

The Relationship between Clinical and Chemical Hyperandrogenism in 14-18-Years- Old Girls

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Article information	Abstract
<p>Article history: Received: 10 May 2011 Accepted: 25 May 2011 Available online: 27 July 2011</p>	<p>Background: One of the most common endocrine disorders in women's medicine is the increased androgen and the symptoms of increased androgens in women such as polycystic ovary syndrome. The two main components to diagnose this syndrome are menstrual disorder and clinical or laboratory hyperandrogenism, but other causes should be ruled out in order to confirm the diagnosis. This study aims to examine clinical Hyperandrogenism in female students of 14 to 18 years old in Shiraz in 2010.</p> <p>Materials and Methods: This cross-sectional study was conducted on 3200 female high school students of 14-18 years old in Shiraz. Data collection tools include questionnaires containing personal details, clinical Hyperandrogenism features (acne, alopecia and hirsutism based on Freeman-Galway scale) and test results. The ultrasound was conducted based on Adams criteria. The data results are analyzed using SPSS-15 software and ² and <i>t</i> statistical tests.</p> <p>Results: In this study, the frequency of hirsutism is 3.2%, prevalence of acne is 5% and alopecia is 4.2%. Mean of free testosterone (1.647±0.835) was higher in the group with hirsutism, acne and alopecia. Independent <i>t</i>-test showed no significant relationship between patients with hirsutism, acne and alopecia and non-affected people in terms of mean of total testosterone and free testosterone. However, there is a significant relationship between people with acne and hirsutism and polycystic ovary compared with those with acne and hirsutism and those without polycystic ovary (<i>p</i> < 0.05).</p> <p>Conclusion: This study indicated that clinical and chemical hyperandrogenism can be a criterion to diagnose with polycystic ovary syndrome, but ultrasound was not helpful.</p>
<p>Keywords: Hyperandrogenism Polycystic Ovary Syndrome Girls</p>	
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Introduction

The most common cause of hyperandrogenism and hirsutism is polycystic ovary syndrome (PCOS), which is also called Stein-Leventhal syndrome. There is strong evidence suggesting that PCOS begins during puberty. It has been suggested that the origin of disorder in the production of ovarian androgens in puberty may be in childhood or even during fetal development [1-3]. According to the recommendations of National Institutes of Health (NIH) in 1990 in America, non-classical adrenal hyperplasia in absence of ovulation hyperandrogenism or hyperandrogenemia and ovulation disorder due to absence of non-classical adrenal hyperplasia are considered as diagnostic criteria of disease, while in Europe these criteria include presence of polycystic ovaries in ultrasound along with one or more of these symptoms: oligomenorrhea, hyperandrogenism, obesity, increased testosterone or LH serum [4]. Therefore, outbreaks in different parts of the world are different based on the diagnostic criteria used, and most studies have reported the prevalence ages of 18-45 to be 2.2-26%, which are about 9.13 in young girls [5]. PCOS

is associated with clinical or biochemical evidence of hyperandrogenemia (for example, acne, hirsutism or increased free testosterone) and anovulation evidence (for example oligomenorrhea or amenorrhea) [6].

Polycystic ovary syndrome is the main cause of effective infertility in approximately 6-8% of women at reproductive age and it is associated with obesity in 60% of cases. The affected women encounter insulin resistance and hyperinsulinaemia in 50-70% of cases, diabetes in 4-10%, and indicators of cardiovascular risk in adolescents in 33% [7-9]. The prevalence of metabolic syndrome with polycystic ovary syndrome is 30-60%, 4 to 5 times the incidence of which is related to age and body mass index [10]. But, the two main components to diagnose this syndrome are menstrual disorder and clinical or laboratory hyperandrogenism, however other causes should be ruled out to confirm the diagnosis [11,12]. Hyperandrogenism clinical symptoms such as hirsutism, acne and male characteristics occur with polycystic ovary syndrome almost in 66% of adolescents. Hirsutism, which is the most common clinical symptom of

hyperandrogenism in polycystic ovary syndrome, is the increased growth of terminal hair in androgen-dependent areas of the body [11]. Other clinical symptoms of hyperandrogenism are typical acne vulgaris, weight gain, menstrual disorders and Acanthosis Nigricans in some women with polycystic ovary syndrome symptoms [12]. In each adolescent, onset of hirsutism leads us to diagnosis of polycystic ovary syndrome. Hyperandrogenemia has been recognized in adulthood as a leading symptom of polycystic ovary syndrome that occurs with higher androgen levels and low fertility level [13]. In addition to the problems of hirsutism, acne, alopecia, obesity, impaired glucose tolerance and insulin resistance and hyperinsulinaemia, adolescents with polycystic ovary syndrome are at risk of infertility, type II diabetes, atherosclerosis, cardiovascular diseases, endometrial cancer and ovarian cancer [11,14]. Therefore, considering the importance of early diagnosis of PCOS, clinical and chemical hyperandrogenism have been reviewed in this article on the student girls of 14 to 18 years old in Shiraz.

Materials and Methods

This is a cross-sectional study which has studied the frequency of clinical and chemical hyperandrogenism. Research environment includes high schools located in different areas of Shiraz. The reason for selecting the above location for research was the greater number of 14-18 year old girls and easy access to the research groups. Using similar studies [15] the sample size, 3200 female students of 14-18 who were studying, was determined. Inclusion criteria included 14-18 years old, willingness to participate in the study and completion of written consent form, lack of adrenal problems, thyroid dysfunction, hyperprolactinemia, not taking any medications except for antihistamines and sedatives for at least 3 months before study, at least 2 years should be passed from their menarche. Data collection tools included questionnaires containing personal details, clinical Hyperandrogenism features, results of test and measurements of weight based on Freeman-Galway scale. The number of samples of each area was determined according to the population covered by it.

From each area 800 students were selected as sample, the schools were selected randomly and 3-4 schools in each district were randomly selected as cluster according to the number of pupils per school. The students were selected based on purposive sampling method. Written informed consent was obtained from students to participate in research. After filling out the questionnaire, which contained demographic information, hirsutism, acne and alopecia and testosterone levels were studied in the research community. The tests included measurement of prolactin (to rule out hyperprolactinemia), dehydroepiandrosterone sulfate (to rule out adrenal diseases), total and free testosterone as well as Thyroid-stimulating hormone (to exclude hypothyroidism). Improved Freeman-Galway scale was used to determine the hirsutism score. In this study, if the total scores were

equal to or more than 6, the person would be Hirsute [16]. The scores of 6-9 were considered as mild hirsutism, the scores of 10-14 moderate hirsutisms and the score of 15 or more were considered severe hirsutism [17]. The severity of acne and alopecia were determined based on clinical symptoms [18].

In this study, a severe form of acne was considered as acne. In this study, based on the severity of clinical symptoms, alopecia was divided into three mild, moderate and severe groups: 1) There is a slight decrease in the density of scalp hair, and thin and small amount of hair, color and forehead hairline are preserved, 2) There is a moderate reduction in scalp hair density and forehead hairline is preserved, 3) There is a sharp decline in scalp hair density and forehead hairline loss [18]. In this study, moderate and severe cases of scalp hair density and forehead lines were considered. Equilibrium dialysis and ultracentrifugation are used to measure free testosterone, which is achieved through dividing the amount of total testosterone by the SHBG concentration and multiplying the obtained number by 100 ($T/SHBG \times 100$). In this study, if the testosterone level is more than 0.65 mg/ml, it is called hyperandrogenemia.

The most acceptable definition of polycystic ovary ultrasound was presented by Adams et al. It is defined as the presence of multiple cysts (10 or more) with 2-8 mm diameter in the ovary as well as the increase of ovarian stroma along with a lower incidence of multiple small 2-4 mm cysts throughout the ovarian stroma [19]. Abdominal ultrasound was performed by an ultrasound specialist and radiologist through 2200 Schimadzu machine with the probe of 3.5 MHz, while the bladder was full. After test results follow-up, those suspected with hyperthyroidism and hyperprolactinemia as well as those with increased testosterone, Clinical Hyperandrogenism (acne, hirsutism, and alopecia) and polycystic ovary syndrome were identified and referred to endocrinology and metabolism specialist for further examination and were treated. Data results have been analyzed using SPSS-15 software and statistical tests of χ^2 and t .

Results

The frequency of severe face and body acne was respectively 143 (0.5%) and 103 cases (3.2%). About 135 cases (4.2%) of the total subjects had moderate to severe alopecia. Approximately 100 people (3.2%) had hirsutism of score 6 and above. 79 cases (2.4%) had mild hirsutism, 17 cases (0.6%) had moderate hirsutism and 4 cases (0.2%) of them had severe hirsutism. The mean of total testosterone level (0.685 ± 0.354) was higher in patients with hirsutism than those without hirsutism (0.582 ± 0.305).

In addition, the mean of free testosterone level (1.647 ± 0.835 ng/ml) was higher in the group with hirsutism. Independent t -test indicated no significant relationship between hirsutism and non-infected people in terms of mean of total testosterone and free testosterone. There was no significant difference between patients with moderate to severe acne and alopecia and non-infected

people in terms of testosterone and free testosterone levels. There was no significant correlation between patients with polycystic ovary alopecia and those with alopecia but without polycystic ovary. Similarly, there was a significant difference between patients with acne, hirsutism and polycystic ovary and patients with acne and hirsutism and without polycystic ovary there. 45 cases (30.8%) of people with clinical Hyperandrogenism had polycystic ovary, while 69.2% of people with polycystic ovary had no hyperandrogenism symptoms (Tables 1 & 2).

Table 1. Mean of testosterone and free testosterone in people

	Testosterone Mean±SD	Free testosterone Mean±SD
Lack of moderate to severe alopecia	0.626±0.343	1.525±0.776
Moderate to severe alopecia	0.588±0.160	1.493±0.523
Lack of hirsutism	0.582±0.305	1.444±0.687
Hirsutism	0.685±0.354	1.647±0.835

Table 2. Frequency of acne, alopecia, hirsutism in terms of polycystic ovary

	PCOS+ (number)	PCOS - (number)	p-Value
Alopecia	8(5.5%)	138(94.5%)	0.202
Acne	19(13%)	127(87%)	0.008
Hirsutism	24(16.4%)	122(83.6%)	0.001

Discussion

In the present study, the prevalence of hirsutism was 3.2%, incidence of acne is 5%, and alopecia is 4.2%. In the study of Hashemipour et al in Isfahan, prevalence of hirsutism has been reported 6%, acne 4.7% and alopecia 3% [15]. Mild hirsutism (score 6-9) is observed in 79 patients (2.4%), moderate hirsutism (score 10-14) in 17 patients (0.6%) and severe hirsutism (score 15 and above) in 4 patients (0.2%). In the study of Akhiani et al on female students of medical schools in Tehran, the prevalence of hirsutism was 22.8%. In this study, 17.3% had mild hirsutism (score 4 to 7), 5.1% had moderate hirsutism (score 8 to 11) and 0/3% had severe hirsutism (score 12 to 16) [20]. The age range of individuals in the study of Akhiani was 18-25 years old. Perhaps due to the higher age of participants in the study of Akhiani, incidence of hirsutism has been reported higher. Hirsutism is less obvious in adolescence [21]. Typically, hirsutism is slowly beginning in polycystic ovary syndrome [22]. It seems that increase of PCOS symptoms is associated with increase of age through gradual accumulation of fat tissue [23]. Another cause of higher incidence of hirsutism in the study of Akhiani is that the subjects completed the questionnaires voluntarily and non-hirsute students might have been less tended to fill out forms. But in our study and the study in Isfahan, the subjects were randomly selected and non-hirsute people also participated in the project. Therefore, prevalence of hirsutism has been estimated to be less. Pilosebaceous unit of armpits and pelvic region is even sensitive to low levels of androgens. On the other hand, hirsutism is not a

hair disorder, but androgens lead to stimulation of hair growth to do which either androgen will be increased or the response of target tissues to androgens will be intensified, which is the increase of blood androgens in more than 80% of cases [24]. Hirsutism which is seen in 5-15% of women is a relative definition rather than an absolute definition; clinical and social reactions and skin sensitivity to androgens are different among races and cultures [14].

Individual susceptibility and genetic factor are involved in clinical symptoms of hyperandrogenism. The studies on twins have shown that genetic factors highly influence the testosterone secretion and conversion of testosterone into dihydrotestosterone [25]. In addition, changes in regulator gene of 5-alpha reductase type 1 (the main enzyme producing dihydrotestosterone in hair follicles) is associated with varying degrees of hirsutism in women [26]. In other words, women with normal levels of androgens are different from women with increased androgen levels in terms of secretion level of androgens and androgen activity in target tissues [27,28]. Initial evaluation of patients with hirsutism includes tests for total testosterone, dehydroepiandrosterone sulfate, prolactin and pelvic ultrasound to examine the ovary. If the patient has other symptoms of this disorder, the evaluation will be conducted according to other studies in terms of Cushing's syndrome, thyroid disorders and acromegaly. Except for several cases of hypothyroidism which were excluded from the study, none of the above cases were seen in our study [29].

Acne is also of hyperandrogenism symptoms [30]. In the present study, the prevalence of severe acne on the face and body of subjects was 5%. In the study of Hashemipour, acne was observed in 4.7%, which is consistent with our results. Hair growth is also inhibited in varying degrees by Gennady androgens. Age and genetics determine the response rate of hair follicles and lead to baldness pattern in forehead and parietal part in men and some women [14,15]. In the present study, the prevalence of individuals with clinical phenotypes of hyperandrogenism and polycystic ovary is 30.8% (45 people). Barber has reported prevalence of this phenotype at 24.6%, which is almost consistent with our results [31]. Our study has shown a higher incidence of individuals with normal ovulation and clinical hyperandrogenism and polycystic ovary (30.8%) compared to other studies (2.4-20%). Diamanti et al in Greece have reported the prevalence of clinical hyperandrogenism and polycystic ovary at 7.4%, Pehlivanov et al in Bulgaria have reported it at 20%, Shroff in America reported it at 13.2%, Blousi in Italy at 5.5% and Hsu in Taiwan have mentioned it to be 21.2% [32-34].

Therefore, early diagnosis and conservative treatment can prevent the complications caused by polycystic ovary syndrome. Since the cause of disease is unknown and there is no certain cure for it, polycystic ovary syndrome is now one of the major priorities in preventive medicine in developed countries which should be considered in adolescence. Although it is difficult to diagnose polycystic ovary syndrome in adolescents, clinical

hyperandrogenism (acne, hirsutism and androgenetic alopecia) and biochemical hyperandrogenism (increased levels of blood androgens) are both more accurate methods to diagnose polycystic ovary syndrome.

In addition, considering that 101 (69.2%) of subjects have no clinical hyperandrogenism, but have polycystic ovary, ultrasound findings and diagnosis of cystic ovarian

did not help to diagnose the disease and there is no need to do it for diagnosis.

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