1%	7.8%	0.000
Heavy menstrual bleeding	7.3%	7.3%	0.982
Dysmenorrhea	58.2%	55.5%	0.419
Family history of PCOS	19	0	0.000
Family history of hypertension	39	13	0.000
Family history of CVD	6	1	0.12
Family history of diabetes	14	7	0.27
Pre-existing hypertension	40 (8.4)	14 (3.3)	0.002
Pre-existing diabetes II	3	0	0.252
Pre-existing CVD	1	3	0.346
Hirsutism			
Any site	34.4%	3.8%	0.000
Leg	25.7%	2.6%	0.000
Arm	18.2%	0.9%	0.000
Pubis	21.9%	1.7%	0.000
Face	1.5%	0%	0.013
Lip	5%	0%	0.000
Chin	0.6%	0%	0.252
Acne	23.8%	5.0%	0.000
Alopecia	8.9%	0.7%	0.000
Acanthosis nigricans	1.5%	0.2%	0.073

CVD, cardiovascular disease.

31.6 years ($P < 0.001$). Polycystic ovarian syndrome subjects presented with primary infertility 74.1% compared to 64.5% in controls ($P = 0.002$). In subjects with secondary infertility, PCOS subjects were less likely to have conceived via natural conception, but instead were more likely to have used medical assistance. Polycystic ovarian syndrome subjects had a shorter duration of infertility by almost 1.5 years at their presentation to a specialist. Polycystic ovarian syndrome subjects were much more likely to have a history of oligomenorrhea or amenorrhea at presentation (55.1% vs 7.8%, $P < 0.001$). Both groups had similar prevalence of self-reported heavy menstrual bleeding and dysmenorrhea. These data demonstrated that the Vietnamese PCOS population was less likely to have a prior conception, had a shorter duration of infertility prior to presentation and much more likely to have oligomenorrhea or amenorrhea compared to controls.

Family history of metabolic disease

Family history of metabolic disease is shown in Table 1. Nineteen subjects from the PCOS group reported a family history of PCOS compared to zero

Table 2 Comparison of pelvis ultrasound parameters between polycystic ovarian syndrome (PCOS) and control subjects

Parameter	PCOS (n = 479)	Control (n = 422)	P value
Left ovarian volume	9.6 ± 6.1	5.6 ± 2.6	0.000
Right ovarian volume	10.6 ± 7.1	5.4 ± 2.2	0.000
Antero-posterior diameter	36.4 ± 5.9	40.0 ± 6.7	0.000
Length of uterus	47.3 ± 7.7	47.4 ± 6.1	0.753
Endometrial thickness	6.2 ± 2.4	6.4 ± 2.5	0.199

of the controls ($P < 0.001$). Thirty-nine subjects from the PCOS group reported a family history of hypertension compared to 13 from the control group ($P < 0.001$). Six subjects from the PCOS group reported a family history of cardiovascular disease compared to one from the control group ($P = 0.12$). Fourteen subjects from the PCOS group reported a family history of diabetes compared to 7 from the control group ($P = 0.27$). These data demonstrate Vietnamese PCOS population was more likely to have a family history of PCOS and hypertension, but no more likely to have a family history of cardiovascular disease or diabetes.

Hyperandrogenism

Prevalence of hirsutism in Vietnamese PCOS patients was 34.4%, significantly higher than the proportion of control group was 3.8%. The mean mFG score of the PCOS group was 1.4, nearly 15 times higher than this score of non-PCOS group. Additionally, our study found that hirsutism at any body's site was noted in 38% of PCOS patients versus 6% of controls ($P < 0.001$). Among nine different body sites observed for hirsutism according to mGF score, it seemed that hirsutism of the chin, lip, chest, abdomen or face was very rare in all Vietnamese subjects, regardless of PCOS status (Table 1). The prevalence of hirsutism at these sites ranged from 0% to 5% in PCOS subjects versus 0% in controls. Polycystic ovarian syndrome subjects were more likely to report hirsutism of the leg, arm and pubis compared to controls, with prevalence ranging from 18.2% to 25.7% at these sites in PCOS subjects versus only 0.9–2.6% in controls (Table 1). PCOS subjects were more likely to had acne, alopecia and acanthosis nigricans (Table 1). These data demonstrate that the Vietnamese PCOS population was more likely to have phenotypic signs of hyperandrogenism and hirsutism, with common sites being the legs, arms, and pubis.

Pelvic ultrasound

Uterine measurements were similar between PCOS and control subjects in uterine length and endometrial thickness (Table 2). However, AP diameter of uterus was smaller in PCOS group compared to control group. Ovarian volumes were nearly twice the size in the PCOS group compared to controls (Table 2b). Left and right ovarian volumes were 9.6 and 10.6 cm^3 respectively in the PCOS group compared to 5.6 and 5.4 cm^3 respectively in the control group ($P < 0.001$).

Metabolic disease

The PCOS group had three subjects with a pre-existing diagnosis of type II diabetes or diagnosed with type II diabetes during evaluation. This was similar to the control group that had zero subjects with type II diabetes ($P = 0.252$). About 8.4% of the PCOS subjects reported hypertension compared to 3.3% in the control group ($P = 0.002$). One of the PCOS subjects had a history of cardiovascular disease compared to three of the controls ($P = 0.346$). Overall there was no higher rate of metabolic disease in the Vietnamese PCOS population compared to the controls (Table 3).

Anthropomorphic

The PCOS group was younger, weighed more, and had a higher BMI compared to the controls ($P < 0.05$) (Table 4). Age was highly correlated to weight and BMI and the differences in weight and BMI persisted after adjusting for subject age. However, PCOS women were still generally lean with a mean weight of 50.8 kg. Waist circumference was on average 2.5 cm wider and the waist : hip ratio was higher in the PCOS group compared to controls ($P < 0.001$). These findings persisted in age adjusted analysis

Table 3 Metabolic profile testing in polycystic ovarian syndrome population

Variable	Abnormal (%)	Mean	Normal range
Cholesterol (mmol/L)	5.6	4.6 ± 0.8	<5.2
Triglycerides (mmol/L)	25.1	1.4 ± 0.1	<1.7
LDL-cholesterol (mmol/L)	23.6	2.9 ± 0.7	<2.6
HDL-cholesterol (mmol/L)	43.4	1.4 ± 0.6	>1.53
G0 (mmol/L)	28.6	5.1 ± 0.5	<6.0
G2 (mmol/L)	22.3	6.7 ± 1.7	<7.8
HbA1c (%)	18.7	5.2 ± 0.4	<5.7
MetS (NIH)	12.5		

G0, fasting glucose; G2, 2-h plasma glucose; HbA1c, hemoglobin A1c; HDL, high density lipoprotein; LDL, low density lipoprotein; MetS, metabolic syndrome; NIH, National Institutes of Health.

Table 4 Baseline characteristics between total polycystic ovarian syndrome (PCOS) population, phenotype group and control group

Characteristics	Control (n = 422)	Total PCOS (n = 479)	P0	Subgroup PCOS population				
				Phenotype A (n = 79) 16.5%	Phenotype B (n = 15) 3.1%	Phenotype C (n = 61) 12.7%	Phenotype D (n = 324) 67.6%	P1
Age	31.65 ± 4.19	29.0 ± 4.12	0.000	28.43 ± 4.19	28.47 ± 3.29	30.46 ± 4.54	28.89 ± 4.00	0.012
BMI (kg/m^2)	20.56 ± 2.20	21.00 ± 2.83	0.017	20.50 ± 2.38	21.06 ± 2.43	21.14 ± 2.92	21.08 ± 2.92	0.693
<18.5	77 (18.25)	75 (15.66)	0.039	16 (20.25)	3 (20.0)	12 (19.67)	44 (13.58)	0.185
18.5–<23.0	287 (68.01)	309 (64.51)		52 (65.82)	7 (46.67)	36 (59.02)	214 (66.05)	
23–<25.0	44 (10.43)	61 (12.73)		8 (10.13)	5 (33.33)	7 (11.48)	41 (12.65)	
≥25.0	14 (3.32)	34 (7.10)		3 (3.80)	0 (0.0)	6 (9.84)	25 (7.72)	
Waist (cm)	70.85 ± 5.49	73.32 ± 7.52	0.000	72.80 ± 7.71	73.95 ± 8.20	73.63 ± 7.97	73.36 ± 7.39	0.888
Hip (cm)	88.39 ± 5.54	88.95 ± 6.38	0.165	88.20 ± 5.87	88.60 ± 4.88	89.31 ± 7.48	89.08 ± 6.35	0.838
WHR	0.80 ± 0.06	0.82 ± 0.06	0.000	0.83 ± 0.07	0.83 ± 0.07	0.83 ± 0.08	0.82 ± 0.06	0.856
mFG	0.12 ± 0.61	1.49 ± 2.24	0.000	4.58 ± 2.32	4.20 ± 2.40	2.10 ± 2.48	0.50 ± 0.99	0.000
Basal FSH (IU/L)	6.58 ± 1.77	5.58 ± 1.65	0.000	5.39 ± 1.74	5.21 ± 1.61	5.81 ± 1.53	5.60 ± 1.66	0.402
Basal LH (IU/L)	5.14 ± 2.34	10.57 ± 6.43	0.000	12.18 ± 7.12	9.16 ± 4.77	8.31 ± 4.22	10.67 ± 6.56	0.009
LH : FSH ratio	0.81 ± 0.40	2.04 ± 1.45	0.000	2.49 ± 1.76	1.81 ± 0.79	1.52 ± 0.89	2.04 ± 1.44	0.001
Basal estradiol (pg/mL)	38.38 ± 18.67	44.33 ± 26.46	0.0001	47.11 ± 28.42	29.31 ± 14.71	47.78 ± 31.39	43.69 ± 25.17	0.025
Testosterone (nmol/L)	0.18 ± 0.12	0.36 ± 0.25	0.000	0.50 ± 0.42	0.38 ± 0.17	0.35 ± 0.31	0.33 ± 0.17	0.000
AMH (pmol/L)	3.40 ± 2.07	8.92 ± 5.88	0.000	9.81 ± 5.94	9.11 ± 5.95	8.65 ± 5.68	8.74 ± 5.90	0.406
Prolactin (IU/L)	389.81 ± 459.32	391.82 ± 600.09	0.956	316.43 ± 236.49	80.97 ± 189.83	363.86 ± 228.26	429.85 ± 707.60	0.000

BMI, body mass index; mFG, modified Ferriman–Gallwey; P0: significant level as comparison between PCOS and non-PCOS group; P1, significant level as comparison between phenotypes in PCOS group; WHR: waist–hip ratio.

(Table 4). Both PCOS and the control groups had a majority of subjects with a BMI <25 (92.9% vs 96.7%). The majority of subjects in both groups also had a BMI <23, consistent with World Health Organization guidelines for a normal Asian BMI (80.2% and 86.3% respectively). While both groups were primarily lean, PCOS subjects were less likely to be classified as BMI normal in both unadjusted and adjusted analyses (Table 4). Overall, these data demonstrated that the Vietnamese PCOS population was lean but weighed more, had a higher BMI and greater central adiposity compared to controls.

Hormonal profile

Serum hormone profiles are presented in Table 4. Day 3 basal FSH was higher in controls compared to PCOS subjects, however that absolute difference was small at 1 IU/L. Day 3 basal LH significantly higher in PCOS subjects compared to controls (10.6 vs 5.1 IU/L, $P < 0.001$). The LH : FSH ratio was 2.0 in PCOS subjects, compared to only 0.8 in controls ($P < 0.001$). There was no difference in prolactin levels in PCOS versus control subjects. Day 3 basal estradiol, testosterone and AMH were all significantly higher in PCOS subjects compared to controls ($P < 0.001$). These data demonstrate that the Vietnamese PCOS population had higher LH, LH : FSH ratio, AMH and testosterone.

Metabolic profile

Fasting cholesterol profiles and HbA1C were not performed on control subjects as it was not indicated for their standard care. Fasting lipid, HbA1C and 2-h GTT values are shown in Table 3. The lipid profile in PCOS subjects was on average in the normal range, with mean total cholesterol of 4.6 (mmol/L),

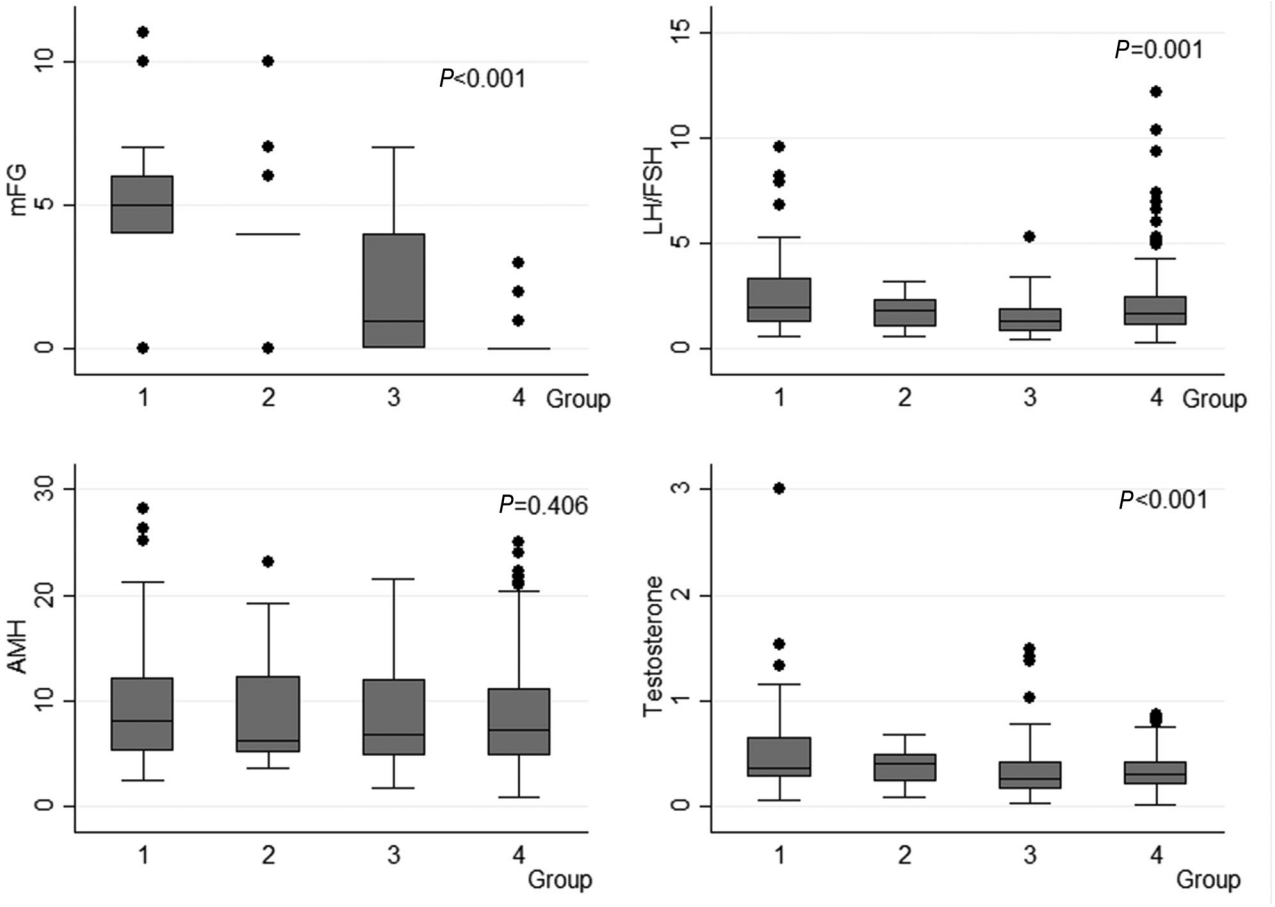

Figure 1 Values of modified Ferriman–Gallwey (mFG), luteinizing hormone (LH) : follicle stimulating hormone (FSH) ratio, testosterone and anti-Mullerian hormone (AMH) in four groups of PCOS phenotypes.

triglycerides of 1.4 (mmol/L), HDL of 1.4 (mmol/L) and low density cholesterol (LDL) of 2.9 (mmol/L). The majority of PCOS subjects had a normal cholesterol levels with only 5.6% having high cholesterol. Only 76.4% of PCOS subjects had an optimal LDL. Only 43.4% of PCOS subjects had normal HDL levels. Triglyceride levels were desirable in 74.9% of PCOS subjects and high or very high in only 25.1% of subjects. HbA1C was on average in the normal range at 5.2% in PCOS subjects with only 16.5% demonstrating values >5.7%. Fasting glucose was normal in 71.4%, and 2 h GTT in 77.7% of PCOS subjects. Only 12.5% of the PCOS patients met NIH criteria for metabolic syndrome. These data demonstrate the Vietnamese PCOS population did not demonstrate significant metabolic abnormalities in total cholesterol or glucose testing, but a majority of PCOS subjects had suboptimal LDL and HDL levels.

Distribution of PCOS phenotypes

Table 4 shows the distribution and baseline characteristics in the PCOS population, control group and among the phenotypes. The classical phenotype (O + H + P) occurred in 16.5% of PCOS women. Phenotype B characterized by O + H but lacking PCOM accounted for 3.1% of Vietnamese PCOS women. Together they represented the phenotypes that would have also been diagnosed with PCOS according to the 1990 NIH criteria, made up 19.6% of the study cohort. The percentages of the patients with the two newly extended phenotypes under the Rotterdam consensus criteria were as follows: 67.6% had PCOS without HA and 12% had PCOS without Oligo-an. The four subgroups presented mostly with similar physical characteristics, including BMI, waist, WHR, alopecia and acanthosis nigricans. However, there was a significant difference of mFG score and presence of acne among four subgroups of PCOS. The mFG score was the highest in the classical PCOS group (O + H + P) and the lowest in group D (O + PCO) (4.58 vs 0.50). Acne usually occurred in group A in comparison with the other groups (45.6% vs 26.7%, 21.3% and 18.8%). Except AMH and FSH, a significant difference was observed in levels of the remaining hormones. Luteinizing hormone and the LH : FSH ratio were lower in cases with phenotype C (H + P) compared with that in phenotype A group (O + H + P). The highest levels of testosterone were observed in groups diagnosed by NIH 1990 criteria while the newly extended subgroups diagnosed by Rotterdam criteria had the lowest testosterone levels as shown in Figure 1. Figure 1 also presents the values of mFG, LH : FSH ratio, testosterone and AMH in four groups of PCOS phenotypes.

Discussion

This large prospective study from three medical centers in Vietnam is among the first to systematically characterize the PCOS phenotype within Vietnam and also in the SE Asian population. Comparison of these results with Asian populations of other regions will help in determining whether there is a different SE Asian PCOS phenotype. Data on PCOS in Asian populations primarily derive from studies comparing migrant Asians to other ethnicities in the countries in which they reside, or from studies evaluating PCOS patients indigenous to one country. Studies of migrant populations can be useful in determining the impacts of factors including dietary and environmental changes on PCOS phenotypes. In order to determine innate ethnic differences in PCOS, it is important to study indigenous populations within their country of origin. Characterization of different ethnic phenotypes is important to assess for the long-term health risks associated with PCOS.

The data demonstrate the Vietnamese population had a low prevalence of metabolic syndrome at only 12.5%. Other Asian populations with PCOS have been found to have an elevated prevalence of metabolic syndrome. Migrant South Asian women with PCOS have higher rates of metabolic syndrome, insulin resistance, type 2 diabetes mellitus and acanthosis nigricans at a lower average BMI compared to Caucasian Europeans.[7,8,10] Studies of indigenous Asian PCOS patients show consistent results. One-third of Chinese PCOS patients are insulin resistant.[13] Metabolic syndrome was found in 14.5% South Korean PCOS women, in 16% in Taiwanese PCOS women and in up to 24.9% Hong Kong Chinese PCOS women while the percentage of MetS was only 6.4% in Chinese PCOS cohort.[18] Sri Lankan patients with PCOS have a higher prevalence of the metabolic syndrome and type 2 diabetes than non-PCOS controls, and also have increased waist circumference, hypertension and hypercholesterolemia. Central obesity predicts metabolic risk more than BMI in this population.[10] Subcutaneous fat volume was independently associated with insulin resistance among Indian women with PCOS.[19] Among Thai PCOS women, however, acanthosis nigricans, a marker of the metabolic

syndrome, was found to be uncommon.[9] It has been suggested that, with adoption of a Western lifestyle and the introduction of fast food diets, Asian populations tend to increase the risk of metabolic abnormality and metabolic syndrome.[18]

In our study, PCOS subjects had significantly higher waist circumference and weight than non-PCOS subjects, suggesting that PCOS has a greater association with central fat deposition than overall BMI. Our findings are consistent with data from prior studies of Asian PCOS patients, though with small absolute differences in metabolic parameters and a low overall rate of type 2 diabetes and metabolic abnormalities. Although PCOS patients had more central adiposity and weight, they were on average leaner than many other PCOS populations characterized in the literature.

These data demonstrated the Vietnamese PCOS subjects were more likely to have hirsutism, with the average of mFG score of 1.4, especially at nonfacial sites. Low rates of hirsutism have been observed among East Asian women of Chinese, Korean, Thai and Japanese origin, possibly due to lower activity of 5-alpha-reductase in their hair follicles.[15,20] Use of an ethnicity-specific Ferriman–Gallwey cutoff point to diagnose hirsutism in these populations has been suggested. In our study, because of lack of a Vietnamese mFG cutoff point for hirsutism diagnostic, we chose a cutoff of 5 based on several studies performed in Chinese and other East Asian populations.[15] However, we observed a high percentage of Vietnamese PCOS subjects had mFG scores of under 5. A study of Indonesian PCOS patients suggested that Asian PCOS population had a lower cutoff of Ferriman–Gallwey in comparison with European and Western populations. A study of healthy Thai women found that 97.8% of subjects had Ferriman–Gallwey scores of 0, 1 or 2. The authors recommended a Ferriman–Gallwey cutoff of 3 to diagnose hirsutism in Thai women.[6] Hirsutism was found to be uncommon in Thai women with PCOS as well.[9] Among Chinese women with PCOS, 6.1% had hirsutism, 13.3% had acne, and 21.1% had hyperandrogenism, with higher Ferriman–Gallwey scores compared to non-PCOS controls.[13] Similarly, a large community based study involving 10 120 Chinese women concluded that mFG score >4 could be made to diagnose hirsutism.[15] Hyperandrogenism was found to be significantly associated with the metabolic syndrome in nonobese PCOS subjects in Korea, but this association was not found in obese PCOS subjects.[11] In contract to East Asians, South Asians in Europe have been observed to have higher Ferriman–Gallwey scores and more acne than Caucasians.[7,12] Even in one study, the mean score of mFG in this population could be as high as 18.[15] Although PCOS subjects in our study had a 31% rate of hirsutism at any sites, which is higher than that reported in populations from adjacent regions and seems to be similar to that of South Asians; they have exceedingly lower score of mFG compared to South Asian population. This suggests a phenotype closer to that of East Asians than South Asians with regard to symptomatic hyperandrogenism. This finding further reinforces that ethnic differences in hirsutism among PCOS do exist, and such differences may contribute to varying rates of PCOS in different populations.[15]

Hyperandrogenemia has consistently been seen among Asian PCOS patients despite a lack of hirsutism in some groups. Chinese PCOS women had elevated total testosterone compared to non-PCOS controls.[13] Thai PCOS subjects had a rate of hyperandrogenemia of 37.1%, with elevated serum androstenedione rather than elevated testosterone.[9] Testosterone levels were found to be similarly elevated among South Asian and Caucasian women with PCOS.[10] Consistent with this data, PCOS subjects in our cohort had significantly elevated testosterone compared with controls. However, evidence for ethnic differences in androgen production is scanty and unclear. The Japanese Society for Obstetrics and Gynecology no longer uses serum androgens for diagnosis of PCOS because of the low prevalence of elevated androgen in Japanese population. Testosterone was recommended only as a complementary factor for diagnosis of PCOS.[15]

South East Asian PCOS subjects had elevated estradiol levels compared to controls, though estrogen levels are lower overall in Asian compared to Caucasian women with PCOS.[16] LH : FSH ratio was elevated among our PCOS patients, which was also seen in Chinese PCOS women.[13] In contrast, the recent research on PCOS phenotypes in Jordanian population has not found a significant difference of this ratio among the PCOS group compared to the control group.[21] Average AMH was almost three times as high in our PCOS patients than in controls, at 8.9 compared to 3.4. To the best of our knowledge, differences in AMH in SE Asian populations have not been described previously.

The Vietnamese PCOS cohort had a significant increase in ovarian size compared to controls, which

is consistent with findings in other populations. Thai PCOS subjects had larger ovarian volume than controls,[9] and 94.2% of Chinese women with PCOS had polycystic ovaries on ultrasound.[13] Studies comparing polycystic ovarian morphology have not found clear differences based on ethnicity.[16]

Migrant South Asians with anovulatory PCOS presented at a younger age and had more severe symptoms at a younger age than Caucasian Europeans.[7,12] In a study of Thai women, the mean age of PCOS patients was lower than that of non-PCOS patients.[9] Similarly, the mean age of PCOS patients in our cohort was significantly lower than the mean age of controls.

One of the main findings of the current study is the distribution and baseline characteristics in the four phenotype groups in Vietnamese PCOS population. Our study reported a very high percentage of phenotypes D which was the new PCOS subtypes under the Rotterdam consensus criteria. This result was different from multiple studies from different regions around the world. Overall, published data indicated that more than half of PCOS identified within the clinical setting demonstrated phenotype A,[10,22,23] whereas the other three phenotypes had almost equal prevalence. The classic form of PCOS (phenotypes A and B) constituted approximately two-thirds of the total of PCOS patients identified within the clinical setting.[22] Similarly, in Asia, Liang and colleagues found that in Taiwanese PCOS population, 18% had PCOS without HA and 21% had PCOS without OA.[24] In contrast, based on the results of a study of 719 PCOS patients in a large-scale Chinese population, Zhang and colleagues reported a very high proportion of the composition of the two new phenotypes created by Rotterdam criteria at 70.8%.[25] Our study therefore supports using the Rotterdam criteria for diagnostic of PCOS in Vietnamese women. In addition, our study observed differences among the four phenotype groups in baseline and hormonal characteristics. Previous study has confirmed this result that BMI, WHR, mFG and testosterone levels were highest in classic group (O + H + P) and lowest in O + P group.[15,25] The highest AMH levels were also found in patients with classic PCOS.[15] These two subgroups were related to an increased risk of metabolic syndrome.[8,18,25] In majority of studies, patients with non-hyperandrogenic PCOS had the mildest degree of endocrine and metabolic dysfunction and the lowest prevalence of metabolic syndrome as compared with healthy controls.[15]

The strength of this study is that it included a large cohort of 901 patients and prospective collection of anthropomorphic, serum and ultrasound data. It is the first study to characterize the manifestations of PCOS in the Vietnamese population, which enhances our knowledge of the SE Asian cohort and allows us to compare groups within this geographic region. Our conclusions are limited, however, to Vietnamese patients and may not be generalizable to other SE Asian populations. As this was a cross-sectional study, we were able to evaluate metabolic risk factors as a single point in time. Longitudinal studies in this patient population are needed to further assess long-term health risks.

Conclusion

The Vietnamese PCOS population is characterized by a lean body type, nonfacial hirsutism, anovulatory, enlarged ovaries and typical PCOS serum hormone markers. The Vietnamese PCOS population also has low risk factors for metabolic syndrome.

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Disclosure

None declared.

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