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Prevalence of hyperandrogenism in Iraqi women with polycystic ovary syndrome

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Abstract

Polycystic ovary syndrome (PCOS) is a mainly common endocrine disorder. Hyperandrogenism is the major standard in the diagnosis of PCOS development. Eighty women diagnosed with PCOS and twenty healthy women (aged 20-40 years) were enrolled in this study which was conducted at the infertility clinic of Kamal AL-Samaray Hospital/ Baghdad. The diagnosis of PCOS was made according to the Rotterdam criteria. Body mass index (BMI, Kg/m²) was calculated by a specific formula. History of menstrual irregularity, hirsutism, acne, and alopecia was taken. Hormone levels in serum, namely luteinizing hormone (LH), follicle stimulating hormone (FSH), and testosterone were measured in all patients and control subjects. There was a statistically significant difference ($P < 0.05$) in the BMI between the PCOS and control women. Also, the prevalence of overweight and obesity was much higher in PCOS women than in their matching control. The serum levels of LH, FSH, and testosterone were significantly different ($P < 0.05$) in PCOS as compared to healthy women. Clinical hyperandrogenism (hirsutism and alopecia) were present in most of PCOS women, while acne was a less useful clinical sign of hyperandrogenism. In addition, the prevalence of hirsutism and alopecia was increased in obese when compared with overweight and lean PCOS women.

Keywords: Polycystic ovary syndrome, Body mass index, Luteinizing hormone, Follicle stimulating hormone. Gonadotropin releasing hormone

انتشار فرط افراز المذاكر في النساء العراقيات المصابات بمتلازمة تكيس المبيض المتعدد

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الخلاصة

تعتبر متلازمة تكيس المبيض المتعدد هي اضطراب الغدد الصم الاكثر شيوعا. فرط افراز المذاكر هي المعيار الرئيسي في تطور تشخيص متلازمة تكيس المبيض المتعدد. ثمانون امرأة شخصت بأصابتها بمتلازمة تكيس المبيض المتعدد و 20 امرأة غير مصابة، اعمارهم تتراوح بين (20-40) سنة تم تسجيلهم في هذه الدراسة من العيادة الخارجية لمرضى العقم في مستشفى كمال السامرائي/ بغداد. في هذه الدراسة تم تشخيص النساء المصابات بمتلازمة تكيس المبيض المتعدد اعتمادا على معيار روتردام . تم حساب دليل كتلة الجسم باستخدام معادلة [الوزن/(الطول)²]. تم اخذ المعلومات من المريضات فيما يخص عدم انتظام الدورة الشهرية، كثرة ظهور الشعر ، الحبوب في الوجه، وتساقط الشعر. تم قياس مستوى الهرمونات (الهرمون اللوتيني، الهرمون المحفز للجريبات، الهرمون الذكري، ونسبة الهرمون اللوتيني الى الهرمون المحفز للجريبات). وجد ان

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هناك فرق معنوي ($P < 0.05$) في دليل كتلة الجسم ، كذلك لوحظ انتشار الوزن الزائد والسمنة في النساء المصابات بمتلازمة تكيس المبيض المتعدد اعلى بكثير من مجموعة السيطرة المطابقة لها. وجد فرق معنوي ($P < 0.05$) في مستوى الهرمونات (الهرمون اللوتيني، الهرمون المحفز للجريبات، الهرمون الذكري، ونسبة الهرمون اللوتيني الى الهرمون المحفز للجريبات) في كلي من النساء المصابات بمتلازمة تكيس المبيض المتعدد والنساء غير المصابات. فرط افراز المذاكر السريري (كثرة ظهور الشعر، وتساقط الشعر) كانت موجودة في اغلب النساء المصابات بمتلازمة تكيس المبيض المتعدد، بينما ظهور الحبوب في الوجه هي اقل علامة سريرية مفيدة لفرط افراز المذاكر، بالاضافة لوحظ زيادة انتشار كثرة ظهور الشعر وتساقط الشعر في النساء البدنيات اكثر من النساء ذوات الوزن الزائد والنحيفات المصابات بمتلازمة تكيس المبيض المتعدد

1-Introduction

Polycystic ovary syndrome (PCOS) is a widespread endocrine disorder affecting 5.6–21.3% of women of reproductive age worldwide [1, 2]. The diagnosis of PCOS was performed according to the Rotterdam criteria. This diagnosis was founded on two of the following three criteria: oligo- and/or anovulation, clinical hirsutism and/or high testosterone, and polycystic ovarian morphology as estimated through antransvaginal ultrasound [3]. Oligo-anovulation was defined by the connection between oligo-amenorrhea and a progesterone level less than or equal to 2 ng/mL in the luteal phase of the last cycle [4], while biochemical hyperandrogenism was defined by a testosterone level more than or equal to 0.454 ng/mL [5].

Androgen excess is a main pathophysiological characteristic of PCOS, with 60–80% incidence [6]. Hirsutism is a familiar clinical appearance of hyperandrogenism reported in up to 70% of women with PCOS [7]. In typical women, androgens are secreted in approximately equal quantities by both adrenals and ovaries. On the other hand, androgen secretion from more than one source is familiar in 35% of women with PCOS. The ovary is the major androgen source in PCOS, while adrenal hyperandrogenism in PCOS is possibly the result of several factors including hyperinsulinemia, changed cortisol metabolism, and augmented ovarian steroid production [8]. In adult women with PCOS [9] and in hyperandrogenemic adolescents [10], androgen excess has been related with persistently augmented pulse rate of gonadotropin releasing hormone (GnRH), which has been connected to the androgen-induced resistance of the GnRH pulse associated with negative progesterone feedback. This irregularity could result in excessively elevated LH secretion, which may be responsible for ovarian androgen production and ovulatory dysfunction, causative to the adult PCOS phenotype [11, 12].

Hyperandrogenism is the most important criterion in the diagnosis of PCOS development. According to the present criteria, it can be unclearly defined by either hirsutism and/or excess of blood testosterone level. However, the majority but not all PCOS women are hirsute, and no more than 50% have increased testosterone levels measured by the usually used immunoassay methods [13].

Objective: This study was designed to inspect the risk of PCOS in the modification of the hormonal profile, and to compare the clinical signs such hirsutism, acne, alopecia, and menstrual cycle dysfunction among lean, overweight and obese PCOS women.

2-Materials and methods

Eighty women already diagnosed with PCOS (by clinical and biochemical indication) and 20 age-matched control women who had no clinical or hormonal abnormalities were recruited into the study. Subject's age ranged between 20 and 40 years.

Patients were examined and diagnosed as having PCOS by gynecologists at the outpatient clinic of Kamal AL-Samaraay Hospital/ Baghdad.

Anthropometry included the measurement of height, weight, and body mass index (BMI), according to the WHO guidelines shown in table 1. BMI was calculated by the routine formula: $BMI (kg/m^2) = \text{weight (Kg)} / [\text{height(m)}]^2$ [14]. Weight in Kgs and height in meters were measured with an electronic scale.

Patients with PCOS had clinical illnesses of either: (1) Irregular menstrual cycles in the form of (oligomenorrhea, amenorrhea) (menstrual cycles < 21 or > 38 days), (2) Hirsutism, acne, or alopecia; hirsutism score by Ferimann Galloway scoring, or (3) Obesity.

Diagnosis of PCOS in the patients was confirmed by:

- Ultrasound of the ovaries (presence of 8 or more subcapsular cysts ≤ 10 mm in diameter with augmented ovarian stroma).
 - The laboratory results which included endocrine secretion evaluation by measurement of hormone levels in serum, namely, luteinizing hormone (LH), follicle stimulating hormone (FSH), and Testosterone (T). Serum concentrations of three hormones were measured by using mini-VIDAS (VIDAS 12 model, 1992), through an enzyme linked fluorescent assay (ELFA) technique.
 The exclusion criteria included the use of hormonal contraception, fertility medications in the three months prior to enrollment, hyperprolactinemia, thyroid dysfunction, Cushing's syndrome, and congenital hyperplasia.

Statistical analysis of data was carried out using (SPSS Version 20). Significance of variances was assessed using t-test and a P value ≤ 0.05 was considered to be significant.

Table 1- The international classification of adult underweight, overweight and obesity according to BMI (WHO, 2004).

Classification	BMI(kg/m ²)	
	Principal cut-off points	Additional cut-off points
Underweight	<18.50	<18.50
Severe thinness	<16.00	<16.00
Moderate thinness	16.00 - 16.99	16.00 - 16.99
Mild thinness	17.00 - 18.49	17.00 - 18.49
Normal range	18.50 - 24.99	18.50 - 22.99
		23.00 - 24.99
Overweight	≥ 25.00	≥ 25.00
Pre-obese	25.00 - 29.99	25.00 - 27.49
		27.50 - 29.99
Obese	≥ 30.00	≥ 30.00
		30.00 - 32.49
Obese class I	30.00 - 34.99	32.50 - 34.99
Obese class II	35.00 - 39.99	35.00 - 37.49
		37.50 - 39.99
Obese class III	≥ 40.00	≥ 40.00

Source: Adapted from WHO, 1995, WHO, 2000 and WHO 2004.

3-Results

Body mass index (BMI)

An increase in BMI was found in PCOS patients as compared with the control group. There was a significant ($P < 0.05$) difference in the mean of BMI between the PCOS group ($32.3 \pm 0.5 \text{ g/m}^2$) and the control group ($28.8 \pm 1.0 \text{ kg/m}^2$) as shown in table 2.

Table 2- Comparison of BMI value in PCOS patients and control women.

Studied group	No.	BMI (Kg/m ²) (mean \pm SE)
PCOS patients	80	(32.3 ± 0.5)*
Control women	20	(28.8 ± 1.0)

-The difference between the two groups was statistically significant (*= $P < 0.05$).

In the present study, we classified the body weight in the studied groups according to BMI, as shown in table 3. The prevalence of overweight and obesity in women with PCOS is much higher than in their matching control.

Table 3- The classification of body weight according to BMI in the studied groups.

Body weight classification	PCOS patients (n=80)	Control group (n=20)
Lean	3 (3.75%)	11 (55.0%)
Overweight	28 (35.0%)	5 (25.0%)
Obese	49 (61.25%)	4 (20.0%)
Degree of significance	28.676*	

(* = $P < 0.05$) = Significant)

Clinical hyperandrogenism (Hirsutism, Acne, and Alopecia)

It was found that the percentage of hirsutism in PCOS patients was 63.75%; in lean (3.92%), in overweight (29.41%) and in obese (66.67%). The percentage of acne was 30%; in lean (4.17%), in overweight (29.17%) and in obese (66.67%), while the percentage of alopecia was 65%; in lean (3.85%), in overweight (30.77%) and in obese (65.38%) (table 4).

Table 4- Clinical hyperandrogenism and their relation to BMI in PCOS patients

Clinical hyperandrogenism	PCOS subgroups				Degree of significance
	Total No.	Lean	Overweight	Obese	
Hirsutism	51 63.75%	2 3.92%	15 29.41%	34 66.67%	12.435*
Acne	24 30.0%	1 4.17%	7 29.17%	16 66.67%	9.055*
Alopecia	52 65.0%	2 3.85%	16 30.77%	34 65.38%	7.064*

(*P<0.05)= Significant

Menstrual cycle dysfunction

In the present study, the whole PCOS group was split into three subgroups according to the menstrual status; fourteen patients were with eumenorrhea (17.5%), eight patients were with abnormal uterine bleeding (10.0%), forty seven patients were with oligomenorrhea (58.75%) and eleven patients were with amenorrhea (13.75%), as shown in table 5. The differences were significant (P<0.05) among lean, overweight, and obese PCOS patients.

Table 5- Menstrual cycle dysfunction in PCOS subgroups.

menstrual status	PCOS subgroups				Degree of significance
	Total No.	Lean	Overweight	Obese	
Eumenorrhea	14 17.5%	6 42.86%	8 57.14%	0 0%	33.140*
Abnormal uterine bleeding	8 10.0%	0 0%	4 50.0%	4 50.0%	33.140*
Oligomenorrhea	47 58.75%	3 6.38%	15 31.91%	29 61.70%	33.140*
Amenorrhea	11 13.75%	0 0%	1 9.09%	10 90.91%	33.140*

*P<0.05= Significant

Hormonal measurements**Serum LH**

The mean serum level of LH within the control group was 3.2±0.2 mIU/ml whilst, in the PCOS patients, it was 7.8±0.6 mIU/ml, as shown in Table-6. The difference between the two groups was statistically significant (P <0.05).

Serum FSH level

The mean serum level of FSH for the control group was 7.1±0.4 mIU/ml, whereas, in the group of PCOS patients, it was 4.2±0.5 mIU/ml, as shown in table 6. The difference between the two groups was statistically significant (P <0.05).

Serum testosterone level

The mean serum level of testosterone within the control group was 0.3±0.03 ng/ml, while, in the group of PCOS patients, it was 1.05±0.1 ng/ml, as shown in table 6. The difference between the two groups was statistically significant (P <0.05).

LH/FSH ratio

The LH/FSH ratio for patients with PCOS was 1.8 ± 0.6 and for the control group was 0.5 ± 0.3 , with a significant difference between the two groups, as shown in table 6.

Table 6- Comparison of hormonal levels in PCOS patients and control women.

Parameters	Mean \pm SE	
	Control women	PCOS patients
LH (mmol/L)	(3.2 \pm 0.2)	(7.8 \pm 0.6) *
FSH (mIU/ml)	(7.1 \pm 0.4)	(4.2 \pm 0.5) *
LH/FSH ratio	(0.5 \pm 0.3)	(1.8 \pm 0.6) *
Testosterone (ng/ml)	(0.3 \pm 0.03)	(1.05 \pm 0.1) *

-The difference between the two groups was statistically significant (*= P <0.05).

4-Discussion

Results of this study showed that women with PCOS had higher BMI than age-matched controls. Also, the prevalence of overweight and obesity was much higher in PCOS women than in their matching controls. Obesity condense the metabolic disorder and clinical criteria in women with PCOS. This finding was in agreement with a study by [15] which indicated that obesity is a familiar morbidity associated with PCOS and that the accompanying insulin resistance is a key pathogenesis of PCOS. The relationship of obesity with PCOS was already illustrated, which gives insight into the expansion of typical criteria for obesity in PCOS. Similar results by other reports [16, 17] were concluded in women with PCOS, where mean BMI in PCOS women was significantly higher than the control groups. Valkenburg *et al* [18] revealed that obesity (BMI \geq 30 kg/m²) occurred more recurrently in PCOS women compared with the control group, while another study [19] indicated that the threat of PCOS is minimally enhanced with obesity, though the degree of obesity of PCOS patients has augmented, similar to that observed in women without PCOS in the present study. This information indicates that obesity in PCOS women reflects environmental factors to a great degree. Apridonidze *et al* [20] stated that the increased weight and obesity (mostly abdominal) were widespread in women with PCOS, while another investigation found no difference in BMI between any of the PCOS groups and their matching controls [21].

Clinically, hyperandrogenic women with PCOS demonstrated hirsutism, acne, and temporal balding. The current study revealed that the frequency and percentage of clinical hyperandrogenism were augmented with increased BMI and that there were significant differences (P<0.05) in hirsutism, acne, and alopecia among lean, overweight, and obese PCOS patients. The clinical hyperandrogenism is augmented by overweight and obesity. We found that obese women with PCOS had a higher prevalence of clinical hyperandrogenism and, hence, obesity was considered to be responsible for hyperandrogenemia and the resulting hormonal abnormality and reproductive disorder in women with PCOS. These results agree with other authors [22] who found that PCOS women with obesity are susceptible to have higher hirsutism and acne signs than their lean counterparts. In fact, sex hormone binding globulin levels are decreased in obese women with PCOS, particularly if they present with abdominal obesity. It was found that overweight girls had significant hyperandrogenemia compared to their counterparts with normal weight [23], findings indicating that obesity plays an exciting role in the early progress of androgen excess, which may render PCOS more rapid. Corbould [24] reported that a key feature of PCOS is the increased levels of androgens. A side from their effects on ovarian function and phenotypical features, like alopecia, they also affect where fat is stored in the body. Majumdar and Singh [25] found that hyperandrogenism was present with hirsutism and acne was significantly higher in the overweight PCOS women.

A study conducted in Iran reported that women who had hirsutism were significantly more obese and younger than those without hirsutism [26]. Another study from Germany assessed the class of life reported by 120 PCOS women and the outcome revealed obesity and hirsutism to be associated to lower class of life scores [27].

It was also reported that the prevalence of menstrual irregularity and the clinical features of hyperandrogenism (hirsutism, acne, alopecia) were elevated in obese than in lean women with PCOS, but there was no statistically significant difference between the two studied groups [28]. However, another study demonstrated that 42% of the PCOS women had typical BMI (lean), but the clinical signs (hirsutism and acne) were analogous to PCOS women with increased BMI (overweight/obese) [29]. Norman *et al* [30] reported that PCOS is a varied endocrine disorder. The main endocrine disturbance is an extreme androgen secretion or activity, with frequent clinical signs of hyperandrogenism such as hirsutism, acne, and alopecia can appear as a result of hypersecretion of androgen by the ovary. Azziz *et al* [13] showed that about 60% of PCOS women are hirsute, which is the most common clinical feature of hyperandrogenemia. Ikhen *et al* [31] mentioned that scalp hair thinning is a prevalent sign in PCOS women. Tissue, rather than systemic endocrine environment appear to be of significance for scalp hair growth and density. Birch *et al* [32] found that PCOS women were six times more possible to distinguish scalp hair thinning compared with 6% incidence described in their matching controls. In the present study, we showed that 65.0 % of PCOS patients had clinical signs of alopecia, while a previous study [33] reported that alopecia is common in 22% of women aggregating diagnostic criteria for PCOS. Androgenic alopecia is linked with other aspect of clinical hyperandrogenism, but not with more risk of biochemical hyperandrogenemia or metabolic disorder than with PCOS alone.

Menstrual disturbance was the main frequently present complaint in PCOS women. The present study showed that 82.5 % of PCOS patients had clinical signs of menstrual disturbance (abnormal uterine bleeding, oligomenorrhea and amenorrhea) compared to 94% in a previous study [28]. Results of this study showed that obese PCOS women had a higher occurrence of menstrual dysfunction (abnormal uterine bleeding, oligomenorrhea, and amenorrhea) than lean and overweight PCOS women. This explains the fact that increased BMI was also associated with an increased rate of menstrual dysfunction. High serum levels of LH and testosterone in PCOS women may be associated with menstrual cycle dysfunction.

However, it was demonstrated that 79.2% of PCOS women with BMI > 23 and 44% of those with BMI ≤ 23 were with menstrual disturbance [25]. Other studies [22, 34, 35] showed that, as compared to non-obese PCOS women, obese women with PCOS have more menstrual irregularity and uterine dysfunctional bleeding, in addition to an increased occurrence of infertility, which were also related with an abdominal distribution of fat. Harris *et al* [36] reported that extended and irregular menstrual cycles, a feature of PCOS, was related with elevated androgen and slight sex hormone binding globulin levels, and that this altered hormonal environment may raise the risk of certain histologic ovarian cancer. Azziz *et al* [37] found that 75-85 % of women with PCOS had clinically obvious menstrual disturbance, while another study found that 75% of PCOS patients were with clinically obvious menstrual disturbance [38]. It was reported that irregular menstrual cycle was analogous in the lean and overweight/obese PCOS groups [29].

The results of LH, FSH, and testosterone levels as well as LH/FSH ratio in the present study were in agreement with the results of previous investigations [39-42] who showed that the elevations in testosterone and LH levels, accompanied by reduced FSH level and higher LH:FSH ratio, were the main endocrine changes observed in women with PCOS. Lewandowski *et al* [43] found that PCOS women have an increased speed of hypothalamic GnRH pulses, leading to an increase in the LH/FSH ratio. Ibrahim and Abdelsalam [44] reported in their study that a significant increase was found in LH, testosterone and LH/FSH ratio, while FSH level was insignificantly increased in PCOS women. Cascella *et al* [45], along with another study [46], reported that the level of LH was significantly elevated in PCOS women than in the control group, while the level of FSH did not alter significantly. In another study [47], elevated levels of FSH and LH were reported in PCOS women. Elevated LH relation to FSH was also documented in PCOS women compared with control subjects [48]. Furthermore, there was an insignificant variation ($P > 0.05$) in LH/FSH ratio between the two groups.

Conclusion

Polycystic ovary syndrome is a frequent endocrinopathy disturbing women of reproductive age. It is the widespread reason of infertility. Moreover, more than half of the PCOS patients were obese. Based on the available data, clinical symptoms such as menstrual cycle dysfunction and hyperandrogenism present with hirsutism, acne, and temporal balding were excessive in obese women with PCOS. However, the role of weight reduction is useful in the management of PCOS. This study

clearly shows that the majority of patients with PCOS have high levels of testosterone and LH that seem to correlate with clinical hyperandrogenism in PCOS patients.

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