Characteristics of 250 Reproductive-Aged Polycystic Ovary Syndrome Thai Women at Siriraj Hospital

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Objective: *To determine the clinical characteristics of reproductive-aged polycystic ovary syndrome (PCOS) Thai women.*
Study design: *Cross sectional study.*
Settings: *Gynecologic Endocrinology Unit, Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital.*
Subjects: *250 PCOS Thai women who registered at the Siriraj PCOS project from May 2007 to January 2009. PCOS were diagnosed using Revised Rotterdam 2003 criteria. Women who were taking medications affecting sex hormones or lipid metabolism within 3 months before registration were excluded from the present study.*
Material and Method: *Patients were interviewed and examined for weight, height, waist circumference, blood pressure, presence of acanthosis nigricans, and signs of hyperandrogenism. Ovarian ultrasonography was examined using vaginal probe inserting into the vagina or rectum. Venous blood sample of each patient was drawn during 8.00-10.00 o'clock after 12-hour fasting.*
Main outcome measures: *Clinical characteristics and laboratory profiles in PCOS Thai women.*
Results: *Of all participants, 62% were 20-29.9 years old, 30% had high blood pressure, 57% were overweight to obese, 49% had central obesity, and 27% had acanthosis nigricans. Clinical hyperandrogenism was found in 15.6% of the patients. Approximately 7% of PCOS women had impaired fasting glucose and one third had dyslipidemia. Prevalence of the PCOS criteria presenting in the population were oligomenorrhea and/or amenorrhea (98.4%), hyperandrogenism (49.2%), and ultrasonographic polycystic ovary (97.2%). Of all participants, 44% had three components of diagnostic criteria. Among those who had two components, presence of abnormal menstrual cycle plus polycystic ovary was the most common finding.*
Conclusion: *Menstrual problem was the most common presenting symptom among the presented participants. Hyperandrogenism/ -emia adds only a little value on making PCOS diagnosis. Most of the PCOS Thai women have menstrual problem. In these patients, ovarian ultrasonography has high value to diagnose PCOS; addition of androgen blood test can diagnose only 3% more PCOS cases. Although the presented PCOS Thai women are still young, approximately 50% already have some parameters of health risk. It is suggested to provide preventive measures for these patients to prevent long term medical problems.*

Keywords: *Characteristics, PCOS, Polycystic ovary syndrome, Thai*

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Polycystic ovary syndrome (PCOS) is a common female endocrinopathy, affecting approximately 4-7% of premenopausal women[1]. The syndrome encompasses a broad spectrum of signs and symptoms, Its clinical manifestations include menstruation irregularity, sign of androgen excess, obesity, and infertilit[1-3]. The association of polycystic ovaries, amenorrhea, hirsutism, and obesity were first described by Stein and Leventhal in 1935. The first diagnostic criteria for PCOS, proposed at a conference convened by the National Institutes of Health (NIH) in 1990, included hyperandrogenism, menstrual disorders, and others causes of hyperandrogenism must be excluded. Since then, many diagnostic criteria have been developed, however, the Revised Rotterdam Criteria

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2003[4] seem to be the most widely used in the recent PCOS studies.

Pathophysiology of PCOS is complex and not yet well-understood. Many risk factors including genetics, environment, and nutrition factors may induce the manifestations of this syndrome[1], causing abnormalities in hypothalamic-pituitary-ovarian pathway, consequently producing inappropriate hormone secretion and leading to anovulation. The PCOS women in the chronic anovulation stage have menstrual irregularity, specifically oligomenorrhea; their ovaries also produce high amount of androgens, including testosterone, free testosterone, and dehydroepiandrosterone sulfate (DHEAS). These hormones have effect on physical manifestation of hyperandrogenism, *e.g.* acne, alopecia, and hirsutism. They also play an important role in pathophysiology of insulin resistance and multifaceted metabolic derangement in PCOS[5-7]. despite menstrual disorders, infertility, and clinical hyperandrogenism are among concerns of PCOS women, causing them to seek medical advice, the hormonal and metabolic disturbances put them into long-term health risks such as endometrial cancer, hypertension, dyslipidemia, diabetes mellitus, and cardiovascular disease[8-12].

Since PCOS is under the influence of genetic, lifestyle, and nutrition factors, its clinical presentations and hormonal features could vary from region to region. In the present study, the authors aim to evaluate clinical characteristics and hormonal profile of reproductive-aged PCOS Thai women in our clinic.

Material and Method

The present study was a part of Siriraj PCOS project, a registry for PCOS patients established in the Gynecologic Endocrinology Clinic, Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital, Mahidol University in 2007. The present study was conducted in accordance with the ethical principles stated in the latest version of the Declaration of Helsinki, and the study protocol was approved by the Siriraj Institutional Review Board.

Participants

Participants were 250 reproductive-aged PCOS Thai women who registered to the Siriraj PCOS project from May 2007 to January 2009. Women who had previous surgery of at least one ovary, took hormonal treatment or any medication for dyslipidemia within 3 months, or took steroids within 6 months before participation in the present study were excluded.

The participants underwent complete physical examination. Blood pressure was measured at both arms after at least 5-minutes rest in the sitting position, using a digital sphygmomanometer (Microlife, Model BP 3AG1, Microlife AG, Switzerland). Body weight was measured while the patient was wearing light clothes and stood on a mechanical weighting balance (Pro-series, Health o Meter, INC., USA). Height was measured while the patient stood upright on an even floor, using a standometer with a minimal measurement unit of 0.5 cm. Waist circumference (WC) was measured at the midpoint between lower rib and iliac crest while the patient was standing upright on her feet shoulder-width apart and both arms hanging on each side of the body in a relaxed manner. The measurement was taken at the end of a normal expiration using a measurement tape with a minimal measurement unit of 0.1 cm. A slight tension was applied to the tape until a red mark appeared on the skin. The two closest measurements were then averaged. Clinical hyperandrogenism was evaluated using a modified Ferriman-Gallwey score[13].

Venous blood sample was drawn from an antecubital vein of each participant during 8.00-10.00 o'clock after overnight fasting for 12 hours. The blood sample was examined for hormonal profiles including prolactin, cortisol and thyroid stimulating hormone (TSH). These hormones were used to exclude diseases with clinical mimicking PCOS. Blood sample was also assayed for baseline serum levels of carbohydrate metabolism (glucose and insulin), lipid (total cholesterol; triglyceride, TG; high density lipoprotein cholesterol, HDL-C; and low density lipoprotein cholesterol, LDL-C) and androgens (dehydroepiandrosterone sulfate, DHEAS; total testosterone and calculated free testosterone).

Body mass index (BMI) was calculated and categorized into normal (BMI < 23.0 kg/M^2), overweight (BMI 23.0-29.9 kg/M^2) and obese (BMI $\geq$ 30.0 kg/M^2), according to the classification adopted by the World Health Organization[14]. Blood pressure was categorized into normal (sBP < 120 and dBP < 80 mmHg), prehypertension (sBP 120-139 and/or dBP 80-89 mmHg), stage 1 hypertension (sBP 140-159 mmHg and/or dBP 90-99 mmHg) and stage 2 hypertension (sBP $\geq$ 160 and/or dBP $\geq$ 100 mmHg), according to the seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7)[15].

FBS was categorized into normal (< 100 mg/dL), prediabetes (100-125 mg/dL), and diabetes ($\geq$ 126 mg/dL), according to the 2003 American Diabetes

Association (ADA) classification[16,17]. Cholesterol, LDL-C, HDL-C, and TG were categorized according to the National Cholesterol Education Program (NCEP ATP III) classification[18].

The ultrasonography of both ovaries was examined using an ultrasound machine (LOGIG 5 PRO, GE Medical System Asia). A vaginal probe was gently inserted into the vagina or rectum as appropriate.

Diagnostic criteria

PCOS was diagnosed using the Revised Rotterdam criteria 2003[4]. Briefly, the patient must have at least two in three of the following: i) oligomenorrhea and/or amenorrhea, ii) hyperandrogenemia and/or hyperandrogenism, or iii) polycystic ovaries. Moreover, the patient must not have any diseases with clinical signs mimicking PCOS. Such diseases include hyper/hypothyroidism, hyperprolactinemia, Cushing syndrome, congenital adrenal hyperplasia (CAH), or hormonal secreting tumor.

Oligomenorrhea means menstrual cycle length longer than 35 days or menstruation less than 10 cycles per year[19]. Amenorrhea means menstrual cycle length longer than 6 months or no menstruation for more than 3 cycles[20].

Clinical hyperandrogenism means a modified Ferriman-Gallwey score ≥ 8[13]. Hyperandrogenemia means serum level of least one androgen higher than a recommended cutoff, *i.e.* total testosterone > 0.8 ng/mL, free testosterone > 0.006 ng/mL, or DHEAS > 350 μg/mL[20].

Polycystic ovaries means ultrasonogram of at least one ovary showing 12 or more follicles measuring 2-9 mm in diameter[21].

Laboratory assays

All laboratory assays were performed at the laboratory unit of the Department of Clinical Pathology, Faculty of Medicine Siriraj Hospital, Mahidol University, the central laboratory certified by IS0 15189. All assays were done using automatic analyzers, *i.e.* Modular P800, Roche for total cholesterol, HDL-C, LDL-C, triglycerides, and glucose; and Modular E170, Roche for thyroid stimulating hormone (TSH), prolactin, and cortisol. Plasma glucose levels were assayed using glucose hexokinase method. Plasma total cholesterol, HDL-C, LDL-C, and TG were assayed using enzymatic method. TSH and prolactin were measured using chemiluminometric assay technique. All techniques had intra-and inter-assay coefficients of variation (CV) < 5%.

Statistical analysis

Data were presented in mean $\pm$ standard deviation (SD), number (%) with or without 95% confidence interval (CI), or bar graph.

Results

There were 250 PCOS Thai women registered to the Siriraj PCOS project during the study period. Characteristics of the participants were presented in Table 1. Participants were 25.4 $\pm$ 5.8 years old, had BMI of 26.2 $\pm$ 7.6 kg/M^2, and had WC of 82.3 $\pm$ 16.3 cm. Distribution of age, BP, BMI, and WC were shown in Fig. 1. Of all participants, 62% were 20.0-29.9 years old, 30% had BP in prehypertenstion to hypertension ranges, 57% had BMI in overweight to obese categories, and 49% had central obesity (WC > 80 cm).

Acanthosis nigricans was found in 27% of cases. Only 141 patients were fully evaluated for

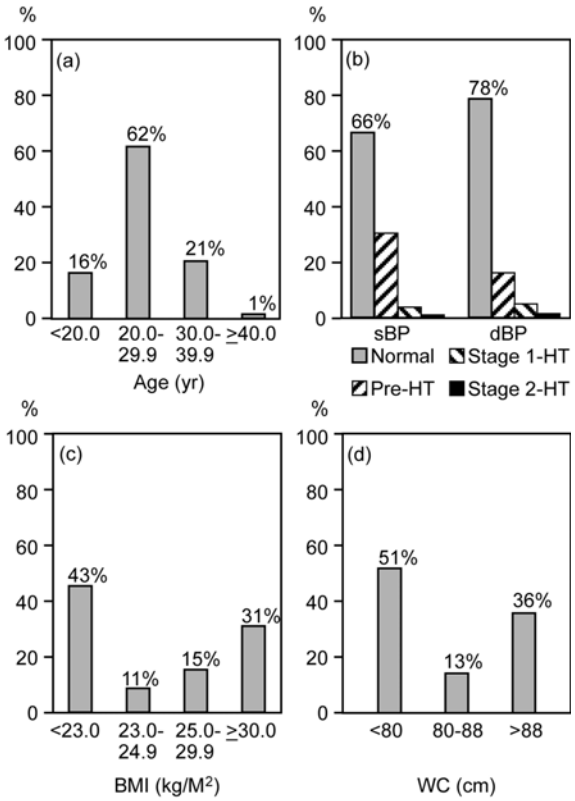

Fig. 1 Clinical characteristics of 250 reproductive-aged polycystic ovary syndrome Thai women at Siriraj Hospital: age (a); blood pressure, BP (b); body mass index, BMI (c); and waist circumference, WC (d) dBP = diastolic BP; sBP = systolic BP; HT = hypertension

Table 1. Characteristics of 250 reproductive-aged polycystic ovary syndrome Thai women at Siriraj Hospital

Characteristics	Mean ± SD or n (%)
Age at registration (yr)	25.4 ± 5.8
Age at menarche (yr)	13.4 ± 5.6
Body mass index (kg/M^2)	26.2 ± 7.6
Waist circumference (cm)	82.3 ± 16.3
Virgin	76 (30.5)
Presence of acanthosis nigricans	68 (27.2)
Clinical hyperandrogenism (n = 141)	22 (15.6)
Rotterdam criteria components*	
Oligomenorrhea and/or amenorrhea	246 (98.4)
Hyperandrogenism and/or hyperandrogenemia	123 (49.2)
Ultrasonographic PCO (n = 249)	242 (97.2)
Number of abnormal components	
1 + 2	8 (3.2)
1 + 3	127 (50.8)
2 + 3	4 (1.6)
1 + 2 + 3	111 (44.4)

* Rotterdam criteria components: oligomenorrhea means menstrual cycle length > 35 days or menstruation less than 10 cycles per year; amenorrhea means no menstruation > 6 months or 3 cycles; hyperandrogenemia means serum androgen (total testosterone, free testosterone, or dehydroepiandrosterone) level higher than recommended cutoff; hyperandrogenism means women who has modified Ferriman-Gallwey score ≥ 8 ultrasonographic; PCO = polycystic ovary means ultrasonogram of at least one ovary showing 12 or more follicles of 2-9 mm in diameter

clinical hyperandrogenism using a modified Ferriman-Gallwey score, 15.6% had hyperandrogenism. None of the women with a score < 8 had hyperandrogenemia. Clinical criteria of PCOS presenting in the population included oligomenorrhea and/or amenorrhea of (98.4%), hyperandrogenism and/or hyperandrogenemia of (49.2%) and ultrasonographic polycystic ovary of (97.2%). Of all participants, 44% had three components of diagnostic criteria. Among those who had two components, presence of abnormal menstrual cycle plus polycystic ovary was the most common finding.

Metabolic profiles are illustrated in Fig. 2. Approximately 7% of the participants had impaired fasting glucose or type 2 diabetes. Dyslipidemia was found as the following: hypercholesterolemia (36%), hypertriglyceridemia (20%) and low level of HDL-C (40%). Suboptimal cholesterol to HDL-C ratio (≥ 4.5) and LDL-C to HDL-C ratio (< 3) was found in 21% and 82%, respectively.

Discussion

PCOS is considered a genetic disease that begins to manifest in reproductive age. Age at clinical manifestation varies among different racial groups[22]. Lifestyle and nutrition are deemed to be important factors for clinical manifestation of the syndrome. In the present study, most of the patients had symptoms that began in the early reproductive period. Although

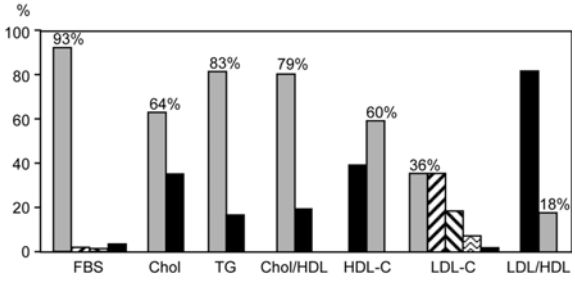

Fig. 2 Metabolic profiles of 250 reproductive-aged polycystic ovary syndrome Thai women at Siriraj Hospital. Meanings of bar from left to right
FBS = fasting blood sugar (< 100, 100-109, 110-125, and ≥ 126 mg/dL); Chol = cholesterol (< 200, and ≥ 200 mg/dL); TG = triglyceride (< 150, and ≥ 150 mg/dL); Chol/HDL = Chol to HDL ratio (< 4.5, and ≥ 4.5); HDL-C = high density lipoprotein cholesterol (< 50, and ≥ 50 mg/dL); LDL = low density lipoprotein cholesterol (< 100, 100-129, 130-159, 160-189, and ≥ 190 mg/dL); LDL/HDL = LDL to HDL ratio (< 3, and ≥ 3)

the most common age at registration was 20.0-29.9 years old, the patients had symptoms for some time before registration, and some of them had already sought many medical consultations. The age group of the presented patients was similar to that of other Asian populations[23], whose age group was usually younger than that of non-Asian populations[24,25].

It is unknown whether the age at clinical manifestation would associate with types and severity of the consequent medical problems of PCOS. It is reasonable to consider that young PCOS women would encounter medical problems early and carry long-term health-risk throughout life. In the present study, although the participants were relatively young PCOS women, approximately 50% already had at least one parameter of health risk such as overweight or obese, central obesity, suboptimal BP or hypertension, impaired fasting glucose or type 2 diabetes, and dyslipidemia, Moreover, one case had endometrial cancer at 20 years old (data not shown). The improvement of these health parameters can be achieved with preventive measures including universal lifestyle modification and prophylaxis medical or hormonal treatments as indicated. However, long-term prospective large scale studies are needed to elucidate whether these preventive measures would improve overall health status of this specific population.

The most common presenting symptom in the present study was menstrual abnormality, *i.e.* oligomenorrhea and/or amenorrhea, which was a complaint in 98.4% of the patients. This complaint was more prevalent than that in previous studies which reported this problem in 34% to 79% of their population[26,27]. This may be explained by the fact that because the present study was conducted in a Gynecologic Endocrinology Clinic, to which women with abnormal menstruation were referred. Among 246 cases with menstrual problem, only eight cases (3.3%) had non-PCO pattern on ovarian ultrasonogram; these cases needed blood tests for androgens as the second diagnostic criterion in order to fulfill the PCOS criteria. Therefore, in an institute that blood tests for androgen are not available, almost 97% of women with oligomenorrhea and/or amenorrhea can be confidently diagnosed of PCOS after performing ovarian ultrasonography. Only four cases (1.6%) without menstrual problem presented with clinical hyperandrogenism; in theses cases, PCOS was diagnosed using ovarian ultrasonography.

There were 44.4% of the presented population who had three components of Rotterdam criteria. Such a finding was well-suited with pathophysiology of PCOS, *i.e.* chronic anovulation causes oligo/amenorrhea; ovaries in chronic anovulation stage have PCO morphology; and the PCO produces a large amount of androgens. It is inconclusive why some PCOS women have only two abnormal components. Previous study showed large variation in prevalence of each combination, e.g 18% of PCOS women had both ovulatory dysfunction and PCO, 9% had ovulatory dysfunction plus androgen excess, and 21% had androgen excess plus PCO[26]. In the present study, 55.6% of the patients had a 2-component combination which comprised oligo/amenorrhea plus PCO of 50.8%, oligo/amenorrhea plus hyperandrogenism of 3.2% and hyperandrogenism plus PCO of 1.6%. Currently, it is unknown whether the three types of PCOS grouping by permutation of two in three components of the Rotterdam criteria are really the same disease or actually they are three different entities.

In conclusion, 98.4% of PCOS women in the presented registry have menstrual problem; 44.4% have three components of Rotterdam criteria. Among those who have only two criteria, the combination of oligo/amenorrhea plus PCO is the most common finding. Ovarian ultrasonography has high value to diagnose PCOS in the patients who have oligo/amenorrhea; addition of androgen blood test can diagnose only 3% more PCOS cases. Although the presented PCOS Thai women are still young, 50% already have some parameters of health risk. It is suggested to provide preventive treatment such as dietary control, exercise, life style modification and metabolic screening for these patients to prevent long term medical problems.

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ลักษณะทางคลินิกของโรคกลุ่มอาการถุงน้ำรังไข่ในสตรีไทย จำนวน 250 ราย ในโรงพยาบาลศิริราช

ธันยารัตน์ วงศ์วนานุรักษ์, สุชาดา อินทวิวัฒน์, มณี รัตนไชยานนท์, กิติรัตน์ เตชะไตรศักดิ์, พิชัย ลีระศิริ, ประสงค์ ตันมหาสมุทร, สุรศักดิ์ อังสุวัฒนา, จงดี แดงรัตน์

จุดประสงค์: *เพื่อศึกษาลักษณะทางคลินิกของโรคกลุ่มอาการถุงน้ำรังไข่ในสตรีไทย*

วัสดุและวิธีการ: *ได้ทำการศึกษาแบบตัดขวาง ในสตรีโรคถุงน้ำรังไข่ จำนวน 250 ราย ตามเกณฑ์การวินิจฉัยของRotterdam 2003 ที่คลินิกต่อมไร้ท่อทางนรีเวช โรงพยาบาลศิริราช ระหว่างเดือนพฤษภาคม พ.ศ. 2550 ถึงเดือนมกราคม พ.ศ. 2552 ผู้ที่กำลังได้รับการรักษาด้วยยาที่มีผลต่อฮอร์โมนเพศ หรือต่อเมตาบอลิซึมของไขมันจะถูกคัดออกจากการศึกษา ผู้ร่วมศึกษาได้รับการสัมภาษณ์ตรวจร่างกาย ชั่งน้ำหนัก วัดส่วนสูง วัดความดันโลหิต ตรวจหาอาการแสดงของภาวะแอนโดรเจนสูง ตรวจอัลตราซาวด์รังไข่ และตรวจเลือดในช่วงเวลา 8.00 ถึง 10.00 นาฬิกา หลังจากการอดอาหารนาน 12 ชั่วโมง*

ผลการศึกษา: *ผู้ร่วมศึกษาร้อยละ 62 มีอายุในช่วง 20.0-29.9 ปี ร้อยละ 30 มีความดันโลหิตสูง ร้อยละ 57 มีภาวะน้ำหนักตัวเกิน ร้อยละ 49 มีภาวะอ้วนลงพุงถึง ร้อยละ 27 มี acanthosis nigricans ร้อยละ 15.6 ตรวจพบอาการแสดงของแอนโดรเจนสูง ผลการตรวจเลือดอยู่ในภาวะเสี่ยงต่อการเป็นเบาหวานร้อยละ 7 และพบภาวะไขมันในเลือดสูงถึงหนึ่งในสามของผู้ร่วมศึกษา ความชุกของเกณฑ์ในการวินิจฉัยโรคกลุ่มอาการถุงน้ำรังไข่ ได้แก่ ระดูผิดปกติ (ร้อยละ 98.4) ภาวะแอนโดรเจนสูง (ร้อยละ 49.2) และอัลตราซาวด์พบ polycystic ovary (ร้อยละ 97.2) ผู้ป่วยร้อยละ 44 มีความผิดปกติทั้งสามเกณฑ์ เกณฑ์ที่พบร่วมกันได้บ่อยที่สุด คือ ระดูผิดปกติ และอัลตราซาวด์พบ polycystic ovary*

สรุป: *ระดูผิดปกติเป็นอาการสำคัญที่พบได้บ่อยในโรคกลุ่มอาการถุงน้ำรังไข่ สำหรับภาวะแอนโดรเจนสูงมีความสำคัญเพียงเล็กน้อยที่จะใช้วินิจฉัยโรค เกือบทั้งหมดของสตรีไทยที่เป็นโรคกลุ่มอาการถุงน้ำรังไข่มีระดูผิดปกติ การตรวจอัลตราซาวด์ของรังไข่มีประโยชน์อย่างมากในการวินิจฉัยโรคกลุ่มอาการถุงน้ำรังไข่ในสตรีกลุ่มนี้ ซึ่งการตรวจวัดระดับแอนโดรเจนในเลือดสามารถให้การวินิจฉัยเพิ่มขึ้นได้อีกเพียงร้อยละ 3 เท่านั้น แม้ว่าสตรีไทยที่เป็นโรคกลุ่มอาการถุงน้ำรังไข่จะมีอายุน้อยแต่พบว่าสตรีร้อยละ 50 มีปัจจัยเสี่ยงด้านสุขภาพบางอย่างอยู่แล้ว ดังนั้นสตรีกลุ่มนี้ควรได้รับคำแนะนำในการดูแลสุขภาพและการป้องกันโรคในระยะยาว*