Prevalence of Polycystic Ovary Syndrome among Malaysian Female University Staff

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ARTICLE INFO	ABSTRACT
Article type: Original article *Article History:* Received: 06-Mar-2018 Accepted: 02-May-2018 *Key words:* Epidemiology Malaysia Polycystic ovary syndrome Prevalence Women's health	***Background & aim:*** Polycystic ovary syndrome (PCOS) is a metabolic disease with diverse etiologies. The prevalence of PCOS varies among different ethnicities and across various geographical and social settings. Scarce data exist on the prevalence of PCOS in Asia, especially in Malaysia. Regarding this, the present study was conducted to assess the prevalence of PCOS and its subtypes among the Malaysian University staff. ***Methods:*** This cross-sectional study was performed on females of reproductive age working at University Putra Malaysia, Selangor, Malaysia. The study population was selected through simple random sampling technique. The women with thyroid abnormalities or adrenal hyperplasia were excluded from the study. The participants were screened based on anthropometric measurements, medical history, blood pressure, and pelvic examination, as well as the presence of hirsutism, acne, and alopecia. The participants were also assessed for total and free testosterone levels and subjected to ultrasonography. The PCOS diagnosis was based on Rotterdam criteria. The data were analyzed using Mann-Whitney U test, t-test, Chi-square test, and logistic regression at the significance level of 0.05. ***Results:*** A total of 675 females with the mean age of 26.01±7.14 years participated in this study. The prevalence rate of PCOS was obtained as 12.6%. All PCOS subjects were detected with hyperandrogenism and polycystic ovary, while anovulation was present in only one participant (1.2%). Odds of PCOS diagnosis was significantly related to increased body mass index (OR=1.14, 95% CI: 1.05-1.25), higher waist circumference (OR=1.06, 95% CI: 1.01-1.11), hirsutism (OR=20.83, 95% CI: 5.35- 81.13), and amenorrhea (OR=0.18, 95% CI: 0.04-0.69). ***Conclusion:*** This study revealed a high prevalence of PCOS and a specific phenotype of PCOS among the Malaysian employees.

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Introduction

Polycystic ovary syndrome (PCOS) is considered a common metabolic dysfunction that has a heterogeneous endocrine background in women of reproductive age (1). The features of PCOS include hyperandrogenism, hyperinsulinemia, luteinizing hormone hypersecretion, menstrual dysfunction, hirsutism, infertility, and pregnancy and neonatal complications (1-3). The PCOS also contributes to long-term metabolic and physiological complications, including type II diabetes mellitus, cardiovascular disease (CVD), and venous thromboembolism. Moreover, this syndrome may result in poor self-esteem and anxiety, which require medical and social support (4-12). Different prevalence rates have been presented for PCOS in various countries. Most of the prevalence rates have been estimated based on small populations (13, 14). The prevalence of PCOS has been reported to range from 5% to 10% in the majority of the studies (5, 13-15).

The Rotterdam and National Institute of Health criteria for PCOS are among the most common diagnostic tools for this syndrome (16, 17). The diagnostic criteria in these tools include the detection of toligoovulation or anovulation, hyperandrogenism (based on clinical or biochemical findings), and polycystic ovaries (based on ultrasound scan). The PCOS might have various clinical manifestations due to its diverse symptoms.

Based on the Rotterdam criteria, PCOS features can be divided into four categories: 1) the first phenotype is defined as the presence of a combination of hyperandrogenism (H) and chronic anovulation (O) in the presence of normal ovaries (H+O), 2) the second phenotype includes hyperandrogenism and polycystic ovaries with ovulatory cycles (H+P), 3) the third phenotype entails a combination of chronic anovulation and polycystic ovaries without clinical or biochemical indicators for hyperandrogenism (O+P), and 4) the fourth phenotype includes the simultaneous presence of hyperandrogenism, chronic anovulation, and polycystic ovaries (H+O+P) (16).

Phenotypic variability of PCOS could be due to various factors, including difficult diagnosis, need for blood or ultrasound assessments, and variability of diagnostic criteria (e.g., NIH criteria or the Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group criteria). There is a paucity of large-scale studies investigating the prevalence of PCOS even in developed countries (5, 18). Furthermore, with regard to the rapid changes in lifestyles in developing countries like China, there is concern that PCOS may become epidemic (19).

The prevalence of PCOS is not well defined in Southeast Asian countries, including Malaysia. Given the health risks of PCOS, it seems both important and necessary to evaluate the current status and features of PCOS in the community and identifies the risk factors for this syndrome to design and implement interventions in order to prevent from this disorder and manage the affected women in the community. With this background in mind, the present study aimed to assess the prevalence of PCOS and its risk factors among the university staff working at a large governmental university of Malaysia.

Materials and Methods
Study design and research population

This cross-sectional study was conducted on females at the risk of PCOS working at 16 faculties of University Putra Malaysia, Selangor, Malaysia. The study population was selected through random sampling technique based on a list obtained from the University Human Resource section. Announcements were provided prior to visiting each faculty, and the female staff were informed about the venue and objectives of the research. In order to reduce the dropout rate and subject refusal, researchers referred to each university faculty at the due date to obtain measurements and perform sampling. The women of childbearing age (i.e., 18-49 years) and those willing to participate were included in the study. On the other hand, the exclusion criteria were: 1) consumption of oral contraceptives for more than 4 weeks, 2) use of hormonal treatment or insulin-sensitizing agents for more than 2 weeks, 3) abnormal thyroid findings, 4) nonclassical adrenal hyperplasia, 5) diagnosis with such conditions as hyperprolactinemia, hypogonadotropic hypogonadism, premature ovarian failure, ovarian cysts or tumors, congenital adrenal hyperplasia, androgen-secreting tumor, Cushing's syndrome, uterine

disorders, and chromosomal anomalies, 6) pregnancy, and 7) menopause.

Screening protocol and assessment criteria

The data were collected using a questionnaire, including items regarding personal information, menstruation and obstetric history, dermal features of hyperandrogenism, and endocrine and metabolic diseases. The participants were subjected to out of charge physical, pelvic, and ultrasound examinations.

Research instrument

The questionnaire covered patients' information, including age, age of menarche, menstruation history, family history, hyperandrogenism-related skin problems (e.g., hirsutism, acne, and premature alopecia), metabolic diseases, and other gynecologic diseases. Oligomenorrhea was defined based on such criteria as fewer than eight menstrual cycles per year or elongated menstrual cycle duration for more than 35 days. Furthermore, amenorrhea was considered as the lack of menstruation for 3-6 consecutive menstrual cycles, or $4 \geq$ menstrual periods per year (20).

The questionnaire was developed by the researchers based on literature review. The face and content validities of the questionnaire were assessed by a panel of experts in reproductive medicine and epidemiologists prior to the study. Three interviewers (i.e., one postgraduate student studying at the university under investigation and two research assistants) were fully instructed to use the standardized questionnaire and perform the required physical examinations.

Physical examination

Physical examination included the measurement of blood pressure, calculation of body mass index (BMI) based on weight and height measurements, and examination of breast and thyroid gland. Hirsutism was assessed based on the modified Ferriman-Gallwey (mF-G) score. Other features of hyperandrogenism, including acne and premature alopecia, were also assessed during the physical examination. Additionally, physical and pelvic examinations were performed for each participant to determine the presence of any uterine or ovarian disorders.

The mF-G scoring system classifies the severity of hirsutism by providing a scoring system for the presence of terminal hair in nine body areas (21, 22). The final score is obtained by summing up the score of each area (maximum score: 36). Each area is rated on a five-point Likert scale ranging from 0 (i.e., absence of terminal hair) to 4 (i.e., extensive terminal hair growth). Terminal hair was distinguished from villus hair based on the length (longer than 0.5 cm) and pigmentation. An mF-G score of ≥ 6 is considered as hirsutism (23).

The grading of acne was performed based on the evaluation of the acne features, including papules, pustules, and nodules, as well as its distribution in various regions, including the cheeks, neck, chest, and upper back. The Consensus Conference on Acne Classification grading was used for grading the severity of acne in the study participant (24).

Ultrasound examination

Each participant underwent an ultrasound scan during the clinical examination to determine the number of follicles and ovarian volume. Diagnosis of PCOS was based on the observation of 12 or more follicles with a diameter range of 2-9 mm in each ovary and/or enhancement of each ovary volume by at least 10 ml (16).

Metabolic and other assessments

Metabolic syndrome was identified based on the modified National Cholesterol Education Program adult treatment panel III guidelines in 2005 (25).

Diagnosis of polycystic ovary syndrome

The Rotterdam criteria were used to diagnose PCOS. The diagnosis of this syndrome was confirmed by the presence of at least two of the three criteria, namely oligo/amenorrhea, clinical and/or biochemical hyperandrogenism, and polycystic ovaries. Oligo/amenorrhea is defined as the lack of menstruation for at least 35 days or 3-6 consecutive menstrual cycles, or ≤ 4 menstrual periods per year. Hyperandrogenism was identified based on the clinical and biochemical indicators of hyperandrogenism, including mF-G score of ≥ 6 with or without acne, and/or androgenic alopecia. Furthermore,

laboratory measurements were performed to assess hyperandrogenism including serum androstenedione of 10.8 nmol/l or total testosterone of 2.81 nmol/l. Anovulation was assessed by measuring serum luteal progesterone in subjects with a history of oligo/amenorrhea. A minimum progesterone level of 10 nmol/l was considered as oligoovulation.

Hormonal assays

Participants with a confirmed diagnosis of PCOS based on the Rotterdam criteria were subjected to clinical examinations, ultrasound examinations, and hormone tests. All blood samples were collected in the morning after fasting for at least 8 h. Total and free testosterone levels were assessed by chemiluminescence using the Immulite 1000 (DPC, USA). For all measurements, the inter- and intra-assay coefficients of variation were < 10% and < 15%, respectively. In addition, fasting glucose, cholesterol, triglyceride, low- and high-density lipoprotein, thyroid stimulating hormone, and T4 were measured in all participants.

Statistical analysis

Statistical analysis was performed in SPSS software for Windows, version 21 (SPSS, Inc., Chicago, IL, USA). Descriptive statistics were used to assess data distribution to compare variables between groups. Continuous variables were checked for normality using Shapiro-Wilk test. The data were presented as mean, standard deviation, median, and interquartile range (IQR). The comparison of the continuous variables was compared using Student's t-test or Mann-Whitney U test.

In addition, the categorical variables were presented as frequency and percentage and compared using Pearson's Chi-square test. Univariate logistic regression was used to examine the independent predictors. Multivariate logistic regression was also utilized to adjust for other variables using PCOS diagnosis as a dependent variable and other variables as independent variables. The weight and body fat percentage were excluded from the model due to the association between these variables; however, the BMI was remained in the model. P-value less than 0.05 was considered statistically significant. The odds ratios (ORs) was modeled to analyze the risk factors for PCOS.

Results

Based on the list obtained from the Human Recourse office of the UPM, 1,424 females were working at this university. Out of 1,424 female university staff, 26 cases were excluded due to lacking the eligibility criteria; therefore, 675 (47.4%) subjects participated in the study. The main reasons for refusal to participate in the study were lack of time, schedule mismatch between sampling time and university programs, sick leave, and fear of blood withdrawal.

Table 1 presents the demographic characteristics of the participants. Out of 675 participants, 85 (12.6%) cases were diagnosed with PCOS according to the Rotterdam criteria. A total of 85 PCOS women responded to the questionnaire and underwent physical examination, ultrasound, and blood tests. All participants had elevated levels of total and free testosterone. In this regard, the median and IQR of total testosterone were both 0.9, and the

Table 1. Characteristics of patients with polycystic ovary syndrome and normal participants

	Total n=675	Normal n=590	PCOS n=85	P-value
Age (years)†	26.01±7.14	25.11±6.76	32.43±6.44	<0.001**
Weight (kg)†	59.57±14.63	57.57±12.79	73.84±18.60	<0.001**
Height (cm)†	156.12±6.43	156.29±5.46	154.89±11.11	0.06
BMI (kg/m²)†	24.47±6.09	23.55±5.02	31.03±8.58	<0.001**
Waist circumference (cm)†	77.57±11.33	75.97±10.12	88.93±12.96	<0.001**
Body fat (%)†	31.99±6.92	31.10±6.62	38.41±5.51	<0.001**
SBP (mmHg)†	114.80±12.25	113.90±11.24	121.15±16.64	<0.001**
DBP (mmHg)†	70.23±9.47	69.58±9.14	74.85±10.48	<0.001**
Acne‡	274 (40.6%)	256 (43.2%)	18 (21.7%)	<0.001**
Hirsutism‡	52 (7.7%)	30 (5.1%)	22 (26.5%)	<0.001**
Amenorrhea§	3 (0.4%)	2 (0.3%)	1 (1.2%)	0.33

PCOS: polycystic ovary syndrome, BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure
† Data were shown as mean and SD, and independent t-test was used for comparison.
‡ Data were shown as frequency and percentage, and Chi-square test was used for comparison. Percentages represent the number of participants divided by the adjacent group population multiplied by 100.
§ Data were shown as frequency and percentage, and Fisher's exact test was used for comparison. Percentages represent the number of participants divided by the adjacent group population multiplied by 100.
** Significant at α=0.01

Table 2. Relationship between polycystic ovary syndrome diagnosis and study variables

Variable	P-value	OR	95% CI		Adjusted regression P-value	Adjusted OR	95% CI	
			Lower	Upper			Lower	Upper
Age (years)	<0.001**	1.08	1.04	1.12	0.76	1.01	0.93	1.01
Weight (kg)	0.23	0.96	0.91	1.02	-	-	-	-
BMI (kg/m²)	0.04*	1.16	1.00	1.35	0.003**	1.14	1.05	1.25
Waist circumference (cm)	0.71	1.01	0.97	1.05	0.02*	1.06	1.01	1.11
Body fat (%)	0.10	1.07	0.99	1.16	-	-	-	-
SBP (mmHg)	0.63	0.99	0.96	1.02	0.79	1.01	0.95	1.07
DBP (mmHg)	0.26	1.03	0.98	1.07	0.06	1.07	0.99	1.14
Acne	0.13	0.63	0.34	1.16	0.76	1.12	0.34	4.36
Hirsutism	<0.001**	4.82	2.37	9.80	<0.001**	20.83	5.35	81.13
Amenorrhea	0.63	0.54	0.04	6.53	0.01*	0.18	0.04	0.69

BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure
* Significant at α=0.05
** Significant at α=0.01

mean level of free testosterone was 12.38±2.90. Furthermore, they had positive ultrasound findings for polycystic ovary. Anovulation was present in only 1 (1.2%) participant (H+P+O subtype), while the rest of the participants (98.8%) were in the H+P subtype. No other subtypes of PCOS were observed in the study population.

Based on the findings of the univariate logistic regression, the participants with PCOS diagnosis had significantly higher age (OR=1.08, 95% CI: 1.04-1.12, P<0.001), BMI (OR=1.16, 95% CI: 1.00-1.35), and hirsutism prevalence (OR=4.82, 95% CI: 2.37-9.80), compared with the normal participants (Table 2). Table 2 summarizes the results of multivariate regression analysis. The odds of PCOS diagnosis was significantly related to increased BMI (OR=1.14, 95% CI: 1.05-1.25), higher waist circumference (OR=1.06, 95% CI: 1.01-1.11), hirsutism (OR=20.83, 95% CI: 5.35-81.13), and amenorrhea (OR=0.18, 95% CI: 0.04-0.69).

Discussion

The prevalence of PCOS reportedly ranges from 2.4% to 52% (2, 26-29). According to the literature, the prevalence of this syndrome is affected by the applied diagnostic criteria and geographical diversity given the role of the genetic and environmental factors in this disorder (2, 26, 27). There is a paucity of data regarding the prevalence of PCOS in the South Asian regions. Moreover, the existing data are inconsistent mainly due to the differences in the chosen diagnostic criteria (30).

The prevalence rate of PCOS in the Asian regions has a range of 2.4-9% in China, Seri Lanka, and India (27, 28, 31, 32). In this study, the prevalence of PCOS among the Malaysian university staff was obtained as 12.6%, which is close to the rates previously reported for the Asian population. In the previous studies, the prevalence of PCOS was reported to be higher in the Asian population from the Indian subcontinent origin, compared with that in the White Asians. In addition, the highest prevalence of PCOS among the Indian population was observed in the immigrant Indians in the United Kingdom (52%) in 1988 (29, 33).

In contrast, the observed prevalence of PCOS in this study was higher than the prevalence rates reported for the Chinese community-dwelling women (5.6% and 2.4%) and Indian adolescents (9%). The reason for this difference might be due to the variations in study participants. While the aforementioned studies were mainly conducted on community-dwelling adults or adolescents, the current study was

performed on female employees, who are known for their sedentary lifestyle.

Moreover, the criteria for PCOS diagnosis varied among this research and some of the previous studies. Previous studies mainly used Rotterdam criteria for the diagnosis of PCOS; therefore, they could be more easily compared with one another (27, 28, 31). The findings of this study indicated the possibility of higher prevalence of PCOS among the Malaysian population, compared to those in the other Asian countries.

This study revealed that the participants diagnosed with PCOS were significantly older than the normal subjects. It was previously shown that PCOS prevalence reduces with an increase in age from 30 to 34 years, compared with that in individuals aged above 35 years (34). The difference between the observed trend of PCOS diagnosis among older age in the current study might be due to the narrow age range of the participants in this study as most of the participants aged below 35 years. Furthermore, statistical analysis was not applicable to higher age groups due to the small number of the participants older than 35 years. On the other hand, the multivariate analysis revealed no significant relationship between age and PCOS diagnosis, which can also indicate that the age of the subjects was distributed evenly in the study population. Therefore, the higher incidence of PCOS in other age groups was not assessed in the analysis.

The significant association between hirsutism and PCOS diagnosis in this study can be due to the elevated levels of total and free testosterone. Moreover, polycystic ovaries were also positive in all 85 PCOS cases (H+P type). It was previously hypothesized that hyperandrogenism is more prominent in PCOS women of the Asian origin, compared to that in Caucasians (35). This finding can be the reason for the observation of a hyperandrogenism prevalence rate of 100% among PCOS cases in the current study.

In a study investigating ovarian morphology in PCOS women in Japan, the presence of polycystic ovaries was associated with hyperandrogenism (36). On the other hand, polycystic ovaries have been found to be associated with increased insulin resistance, diabetes mellitus, and obesity (37). Our findings

are in line with those of the mentioned studies as the odds of PCOS diagnosis was higher in the participants with higher BMIs (2, 26, 38).

In another study examining the pattern of PCOS subtypes in white and South Asian ethnicities, the odds of PCOS diagnosis was increased with the enhancement of hirsutism prevalence in South Asians, compared with that in the white Asians (39, 40). The findings of this study can also strengthen the hypothesis that a certain PCOS phenotype may exist in the Asian ethnicities (39, 40). This proposed Asian phenotype is also associated with increased prevalence of type II diabetes mellitus, as well as increased systolic and diastolic blood pressure, which were also observed in the current study (39, 40). The reason for the achievement of a high OR in this study might be due to the small number of subjects with hirsutism (7.7%).

Our results revealed that amenorrhea was associated with the reduced risk of PCOS. This finding was in contrast with the definition of PCOS, which includes oligo/amenorrhea (26, 41). This discrepancy might be due to the small number of subjects with amenorrhea and the existence of a different phenotype of PCOS among the subjects. Therefore, further studies should be conducted to identify the PCOS phenotype and association between PCOS diagnostic criteria among Malaysian women.

The significant association between abdominal obesity (i.e., increased BMI and waist circumference) and increased odds of PCOS diagnosis may be also related to the higher prevalence of metabolic syndrome among PCOS women, compared to that in normal population. It was also shown that the prevalence of metabolic syndrome was higher among Asians with PCOS, compared with that in Caucasians (40). Although the prevalence of metabolic syndrome could not be assessed in all study participants due to the financial limitations and restraints in blood sampling, metabolic syndrome could be an underlying cause of insulin resistance and PCOS.

This was the first large-scale study that assessed the prevalence of PCOS among women of reproductive age working at the largest public university in Malaysia. The high prevalence of PCOS (12.6%) among Malaysian women could

be a sign of an emerging public health issue in Malaysia. Regarding this, more studies are required on larger scales to identify the burden of PCOS in Malaysian population. The findings of this study also suggested the necessity for adopting preventive strategies through health education, as well as the prevention and treatment of PCOS in community-dwelling women, especially those who are obese. Further research should examine the prevalence of metabolic syndrome and each of its criteria among Malaysian women with PCOS in order to shed light on the focus of attention in the treatment of women with PCOS in Malaysia.

The strengths of this study are the assessment of the prevalence of PCOS and its subtypes in community-dwelling Malaysian women by using nationally approved diagnostic criteria. This study also evaluated some of the PCOS-associated risk factors for CVD, including BMI, serum lipids, and blood pressure. The most important limitation of this study was the non-implementation of blood sampling for all participants due to financial limitations. Therefore, a number of CVD risk factors and metabolic syndrome criteria could not be assessed in this study. It is recommended to perform further research to assess CVD serum markers in PCOS women.

Conclusion

The findings of the present study revealed a high prevalence of PCOS among Malaysian employees that may require urgent health education interventions in order to prevent the associated consequences. This study also strengthened the hypothesis regarding the presence of a specific phenotype of PCOS among Asian population.

Acknowledgements

Conflicts of interest

The authors declare no conflicts of interest.

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