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RESEARCH ARTICLE

Relationship of Body Mass Index and Hormonal disturbance in patients with Polycystic Ovary Syndrome.

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Abstract

polycystic ovary syndrome (PCOS) and obesity are commonly seen in women of reproductive age . The study includes 50 infertile Iraqi women with polycystic ovary syndrome (PCOS) and 20 healthy women, Blood samples were collected from the Infertility center of AL-Yarmok Teaching Hospital in Baghdad / Iraq. The age of PCOS women and healthy women was ranged from 16 to 45 years. The results were as follows: There is significant ($P < 0.05$) decrease in E2 levels 34.90 ± 2.39 pg/ml and FSH levels 7.0 ± 0.41 µIU/ml in PCOS women. There is significant ($P<0.05$) increase in LH levels 13.51 ± 3.88 µIU/ml in PCOS women and there is no significant differences in Testosterone levels 1.50 ± 0.30 ng/ml . The ratio of LH/FSH was >1.5 but no significantly . The hormonal profile according to BMI was as follows: There is no significant ($P < 0.05$) decrease in E2 levels in overweight PCOS women 29.8 ± 3.0 pg/ml compared with normal weight but no obese PCOS women .Testosterone was significant increase in obese and overweight PCOS women 1.3 ± 0.5 ; 1.2 ± 0.15 ng/ml respectively .There is significant ($P < 0.05$) decrease in FSH level in both overweigh and obese PCOS women 7.9 ± 0.7 ; 5.96 ± 0.43 µIU/ml respectively.

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INTRODUCTION

Polycystic ovary syndrome (PCOS) was first described in 1935 by Stein and Leventhal **(Marx and Mehta, 2003)**. PCOS is a common endocrine disorders in women with reproductive age , is associated with marked increases in ovarian androgen production and insulin resistance .Although the pathogenesis of PCOS remains uncertain , insulin resistance and hyperinsulinmia are found in approximately 80 % affected women. The long-term consequences include increased risk for diabetes mellitus, increased blood lipid (dyslipidimia) and cardiovascular disease(**Guyton and Hall, 2001).**

Several theories have been proposed to explain the pathogenesis of PCOS:

1- An increase in(GnRH) secretion results in increased (LH) secretion (**Tsilchorozidou *et al*., 2004**)
2- An alteration in insulin secretion and insulin action results in hyperinsulinmia and insulin resistance. (**Ehrmann, 2005**).
3- A defect in androgen synthesis that results in an increased ovarian androgen production. **(Hill,2003**)

Obesity is defined as a body mass index (BMI) exceeding 25 or 27. It is estimated that 50% to 90% of women with PCOS are obese, which is higher than the prevalence rate of obesity in the general population (**Franks,1995**). Obesity is a risk factor for diabetes and a centripetal pattern of obesity is seen in women with PCOS (**Legro,2001**).Women with PCOS with a BMI of 23 to 28 were shown to have a relative risk of 3.6 for the development of diabetes when compared with thinner women (BMI of < 22) in the Nurse's Health study(**Zacur,**

2001). Both obese and nonobese women with PCOS have a higher incidence of insulin resistance and hyperinsulinmia than age matched controls. Insulin resistance is known to precede the development of type 2 diabetes mellitus (**Ehrmann, 2005**) .

There have been no genome wide screens of PCOS, and all reported genetic studies have used candidate gene approach in which genes are selected for analysis based on pathophysiology. Acceptable candidate gene for PCOS include those encoding proteins involved in steroid hormone biosynthesis ,Gonadotropin secretion or action, obesity and energy regulation, and insulin action **(Urbanek *et al* ., 1999)** . The aims of this study was to determine the correlation between the BMI and hormonal disturbance in patients with PCOS.

Material and methods:

Two study groups have been investigated: Healthy control group consists of twenty healthy fertile women of different ages, but all of them are chosen dependent on the next criteria (**Macklon and Fauser, 2000**)

- Regular menstrual cycle (26 to 30 days)
- Normal body mass index (18 to 25 Kg/m²),
- No history of endocrine disease
- No use of medication or oral contraceptives.
- Ultrasongraphic and blood sampling were collected during the follicular phase (3, 4, or 5 day).

Patients group include fifty Iraqi women with PCOS. Patients were selected from the Infertility Center of Al-Yarmouk Teaching Hospital. All subjects were mostly from the capital Baghdad /Iraq. *To enroll the subjects with PCOS should include* at least two of the following three features (**Mulders *et al*., 2005**):

1. The presence of polycystic ovary morphology
2. Oligo and /or anovulation.
3. Clinical and /or biochemical features of hyperandrogenism.

Hormonal assay:

Venous blood sample (5 ml) was collected from both PCOS and healthy control. The serum obtained by putting the blood samples in a plastic tube and allowed to clot at 37°C for 30 minutes before centrifugation. The tubes centrifuged at 5000 rpm for 5 minutes. Hormonal tests was performed by using Addendum-Mini VIDAS apparatus (VIDAS) 12 mode l0, BioMerieux Company, through an enzyme linked fluorescent assay (ELFA) technique. All the assay steps are performed automatically by the instrument. The assay will be completed within approximately 60 minutes . The values of hormonal assays for the subjects were compared with the next normal range: E2 = 18-175 pg /ml, FSH = 3.9-12 µIU/ml, LH =1.5- 8 µ IU/ml, and T = 0.1- 0.9ng/ml.

Body Mass Index:

The female body mass index (BMI) was measured according to the following equation: dividing the weight in kilograms by the height in squared meters (kg/m^2) (**Flegal *et al*., 2005**)**.** The parameter of BMI : Underweight ≤ 18.5 , Normal 18.5-24.9, Overweight 25-29.9 and Obesity ≥ 30. **(European Society of Human Reproduction and Embryology, 2009)**

Statistical analysis:

The statistical analysis system –SAS (2004) program was used to the effect of difference factors in traits in this study. Least significant difference (LSD) test was used to the significant compare between means.

Results and Discussion:

1-Polycystic Ovary Syndrome and hormonal profile :

The results obtained from hormonal analysis revealed that the E2 and FSH have a significant lower levels 34.9±2.39 pg/ml ; 7.0 ± 0.41 **µIU/ml** respectively; than the control group (54.07±7.02 pg/ml; 13.56 ±3.79 **µIU/ml** respectively; in PCOS women . Other parameters such as LH and LH/FSH ratio showed no significant levels. On the other hand, testosterone levels showed elevated level (1.43±0.29) ng /ml than control group (0.60 ±0.13) ng/ml in PCOS women with no significant (P>**0.05) different** (Table :1). Chang and Katiz (1999) showed the E2 level in

PCOS women may be low to normal. The increase in serum **Anti-Müllerian Hormone** (AMH) level in PCOS women resulted from an increased production of this hormone per follicle , the elevated of AMH amount led to an inhibits of aromatase activity therefore the follicle did not produce a sufficient amount of E2 hormone (Agarwal *et al*., 1999).

The elevated of testosterone was related with the LH Hypersecretion which was in positive correlation with the elevated serum of 17-hydroxyprogestrone , androstenedione and testosterone Carmina *et al*.(2006) . Allahbadia and Merchant (2011) listed additional causes of hyperandrogenism as :

- An increased synthesis of testosterone precursors due to a dysregulation of theca cell androgen production.
- An inhibin augmentation of LH-mediated androstenedione production.
- Hyperinsulinmia which has been proposed as the primary event leading to hyperandrogenism.
- An increased serine phosphorylation of the insulin receptor, resulting in an activation of both ovarian and adrenal P450c17α enzymes and promoting androgen synthesis.

The high level of LH which was recorded in this study was explained by **MecCartney *et al*. (2002**) who found that the PCOS women as exhibiting an accelerated frequency and / or higher abundance of LH pulses ,augmentation of LH secretory burst mass, a more disorder in LH secretion. One study reported that 75% of PCOS women have an elevated LH level, because of the elevated insulin levels that cause the abnormalities in hypothalamic-pituitary-ovarian axis that lead to PCOS (**Taylor *et al*., 1997**).

Follicle Stimulating Hormone (FSH) levels was significantly lower in PCOS compared with **healthy group** .The reduction levels of FSH can be explained by :

- High levels of inhibin that have been found in the PCOS women which lead to FSH reduction (**Ehreman *et al*., 1992**).
- Overexpression of Follistatin leading to the increase of ovarian androgen production (**Urbanck *et al*., 1999**).

The results obtained revealed that there was LH/FSH>1.5 in PCOS **women**(1.51±0.168) compared with healthy group (0.991 ± 0.008). there were more than 75% of PCOS **women** with dyesregulation in gonadotropic function and explained that the normal pulsatile secretion of LH was increased by an increased frequency and amplitude of pulses, while that of FSH is unchanged or muted ,therefore the LH values may be elevated; On the other hand, these values may be normal in as many as 10% to 20% of women with PCOS (**Arroyo *et al* .(1997**)

Table (1) : Mean endocrine-metabolic values (± SE) of polycystic ovary syndrome and healthy women.

Hormones	Mean ± SE		LSD value
	PCOS	Healthy control	
E2 (pg/ml)	34.90 ± 2.39	54.07 ± 7.02	17.464 *
T (ng/ml)	1.50 ± 0.30	0.60 ± 0.13	2.102 ns
LH (µIU/ml)	13.51 ± 3.88	10.04 ± 0.98	7.247*
FSH (µIU/ml)	7.0 ± 0.41	13.56 ± 3.79	3.517 *
LH/FSH	1.51 ± 0.168	0.99 ± 0.008	1.203 ns

* (P<0.05) , ns: non-significant. T: Testosterone, E2: 17 β-Estradiol, LH: Luteinizing Hormone, FSH: Follicle Stimulating Hormone, SE: Standard error, PCOS: Polycystic ovary syndrome, LSD: Least Significant Differences .

2-Body Mass Index and Hormonal changes:

The results of this study shown in table(2) indicate that there has been significantly lower (p<0.05) in T hormone levels in obese PCOS women (1.09±0.15)ng/ml and overweight PCOS women (1.26±0.54) ng/ml when compared with normal weight PCOS women (2.78±1.19) ng/ml , current results also showed the FSH levels which were significantly lower (p<0.05) in obese PCOS women (5.96 ± 0.43) µIU/ml when compared with normal weight PCOS women (7.94± 1.33) µIU/ml . There was no significant difference in serum levels of E2 and LH.

Obesity represents a probale pathogenetic factor since the FSH secretion of the pituitary is inhibited by the increased synthesis of E2 in the adipose tissues,the additional cyclic E2 lead to an increase secretion of LH of the pituitary **(Breckwoldt *et al*., 1994)** .

Benson *et al*.(2008) reported the obese and overweight PCOS women who had increase levels of T hormone and LH. **Wang *et al*.(2001)** reported that there was high prevalence of overweight/obesity in PCOS women ,the obesity is associated with insulin resistance and correlated with decreased SHBG which caused an increase in circulating testosterone (**Chang,2004**). Two studies by Arroyo et al [45] and Morales et al[46]addressed the role of obesity in the abnormalities of the gonadotropin axis in PCOS and reported consistent results: accelerated LH pulse frequency is seen in many patients with PCOS, regardless of body weight, but obese patients exhibit lower LH pulse amplitude and mean circulating LH values than lean patients. Factors proposed to account for these differences include variations of insulin and leptin levels, as well as differences in cathecholamine and endorphine metabolism. The exact mechanism, however, remains unclear.

Freytag (2003) proved that hyperandrogenaemia possibly causes android fat after hirsutism in PCOS women and confirmed the suggestion that obesity caused by hyperandrogenaemia is mostly adrenocortical obesity. She also report that both hyperandrogenaemia and obesity are related to the insulin metabolism. In PCOS the estrone level increases due to conversion of androstenedione in adipose tissue which additionally stimulates LH and inhibits FSH (**Marx and Mehata, 2003**).

Table (2): Body Mass Index of polycystic ovary syndrome women and hormonal profile (Mean ± SE).

Hormones	Body Mass Index			LSD value
	Normal weight	Overweight	Obesity	
E2 pg/ml	35.1 ± 6.3	29.8 ± 3.0	39.0 ± 3.93	9.237 ns
T ng/ml	2.8 ± 1.1	1.3 ± 0.5	1.2 ± 0.15	1.231 *
LH µIU/ml	11.6 ± 3.0	11.5 ± 1.6	8.28 ± 1.27	3.924 *
FSH µIU/ml	7.9 ± 1.3	7.9 ± 0.7	5.96 ± 0.43	1.663 *

* ($P<0.05$) , ns: non-significant. E2: 17 β-Estradiol, T: Testosterone, LH: Luteinizing Hormone, FSH: Follicle Stimulating Hormone, SE: Standard error, LSD: Least Significant Differences, BMI: Body Mass Index weight/heigth²)

Conclusions :

Polycystic ovary syndrome can be considered as a complex and heterogeneous metabolic syndrome because of the heterogeneity of this disorder This study confirmed the role of hyperandrogenaemia with both Obesity and overweight in women with PCOS

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