

Evaluation of the Prevalence of Polycystic Ovarian Syndrome among Adolescent (15-18 Years Old) Girls in Tehran during 2005-2006

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Abstract

Background: Polycystic ovarian syndrome (PCOS) was first introduced by Leventhal and Stein in 1935. It has a wide range of manifestations such as hyperandrogenism, irregular menstruation and central body obesity. The lack of definite diagnostic criteria has made the diagnosis a difficult task. Moreover, the disturbing aspects of the syndrome range from hirsutism in an adolescent girl to infertility in a young woman. Based on the Rotterdam 2003 Criteria, current diagnostic criteria must include two of the following three symptoms:

1. Either oligo-ovulation or anovulation,
2. Clinical or laboratory manifestations of hyperandrogenism,
3. Polycystic ovaries on sonographic examination (more than 12 follicles of less than 10 mm in diameter in each ovary).

In this study, we have focused on the enrollment of a large sample size to assess the prevalence and clinical features of PCOS such that a wide range of basic information can be utilized for further investigations.

Materials and Methods: This was a cross-sectional study with multi-stage random sampling. Subjects were selected from 15-18 years old girls from a number of high schools in Tehran. After interview and clinical examination, those individuals with either menstrual irregularities, hirsutism or obesity were referred for further laboratory evaluations and abdominal sonography in order to diagnose PCOS and estimate its prevalence. We also aimed to assess the predominant features of this disorder among adolescents.

Results: The overall prevalence of the syndrome was 3.42%. Out of the 1430 girls, 49 were diagnosed with PCOS.

Conclusion: Despite its high prevalence, this syndrome has not been widely studied. Most of the conducted studies have enrolled small samples within a short time period. Thus, more accurate policy making in this regard can be achieved through definition of the prevalence of PCOS and accurate estimation of its burden.

Keywords: Polycystic Ovarian Syndrome, Obesity, Acne, Infertility

Introduction

Polycystic Ovarian Syndrome (PCOS) is the most prevalent endocrinologic disorder among women of reproductive age (1) whose manifestations include obesity, hirsutism, infertility, amenorrhea or oligomenorrhea (2). Furthermore, PCOS is considered as an endocrinologic disorder which can be manifested with high serum levels of androgen, adrenal hyperplasia, insulin resistance, hyperlipidemia, overweight and obesity, anovulation and infertility, hirsutism, and acne (3). PCOS can be accompanied by a wide range of endocrine and metabolic disorders which predispose the patient

to atherosclerotic cardiovascular disorders, consequently, early diagnosis and recognition of its etiological factors and clinical features are of paramount importance.

Considering the high prevalence of PCOS it seems that little research has focused on the adolescent population, worldwide. The majority of studies conducted on adolescents have enrolled small numbers over a short period of time. Taking the controversial clinical features, laboratory indicators and etiologies into consideration, therefore the conduction of a large basic study on adolescent PCOS is deemed necessary (4). Most studies have focused

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on the signs or symptoms of PCOS, whereas population-based and community-based studies have been the center of less attention (5, 6).

The presence of polycystic ovaries is a common sonographic finding seen in 20-23% of women during reproductive age but not all show the clinical and paraclinical manifestations of PCOS (6). Sonographic examination of PCOS patients reveals polycystic ovaries with a shell-like appearance and sclerosis. Large numbers of fluid-containing cysts reside under this sclerotic membrane.

Clinical manifestations of PCOS include menstrual irregularities, obesity, hirsutism and acne, in addition to biochemical disorders such as increased luteinizing hormone (LH), follicle stimulating hormone (FSH), testosterone and androstendion levels, and insulin resistance (IR). Clinical features of PCOS may range from a single manifestation to the presence of manifestations with variable sonographic findings. Paraclinical manifestations include increased LH/FSH, increased androgen and lipid profile disturbances (7).

Based on previously conducted studies, the prevalence of PCOS has been reported to be 4-12% (average: 7.5%) among women of reproductive age (8). Early diagnosis of PCOS is of paramount importance since progression toward full-blown PCOS can be prevented (8, 6).

Ethnic and nationality factors influence the prevalence of PCOS. For instance, PCOS is significantly more prevalent in southeastern Asian countries such as India and Thailand rather than in Britain (6). Other factors influencing the prevalence and incidence of PCOS include dietary habits, type and nature of physical activity and obesity (6). Genetics is another factor which influences both the incidence and prevalence rates (9). Additionally, PCOS may accompany other endocrine disorders (10).

In this study we have aimed to achieve an accurate estimation of the prevalence of PCOS as well as the predominant clinical features among adolescents in order to facilitate future studies on both the control and treatment of PCOS in its early stages. On the other hand, thorough estimations of the prevalence of this syndrome will provide a complete estimation of the burden of the disease for health policies.

Materials and Methods

This study has been approved by Shahid Beheshti University of Medical Sciences Institutional Review Board and participants signed approved study informed consents.

This is a cross-sectional study conducted on adolescent girls, 15-18 years old in Tehran. Subjects underwent both interviews and examinations. Those

girls with at least one clinical feature that included menstrual irregularity (in all girls who had menstrual irregularity, the onset of menstruation was four or more years prior), hirsutism (Ferryman Gallway score of eight or greater) and obesity (body mass index; BMI) $>30 \text{ kg/m}^2$) underwent blood testing for serum FSH, LH, fast blood sugar (FBS) - insulin and prolactin (PRL) levels (in one reference laboratory) and sonographic examination (by one gynecologist). Confirmed cases of PCOS constituted the basis for calculation of the prevalence of the syndrome. The predominant clinical feature of PCOS among subjects could also be determined. All laboratory investigations were conducted only once, on the first to the fourth day of either a normal menstrual cycle or menstruation following an intramuscular injection of 150 mg progesterone at 8 am and in a fasting condition. Subjects consumed no hormonal agents, such as oral contraceptives or Dian pills, during their prior menstrual cycles. In the next step, a diagnosis of PCOS was confirmed based on the previous definition and the results were subsequently analyzed by SPSS software.

Adolescents who had not experienced puberty, or those with a history of an endocrine disorder diagnosed by an endocrinologist that included Cushing's syndrome, congenital adrenal hyperplasia, adrenal neoplasia, ovarian neoplasia, and hypophysis or hypothalamus dysfunctions were excluded.

Samples were selected through multi-stage random sampling. The size of the sample was calculated based on the mean prevalence ($P=8\%$) with a confidence interval of 90% ($\alpha=10\%$) and relative accuracy of 20% of the prevalence ($d=20\%P$) by use of the sample size formula:

$$(n = Z^2 \cdot \frac{p \cdot (1-p)}{a^2}).$$

Therefore, the sample population was calculated to be 774. Considering the fact that the efficacy of cluster sampling is 60% of the efficacy of simple convenient sampling, the final sample would be 1100 individuals. Thus, 1430 adolescent girls were enrolled in this study in order to increase the confidence.

Each student was examined by a group of physicians and trained midwives. Paraclinical data were obtained by a professional who used identical testing kits. In order to evaluate the consistency of the results of the clinical examinations performed by the groups of examiners, in the first high school the selected sample were re-examined by a second group of examiners. The results of five sonographic examinations were collected by one gynecologist and rechecked. Blood samples were frozen

after the tests were performed and re-tested after three days to determine data reliability.

Statistical analysis

Descriptive statistics was utilized to demonstrate the demographics of the sample population. Quantitative variables including age, age at first menstrual period (FMP), BMI, serum prolactin levels, serum LH, FSH, FBS and insulin levels were analyzed by the t-test. In order to assess the correlation of qualitative variables including hirsutism, frontal hair loss, acne, and menstrual irregularity in the presence of PCOS, the χ^2 test was performed. $P < 0.05$ was considered significant.

Results

The mean age of the participants was 15.84 ± 1.05 years. Of the participants, 12.8% experienced their first menstruation at the age of 14 and 22.4% at the age of 15. Girls who had experienced their FMP at the ages of 16, 17 and 18 constituted 37.3%, 23%, and 4.5% of the sample, respectively (Fig 1).

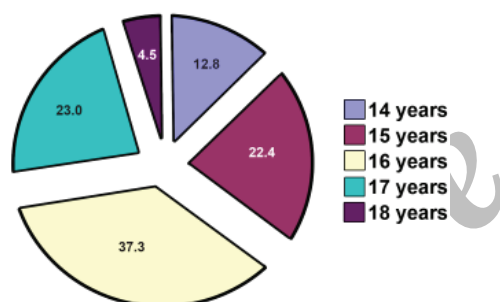


Fig 1: Distribution of participants' ages.

Table 1 represents the mean, minimum, maximum, and standard deviation (SD) of the variables including age, age at FMP, height, weight, BMI, waist circumference and hormonal levels.

Among this sample population, the diagnosis of PCOS was confirmed by means of paraclinical tests and sonographic examination results. Thus, the frequency of the syndrome in this age group was 3.42%. The frequency of PCOS among the four aforementioned age groups was 3.3%, 2.5%, 3.6% and 1.5%, respectively. Although the syndrome was most frequently observed in 17 year-olds, no significant difference was observed among the frequencies calculated for different age groups ($p > 0.05$). Figure 2 depicts the distribution of the syndrome among the different age groups.

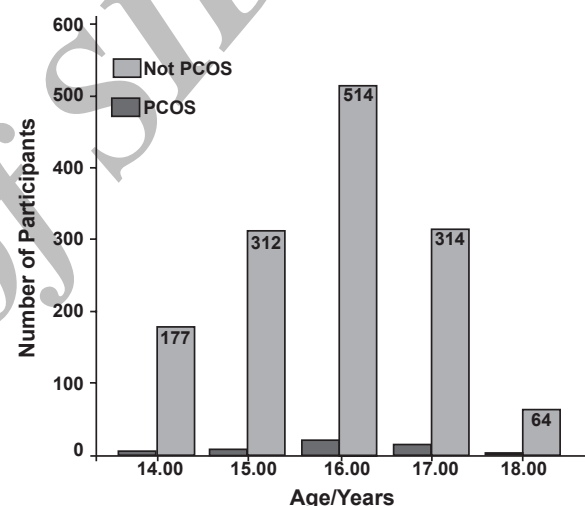


Fig 2: Frequency of PCOS among the different age groups

Table 1: Representation of variables (mean, minimum, maximum and standard deviation)

Variables	Number	Minimum	Maximum	Mean	SD
Height (cm)	1378	140	185	161.78	6.04
Waist (cm)	550	17	127	83.18	10.18
Hip (cm)	541	11	144	98.01	9.17
Weight (kg)	1388	32	122	56.31	11.28
BMI (kg/m ²)	1368	14.61	45.36	21.49	3.95
Age at first menstrual cycle (years)	1391	8	19	12.75	1.18
Testosterone (mg/ml)	73	0.21	8.16	1.10	1.09
LH (IU/ml)	73	0.2	17.4	3.46	3.29
FSH (IU/ml)	73	1.1	16.9	7.36	3.22
LH/FSH	73	0.05	1.58	0.48	0.39
PRL (IU/ml)	73	2.2	211	17.93	26.78
PRL (μg/ml)	73	3.6	5698	480.12	724.95
Glucose (mg/dl)	73	70	133	85.22	10.55
Insulin (IU/ml)	73	1.9	72.5	18.90	14.01

Acne was present in 31.3% of the participants. The frequency of this skin lesion among the different age groups was reported to be 29.8%, 31.9%, 33.6% and 34.4%, respectively. The frequency of acne was not significantly different among the different age groups ($p > 0.05$) as seen in figure 3. In the total sample, the frequency of hirsutism was 10.7%. Within the four age groups of participants, hirsutism was reported in 7.2%, 10.4%, 11% and 18.5%, respectively (Fig 4). Here, a significant difference among the different age groups was observed ($p < 0.05$).

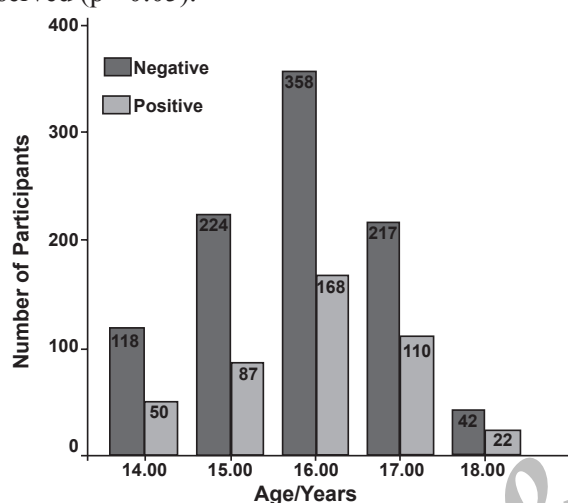


Fig 3: Distribution of Acne among the different age groups.

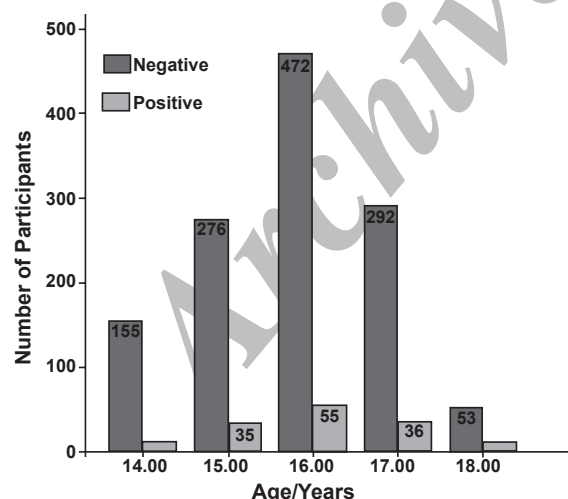


Fig 4: Frequency of hirsutism among the different age groups.

Frontal hair loss was observed in 3.1% of the participants. Among the different age groups, in 3%, 1.9%, 1.8%, and 4.6% frontal hair loss was confirmed as a manifestation of the syndrome, respectively. Here again, a significant difference among the four age groups ($p < 0.05$) was seen (Fig 5).

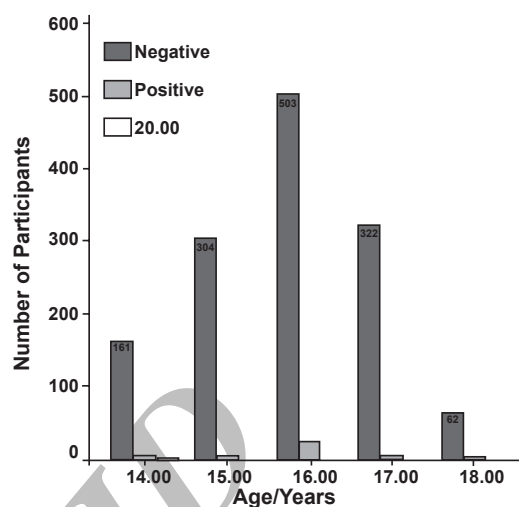


Fig 5: Frequency of frontal hair loss the different age groups.

Discussion

This was the first study that evaluated the frequency of PCOS among a large number of Iranian girls, ages 15-18, in Tehran. Another study was performed in Zanjan in 2008 (11). Previously, minor studies have been performed in Iran such as a study by Hashemi-pour and colleagues in Isfahan (12). As previously mentioned, the main objective of this study was to evaluate the frequency of PCOS among adolescent girls. In case the results may be utilized as an input for policy-making with the aim of prevention of health problems that stem from PCOS; therefore, this study can be deemed essential.

As reviewed earlier, based on the definition of European Society of Human Reproduction and Endocrinology (ESHRE) and American Society of Reproductive Medicine (ASRM), PCOS is diagnosed when two of the three main Rotterdam criteria are found in the patient (5).

It must be noted that the National Institute of Health (NIH) has defined PCOS as the presence of two characteristics, namely, oligo-ovulation and either clinical or paraclinical hyperandrogenemia. When considering the definition provided by ESHRE/ASRM, the frequency of PCOS will be almost 4% while based on the definition of NIH, the frequency of the syndrome would be higher due to the high frequency of hirsutism and menstrual irregularities (10). Meanwhile, based on these frequency rates, comprehensive planning for prevention of the adverse effects of PCOS during adulthood is recommended. The adverse effects of PCOS mainly include:

1. IR: Due to the technical difficulties for measurement of serum insulin levels and IR, accurate

evaluation of the percentage of the patients with IR is difficult. In his study in 1997, Dunaif notified that regardless of obesity or thinness, all patients with PCOS suffer from IR to some degree (3). Through induction of diabetes type II, IR has been recognized to have a high burden on the health economics of different countries. Decreasing this adverse effect among adolescents who suffer from PCOS through lifestyle changes will result in resolution of the high demand on the healthcare system. This change includes change in dietary habits, eating habits and routine physical exercise which can be achieved at school. IR is found in 30% of adolescents suffering from PCOS while 7% of the patients have diabetes type II. These adverse effects can be decreased with proper diet and physical exercise.

2. Dyslipidemia: Dyslipidemia is found in 70% of PCOS patients (increased LDL and triglycerides, decreased HDL) and predisposes them to a higher risk of cardio-vascular diseases. This can be prevented, to a great extent, by means of a proper diet and physical exercise.

3. Obesity: Trunkal obesity and increased waist/hip ratio are frequently observed among patients with PCOS. This can independently increase the risk of cardio-vascular diseases which can be controlled through lifestyle changes. Childhood metabolic syndrome includes IR, obesity, iatrogenic dyslipidemia and hypertension. This syndrome is observed in 45% of patients with PCOS while only 4% of control groups within the same age range manifest this syndrome. Weight loss and lifestyle changes have been recognized to be effective in the control of metabolic syndrome.

4. Endometrial neoplasia: Endometrial neoplasia is three times more prevalent among PCOS patients as compared to the general population. Among these patients, endometrial hyperplasia and cancer in their 40s results in a heavy burden on the family as well as the health system. Early diagnosis of the syndrome in adolescence and prevention of the effects of estrogen on the endometrium when unopposed by progesterone results in prevention of endometrial neoplasia.

5. Adverse effects during pregnancy: There is a 2-3 times greater chance for developing gestational diabetes, pre-eclampsia, preterm labor and prenatal mortality which are among the adverse outcomes of PCOS. Their prevalence can be decreased by means of controlling the adverse effects of PCOS in adolescence.

It must be emphasized that in comparison to the

prevalence rates in Europe and the United States, PCOS is more prevalent in reproductive aged Iranian women. On the other hand, the sequels of the syndrome can be diminished to a significant extent through lifestyle changes. Today unhealthy diets, such as those diets which include fatty foods, high calorie and high-carbohydrate foods, and low fiber foods are more popular. On the other hand, as a consequence of the rapid pace of life and long distances that necessitate using automobiles for transportation, the mean physical activity of individuals has also decreased significantly. In adolescents with early manifestations of PCOS, education about a change in lifestyle and physical activity at schools and universities might result in a decrease in future adverse outcomes of the syndrome, both at the family and social level.

Conclusion

It seems that allocation of additional budgets and the inclusion of larger study samples in which the subjects are more motivated allow for the achievement of more comprehensive and practical results.

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