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The Frequency of Various Phenotypes of Polycystic Ovarian Syndrome in Adolescents, Based on Rotterdam Criteria

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Background: Polycystic Ovarian Syndrome (PCOS) is the most common endocrine disorder among women and is also the cause of infertility due to an- ovulation.

Objectives: This study was carried out to determine the prevalence of PCOS phenotypes in Shiraz.

Patients and Methods: In this cross-sectional study, 3190 female adolescents aging from 14 to 18 years were randomly selected from Shiraz high schools in 2009. Diagnosis of PCOS was carried out through history, examination according to oligomenorrhea (6 cycles or less in a year), and clinical signs of hyperandrogenism including hirsutism (Ferriman-allwey score of 6 and above), severe acne, and androgenic alopecia. Finally, 146 students entered into this study. The ultrasound was conducted based on Adams criteria .The data analyzed using SPSS-16 software and χ^2 and t statistical tests, and $P < 0.05$ was considered as statistically significant.

Results: The prevalence of hirsutism, acne, alopecia, and oligomenorrhea was 3.2% (100 cases), 5% (235 cases), 4.2% (135 cases), and 4.6 % (144 cases), respectively. The incidence rate of menorrhagia was 9.2% (265 cases). Additionally, clinical hyperandrogenism phenotype and oligomenorrhea (HA, OA)were presented in 29 cases (19.9%), clinical Hyperandrogenism phenotype and Polycystic Ovary (HA ,PCO) in 45 cases (30.8%), Oligomenorrhea phenotype and Polycystic Ovary (OA, PCO) in 43 cases (29.5%), and clinical hyperandrogenism phenotype, polycystic ovary, and oligomenorrhea (HA, OA and PCO) in 21 cases (14.5%).

Conclusions: Full-blown phenotype (hyper androgenic, Oligomenorrhea and polycystic ovary syndrome), Lowest frequency and phenotype (hyperandrogenic, polycystic ovary syndrome) was the most frequent in this population of Iranian girls. The risk of sex hormone turmoil, psychological effects of skin symptoms (acne and hirsutism), and the high complications of this syndrome in adolescent group necessitate further investigation.

Keywords: Polycystic Ovary Syndrome; Oligomenorrhea; Adolescent

1. Background

Polycystic Ovarian Syndrome (PCOS), known as Stein–Leventhal syndrome, is the most common endocrine disorder among the women of reproductive age. The prevalence of this disorder has been reported to be 6.5 - 6.8% among the women of reproductive age according to the criteria of National Institute of Health (NIH) (1, 2). There is strong evidence that PCOS begins during puberty (3). The pathophysiology of PCOS is complex, and its etiology remains unclear. This heterogeneous syndrome presents with anovulation, hirsutism, and infertility (4). Both adult women with PCOS (5) and adolescents with Hyperandrogenemia (HA) (6-8) demonstrate altered neuroendocrine function with a persistently rapid Luteinizing Hormone (LH) pulse frequency (and by inference GnRH) as well as elevated serum LH concentrations, which contribute to HA and ovulatory dysfunction. Moreover, recent data suggest that a similar abnormality is present in some adolescents with HA (9). These criteria were meant for adult women, without any consideration for the adolescents. Although the clinical manifestations are believed to be similar in adolescents and adults, anovulation and hyperandrogenism that define PCOS do not always adequately characterize the adolescents with PCOS. Even by the third year after menarche in normal females, 59% of the cycles remain without ovulation (10). In the U.S., based on the recommendation of NIH in 1990, hyperandrogenism or hyperandrogenemia and ovulatory dysfunctions in the absence of adrenal non–classic hyperplasia were considered as the diagnostic criteria of PCOS. In Europe, however, these criteria included cystic ovaries

in ultrasonography accompanied by one or more of the following: oligomenorrhea, hyperandrogenism, obesity, and increasing serum testosterone or LH (11). Therefore, the prevalence of PCOS has been reported to vary from 17% to 22% in different areas of the world according to the used diagnostic criteria.

2. Objectives

The clinical symptoms of this syndrome can also be very different. Thus, with respect to the importance of early diagnosis of this syndrome in female adolescents, this study was carried out on 14 to 18 year old girls in Shiraz high schools in 2009.

3. Patients and Methods

In this study, 3190 female adolescents between 14 and 18 years old were randomly selected from Shiraz high schools in 2009. This study was approved by the ethics committee of Shiraz university of medical sciences. The study sample size was determined according to 3.5% prevalence of PCOS in Hashemipour's study (12) and considering z = 1.96, d = 0.7%, P = 3.5%, and loss rate of 20%, a sample size of 3200 subjects was included in the study. Having obtained the approval of the department of education, the researcher received the list of all the schools in each educational district. The schools were selected as a cluster using one-stage cluster sampling method. The samples of each district were then determined according to its population including 600 - 800 students from each district. The students were selected through purposive sampling. Having described PCOS and its short- and long-term complications, the researcher obtained the written informed consent from all the participants to take part in the study. The students then completed the study questionnaire which included demographic information and investigation of hirsutism, acne, alopecia, and menstrual disorders. The students who met the above-mentioned criteria underwent physical examinations. Oligomenorrhea was defined as 6 or fewer menstrual cycles in a year (13). In addition, the researcher performed the necessary examinations about hyperandrogenism's clinical symptoms, including hirsutism, acne, and androgenic alopecia. Hirsutism was determined according to the Ferriman-Gallwey-score and examination of 9 body areas, including upper lip, chin, and chest, upper and lower areas of the abdomen, thighs, and upper arms, for coarse terminal hair. In each part, the severity of hirsutism was graded from 1 to 4 and the participants with the total score of 6 and above considered as having hirsutism (14). The severe acne accompanied by too many papules, pustules, cysts, and scars was also considered as an inclusion criteria (15). The alopecia was characterized by moderate hair loss and severe reduction in hair density of the frontal hair and forehead.

Adams et al. presented the most acceptable definition of polycystic ovary ultrasound which was defined as the presence of 10 or more ovarian cysts with 2 – 8 mm diameter as well as increasing ovarian stroma with a lower incidence of multiple small 2 – 4 mm cysts throughout the ovarian stroma (16). Abdominal ultrasound was performed by an ultrasound specialist and radiologist using 2200 Schimadzu machine with 3.5 MHz probe, with full bladder (17).

The inclusion criteria of the study were females aged from 14 to18 years and not having consumed any medications, except for anti-allergy medicines and sedatives, for at least 3 months before the study. On the other hand, the exclusion criteria of the study were passage of less than 2 years from the onset of menarche, having adrenal, thyroid, hyperprolactinemia, and amenorrhea disorders, and suffering from severe underlying diseases affecting menstrual cycles, including thalassemia and known endocrinopathy such as Cushing syndrome. In this study, PCOS was diagnosed according to Rotterdom criteria. Based on the definition proposed by the society of reproduction and embryology in Europe and America's fertility committee in Rotterdom conference in 2003, 2 out of the 3 following criteria are used as diagnostic criteria of PCOS: 1) oligoovulation or anovulation, 2) clinical symptoms of hyperandrogenism or hyperandrogenemia, and 3) the evidence of polycystic ovary in sonography with exclusion of other endocrine disorders (18). Therefore, according to Rotterdom criteria, PCOS is presented through the following 4 phenotypes (19): 1) clinical hyperandrogenism phenotype and oligomenorrhea, 2) hyperandrogenism phenotype and polycystic ovary, 3) oligomenorrhea phenotype and polycystic ovary, and 4) hyperandrogenism phenotype, polycystic ovary, and oligomenorrhea.

4. Results

The present study was conducted on 3190 female students aged from 14 to18 years in Shiraz high schools. The demographic characteristics of the participants are shown in Table 1, 2. Accordingly, 11.2%, 21.2% and 20.2% of the students were 14, 15 and years-old 18 years old, respectively. The respective prevalences of hirsutism, acne, alopecia, and oligomenorrhea were 3.2% (100 cases), 5% (235 cases), 4.2% (135 cases), and 4.6 % (144 cases). Besides, the incidence rate of menorrhagia was 9.2% (265 cases). Moreover, 5.5% of the patients with alopesia showed polycystic ovaries in sonography. Also, 13% of the subjects with acne, 16.4% with hirsutism, and 29.5% with oligomenorrhea had special signs of polycystic ovaries in sonography. Furthermore, clinical hyperandrogenism phenotype and oligomenorrhea presented in 29 cases (19.9%), clinical hyperandrogenism phenotype and polycystic ovary in 45 cases (30.8%), oligomenorrhea phenotype and polycystic ovary in 43 cases (29.5%), and clinical hyperandrogenism phenotype, polycystic ovary, and oligomenorrhea in 21 cases (14.5%).

According to Fisher's test, Dehydroepi Androstenedione Sulfate (DHEAS) levels were not significantly different in women having various phenotype and were unaffected by this syndrome (Table 3).

Table 1. The Demographic Characteristics of the Studied Population [a,b]

	OM/HAc/PCO	OM/HAc	HAc/PCO	OM/PCO
Menarche	13 ± 1.14	13 ± 1.10	13 ± 1.22	12.98 ± 1.10
Weight, Kg	66 ± 16.19	63.75 ± 15.05	65.47 ± 14.94	65.07 ± 15.82
Waist circumference, cm	73.11 ± 10.69	72.25 ± 9.63	73.27 ± 10.64	72.68 ± 10.93
BMI, kg/m²	25.35 ± 5.13	24.75 ± 4.84	25.60 ± 5.09	25.19 ± 5.40
Height, cm	160.81 ± 6.11	160.03 ± 6.25	159.52 ± 5.39	160.33 ± 4.86

[a] Data are shown as Mean ± SD.
[b] Abbreviations: HA: clinical Hyperandrogenism, mF–G score: modified Ferriman-Gallwey, OM: Oligomenorrhea, PCO: Polycystic Ovary.

Table 2. The Frequency of Phenotype and Modified Ferriman-Gallwey Score of the Study Participants [a]

	OM/HAc/PCO	OM/HAc	HAc/PCO	OM/PCO
Frequency of phenotype [b]	21 (14.4)	29 (19.9)	45 (30.8)	43 (29.5)
mF–G score [c]	4.62 ± 3.98	5.03 ± 4.37	4.82 ± 4.13	2.93 ± 3.45

[a] Abbreviations: HA: clinical Hyperandrogenism, mF–G score: Modified Ferriman-Gallwey, OM: Oligomenorrhea, PCO: Polycystic Ovary.
[b] Data are presented as No (%).
[c] Data are shown as Mean ± SD.

Table 3. Frequency of Dehydroepi Androstenedione Sulfate (DHEAS) in Patients with Different Phenotypes of Polycystic Ovary Syndrome [a,b]

DHEAS	Without OM/PCO	OM/PCO	Without OM/HAc	OM/HAc	Without HAc/PCO	HAc/PCO
DHEAS < 2.17	(77) 69	(55.8) 24	(68.1) 79	(46.7) 14	(64.4) 65	(62.2) 28
DHEAS > 2.17	(33) 34	(44.2) 19	(31.9) 38	(53.3) 16	(35.6) 36	(37.8) 17

[a] Values are presented as No (%).
[b] Abbreviations: HA: clinical Hyperandrogenism, OM: Oligomenorrhea, PCO: Polycystic Ovary.

5. Discussion

PCOS is a heterogeneous disease which occurs due to a variety of reasons. The sequence of events eventually leads to symptomatic disease, such as hyperandrogenism, abnormality pattern of pulsatile of LH hormone, and menstrual disorders, which may begin from different parts of the body by various processes (19). It should be noted that PCOS is diagnosed by ruling out other disorders, such as oligomenorrhea or hyperandrogenism (20). On the other hand, single girls with PCOS exposed to an increasing level of circulating androgens for a long time, compared to estrogen, are at higher risk for cardiovascular diseases, hyperansulinemia, and diabetes mellitus. Hence, considering the foregoing long term complications, it seems that timely screening of all such complications would contribute to the disease prevention.

In the present study, the prevalence of the patients suffering from PCOS with oligomenorrhea phenotype was 29.5%, which was consistent with the result of the study by SOO Jin in Korea (37.3%) (21). Moreover, the prevalence of the disease was reported as 6.9% in Greece, 10% in Bulgaria, 14.3% in the U.S., 13.3% in Italy, and 18.2% in Taiwan (22-27). In the present study, the prevalence of clinical hyperandrogenism phenotype and polycystic ovary was 30.8% (45 cases). Barber (2007) reported the prevalence of this phenotype to be 24.6% which is almost compatible with our result (28). In this study, the prevalence of this phenotype was higher in comparison to other reports (20, 24). The prevalence of clinical hyperandrogenism and polycystic ovary was reported as 7.4% by Diamanti et al. (1), 20% by Pehlivanov (26), 13.2% by Shroff (27), 5.5% by Belosi (22), and 21.2% by Hsu (25).

In the present study, the prevalence of the patients with clinical hyperandrogenism phenotype and oligomenorrhea was 19.9% (29 cases), which is different from other studies performed in other countries, The prevalence of this phenotype was reported as 40.2% by Diamanti, 11.4% by Pehlivanov, 14.3% by Shroff, 7.5% by Belosi, and 8.8% by Hsu. In Hashemipour's study which was conducted in Iran, the clinical prevalence of PCOS with oligomenorrhea and clinical hyperandrogenism was reported to be 3.4%. In the current study, the prevalence of clinical hyperandrogenism phenotype and polycystic ovary and oligomenorrhea was 14.4% (21 cases), which differs from studies conducted in other countries. In Greece, Diamanti reported the prevalence of this phenotype to be 45.5%. Besides, its prevalence was reported as 58.6% by Pehliva-

nov, 58.1% by Shroff (27), 73.6% by Belosi (22), and 51.8% by Hsu (25) in Taiwanese Chinese women respectively. In this study, the prevalence of this PCOS phenotype was lower (45.5%) compared to other studies (73.6%), which might be due to the younger age of the study population. These studies were carried out on adult women, whereas the participants the current study were 14 to 18 years-old. Thus, more time is needed in order to detect all the symptoms of this syndrome. In one study, Carmina (2006) noted the prevalence of PCOS to be 78.5% according to NIH criteria (29). Also, the prevalence of this syndrome was reported as 79.13% by Belosi (2006) (22). Furthermore, Puzigaca et al. conducted a study in 1991 and showed that anderestondion, testosterone, and DHEAS levels were higher in the patients with polycystic ovaries in sonograghy compared to those with normal sonography although this difference was not statistically significant (30). One of the strengths of our study was that it determined the phenotype of the syndrome in Iran, whereas, except in few studies, most investigations have examined the overall poly cystic ovarian syndrome. Also, most studies were carried out on adults, and few on adolescents.

One limitation of our study was the lack of cooperation of girls during physical examination. Also, in regard to hormonal assay or taking sonography, the girls and their parents did not call on the laboratory and radiology on time.

Our study showed that PCOS was a common endocrine disorder in reproductive ages, which was consistent with the results of other studies. Thus, the individuals with menstrual disorders and especially oligomenorrhea several years after menarche are recommended to be screened for PCOS symptoms and undergo endocrine assay in order to diagnose the underlying causes of this syndrome. In general, the women with anovulation and hyperandrogenism are more exposed to the risk of insulin-independent diabetes. In addition, the beginning of the disease in these women is 30 years earlier than the general population. Therefore, in view of the complications of this syndrome, it is suggested to prevent PCOS from adolescence. Also, the physicians should inform the patients about the importance of changing their lifestyle and diet and doing exercise.

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Authors' Contributions

Akbarzadeh M. and Naderi T. prepared the first draft of the manuscript and Akbarzadeh M. made the critical revisions to the paper and translated it into English. Dabbagh Manesh M. H. had Supervision in the definitive diagnosis of girls with polycystic ovarian syndrome and Tabatabaee H. R. in performed the data analysis.

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