Testosterone level and body mass index in women with polycystic ovary syndrome

Sabah N. Alwachi[1], Yasmin L. Alsaadi[1] and Nuhal N. Jebri[2]

1 Department of Biology, College of Science, Baghdad University.

2 Kamal AL-Samaraay Hospital, Baghdad-Iraq

Abstract:

Background

Elevated serum concentrations of testosterone is common in women with polycystic ovary syndrome (PCOS) but it's relation to body mass index(BMI), is still unknown.

Objective

The present study was conducted to investigate the relationship between testosterone level and body mass index in women with polycystic ovary syndrome.

Methods

A total of eighty PCOS women with average age 27.6±0.7 and BMI 31.9±0.5 were compared with twenty-two healthy women considered as a control group (age 28.2±1.1, BMI 28.8±1.0). Patients and controls were grouped according to (BMI: Lean, overweight and obese. All women in both groups were subjected to the following investigations: evaluation of luteinizing hormone (LH), follicle stimulating hormone (FSH.), prolactin (PRL), testosterone levels and ultrasonography.

Results

The serum levels of LH, LH/FSH and testosterone were significantly higher ($P< 0.05$) in PCOS compared to control women ,while in FSH and PRL the difference was non significant. Obese women with PCOS also had a significantly higher ($P<0.05$) mean level of testosterone (1.33±0.28ng/ml) compared to lean and overweight patients (0.53±0.17, 0.61±0.08 ng/ml respectively). Ultrasound examination was performed in the ovulatory phase during (12-14) days of the cycle in both PCOS patients and controls, and all women with PCOS with evidence of polycystic ovaries on ultrasonography.

Conclusion

Testosterone level was significantly elevated in obese compared to overweight and lean women with PCOS .The role of weight reduction is more beneficial in the management of PCOS and improvement of testosterone level.

Key words: Polycystic ovary syndrome, LH, FSH, Body mass index.

Introduction

The polycystic ovary syndrome is a common endocrine-metabolic disease, affecting 5-10% of women during reproductive age and it is the first cause of infertility in women (1). This syndrome is also called Stein-Leventhal syndrome as was first described in 1935 (2). The diagnosis of PCOS is made when at least two of the following three criteria existed, as proposed at the Rotterdam Consensus Meeting: oligomenorrhea - and/ or anovulation ; Clinical and/or biochemical signs of hyperandrogenism; polycystic ovaries on ultrasonography (3).

However, not all women with polycystic ovary demonstrate the clinical and biochemical features which define the PCOS. These features include menstrual cycle disturbances, obesity, hyperandrogenism, infertility and abnormalities of biochemical profiles including elevated serum concentrations of LH, testosterone, androstenedione and insulin (4). Hyperandrogenemia is the key feature of the syndrome; it is mainly of ovarian origin although an adrenal contribution can not be excluded.

Most, but not all, women with PCOS have high plasma levels of androgens. Androstenedione and testosterone are markers of ovarian androgen secretion and dehydroepiandrostenedione sulfate (DHEAS) is the best marker of adrenal secretion. Hyperandrogenemia is not always linked to hyperandrogenic signs such as acne or hirsutism (5). Obesity, specifically abdominal obesity, is a common PCOS feature (6). Up to 70% of women with PCOS are

obese (7). Abdominal obesity is associated with high oestrogen production, increased serum oestrone concentration, and greater amount of free oestrogen as a result of decreased sex hormone binding globulin (SHBG) concentrations, favouring a hyperoestrogenic state (8).This exerts positive feedback regulation upon LH release and further increasing of ovarian androgen secretion (9).Testosterone is known to facilitate lipolysis, providing increased free fatty acids (FFAs) concentrations (10). And rogens and increased FFAs, common in central abdominal obesity, inhibit hepatic insulin excretion ,resulting in hyperinsulinemia and insulin resistance (11) and induce defects in skeletal muscle cells uptake of glucose and glycogen synthesis (12). Ovarian androgens are produced in theca cells and diffuse across the basement membrane to t he granulosa cells, which in response to FSH stimulation regulate aromatase activity,converting these and rogenic precursors to oestrone and oestradiol (E2). Androgens are obligate substrates for E2 biosynthesis and they promote the growth of small follicles (13). A romatase activity may be decreased in granulosa cells and follicles from women with PCOS, and the possible androgen excess resulting from this decreased activity might contribute to abnormal follicle development (14) .Weight loss may improve menstrual abnormalities , hirsutism and also helps in reducing hyperinsulinemia and IR. In addition, gonadotropin and sex steroid secretion may also be corrected (15) in addition to the increase in SHBG (16).

Materials and methods

Subjects

Eighty women with PCOS (patients group) and twenty two healthy women (control group) were consecutively enrolled in this study at infertility clinic population of Kamal AL-Samaraay Hospital in Baghdad.

All women in the patients group were in reproductive age of (17-40) years old. They also had

one or more of the following symptoms: menstrual cycle disturbances (oligomenorrhea, amenorrhea, abnormal uterine bleeding); Hirsutism, acne, temporal balding, and obesity .

Diagnosis of PCOS in patients were confirmed by:

Ultrasound of the ovaries looking for the morphological changes related to PCOS such as (presence of 8 or more subcapsular cysts ≤10 mm in diameter with increased ovarian stroma), and endocrine secretion assessment by measurement of hormones levels in serum such as (LH , FSH , Testosterone and PRL).

The women in the control group were characterized by the following :

They were in reproductive age of (20-40) years old ; had no hirsutism, acne or temporal balding ; non of them had a past history of primary or secondary infertility and they had a past history of regular menstrual cycles with a normal ovarian morphology on ultrasound examination.

Blood samples

Blood samples were collected between 8-10 AM in the early follicular phase, on days 2 or 3 of the last menstrual period in both PCOS patients and controls. In PCOS patients, the last menstrual period was either spontaneous or induced by the administration of progestin (17).

Ten ml of venous blood samples were collected into disposable plain plastic tubes. Blood was allowed to coagulate at room tempreture and then centrifuged at 3000 rpm for 15 min. Serum was separated and stored at -20°c until hormonal assay.

Body mass index

Body mass index was obtained by the ratio of weight (kg) over height in square meter (m^2), and is expressed in kg/m^2 (18).

The World Health Organization (WHO) international classification system was used in this study regarding to BMI to define lean, overweight and obesity "Table 1"(19).

Hormonal assay

Serum concentrations of four hormones (testosterone, PPL, LH and FSH) were measured by using mini-VIDAS (VIDAS 12 model, 1992), through an enzyme linked fluorescent assay (ELFA) technique (20).

Statistical analysis

Statistical analysis was performed using Statistical Package for Social Science (SPSS) ver.12 . The level of significance was at $P<0.05$. Discribtive analysis was used to show the mean ±SE for age, BMI and hormones. Number and percentage was used to show the distribution BMI groups. Chi-square test was used to check the relationship between BMI groups with patients and control, hirsutism, acne, temporal balding, menstrual cycle and infertility. t- test and ANOVA was used to test the difference for age, BMI and Hormones between BMI groups with patients and controls (21).

Results:

No significant differences ($p>0.05$) were found between the mean age of the PCOS patients and control groups. The mean age of PCOS patients group was (27.6±0.7) and the control group (28.2±1.1).

There was an increase in BMI in PCOS patients (31.9±0.5) as compared with the control group (28.8±1.0), but the difference was non significant ($p>0.05$). Furthermore three patients (3.75%) and four control (18.18%) were within normal body weight range (lean), twenty eight patients (35.0%) and nine control (40.91%) were overweight and fourty nine patients (61.25%) and nine control (40.91%) were obese (Table 2). This difference among BMI subgroups in PCOS women was statistically significant ($p<0.05$).

Table (1) : The international classification of adult lean, overweight and obesity according to BMI (19)

Classification	BMI (Kg/m²)
Lean	18.50-24.99
Overweight	=25.00
Obese	=30.00

Table (2) : The classification of body weight in PCOS women.

Body weight classification	PCOS group (n=80)
Lean	3 (3.75 %)
Overweight	28 (35.0 %) **
Obese	49 (61.25 %) *

*** P < 0.05 = Significantly different than other groups**

**** P< 0.05 =Significantly different than lean group**

The results showed that the percentage of hirsutism in PCOS patients was (63.75%); in lean (3.92%), in overweight (29.41%) and in obese was (66.67%). The percentage of acne was (30%); in lean (4.16%), in overweight (29.17%) and in obese (66.67%) while the percentage of temporal balding was (65%); in lean (3.85%), in overweight (30.77%) and in obese was (65.38%) (Table 3).

Table (3) : Different clinical criteria and their relation to BMI in PCOS

Clinical criteria	PCOS groups			Total number (N=80)
	Lean N=3	Overweight N=28	Obese N=49	
Hirsutism	2 3.92 %	15 29.41 %	34 * 66.67 %	51 63.75 %
Acne	1 4.16 %	7 29.17 %	16 * 66.67 %	24 30.0%
Temporal balding	2 3.85%	16 30.77%	34 * 65.38%	52 65.0%
Eumenorrhea	0 * 0 %	8 57.14 %	6 42.86 %	14 17.5%
Abnormal uterine Bleeding	0 * 0 %	4 50.0 %	4 50.0 %	8 10.0%
Oligomenorrhea	3 * 6.38 %	1 531.92 %	29 61.70 %	47 58.75%
Amenorrhea	0 0 %	1 9.09 %	10 * 90.91 %	11 13.75%
Primary infertility	1 1.85%	1 935.19%	34 * 62.96%	54 67.50%
Secondaryinfertility	2 7.69%	9 34.62%	15 * 57.69%	26 32.50%

*** P<0.05 = Significantly different than other groups.**

In the present study, the whole PCOS group was divided into four subgroups according to the menstrual status, fourteen patients were with eumenorrhea (17.5 %), eight patients were with abnormal uterine bleeding (10 %), forty seven patients were with oligomenorrhea (58.75%) and eleven patients were with amenorrhea (13.75%) (Table 3).Differences were significant (P<0.05) among lean, overweight and obese PCOS patients.

The present study showed that all women with PCOS are infertile. Primary infertility occurred in fifty four PCOS patients (67.5%) and twenty six PCOS patients (32.5%) were with secondary infertility. The frequency and percentage of primary and secondary infertility increased among obese PCOS patients (Table 3) . However, there was a significant differences ($p < 0.05$) among PCOS patient subgroups. While, the high levels of LH and testosterone are due to the persistent anovulation in women with PCOS.

Furthermore , it was also found that the mean serum level of LH, FSH, LH/FSH ratio, testosterone and prolactin were 7.8±0.6 mIU/ml, 6.2±0.5 mIU/ml, 1.3±0.6, 1.05±0.1 ng/ml and 16.3±1.1 ng/ml ,respectively in patients with PCOS. However, the mean serum levels for control group were 3.2±0.2 mIU/ml of LH, 7.1±0.4 mIU/ml of FSH, 0.5±0.3 of LH/FSH ration, 0.3±0.03 ng/ml of testosterone and 15.21±0.9 ng/ml of PRL, respectively (Table 4).

There was a significant (p<0.05) increase in LH, LH/FSH ratio and testosterone level compared to control group, while the levels of FSH and prl were not statistically significant (p>0.05) between PCOS and control groups, although PRL level was elevated (more than 25 ng/ml) in fourteen patients (17.5%) of 80 PCOS patients (Table 4).

The mean serum level of testosterone was elevated in obese and overweight as compared to the lean PCOS patients and this difference was significant (P<0.05) (Table 5).

Table(4): hormonal levels in PCOS and control groups

Parameters	Mean ± SE	
	Control group	PCOS group
LH (mIU/ml)	(3.2±0.2)	(7.8±0.6)*
FSH (mIU/ml)	(7.1±0.4)	(6.2±0.5) N.S.
LH/FSH ratio	(0.5± 0.3)	1.3± 0.6)*
Testosterone (ng/ml)	(0.3±0.03)	(1.05±0.1)*
PRL (ng/ml)	(15.21±0.9)	(16.3±1.1) N.S.

* P<0.05 = Significant compared to control group

N.S. : Non significant

Table (5): Serum testosterone level in PCOS subgroups

PCOS subgroups	Testosterone (mean±SE)
Lean	(0.53±0.17)
Overweight	(0.61±0.08)
Obese	(1.33±0.28) *

* P< 0.05 = Significantly different than other groups

Discussion

In this study, the prevalence of obesity in women with PCOS is much higher than those with no PCOS.Thus, obesity intensify the metabolic disturbances and clinical criteria in women with PCOS . The present result was in agreement with that found by Apridonidze et al. (22) who showed that the increased weight and obesity (mostly abdominal) were common in PCOS women. Vrbikov et al.(23) revealed that PCOS women had a significantly higher BMI than in control. While Yesilada et al. (24) reported non significant difference in BMI between PCOS and control groups.

The frequency and percentage of clinical hyperandrogenism were increased with increased body weight and there are significant differences (P<0.05) in hirsutism, acne, temporal balding among lean, overweight and obese PCOS patients. The clinical hyperandrogenism are amplified by overweight and obesity. We found that obese women with PCOS had a greater prevalence of clinical hyperandrogenism due to elevated serum testosterone level in the obese subjects . This result confirmed what already found by Ducluzeau et al. (25) who showed that obesity in women with PCOS increases the pathology, worsens symptoms , and in some individuals might underlie the clinical presentation . However , Guyatt et al.(26) reported that patients with PCOS frequently developed androgen-related dermatologic complaints, including hirsutism, acne and androgenic alopecia.

Moreover, ,obese women with PCOS was found to have a higher incidence of menstrual dysfunction (oligomenorrhea and amenorrhea) than lean and overweight women with PCOS. Our results confirm that the increase in BMI was also associated with an increase in the rate of menstrual dysfunction. Menstrual dysfunction also reflects chronic anovulation and is characterized by irregular and infrequent bleeding. High serum LH and testosterone levels in women with PCOS were found to be associated with menstrual cycle dysfunction. However, irregular bleeding was a consequence of excessive endometrial proliferation due to unopposed chronic oestrogen secretion. The results of this study was in agreement with the results of Dewailly *et al.*(27) showed that (13.8%) of patients were with

amenorrhea and (62.1%) with oligomenorrhea. Haddad et al. (28) also found that (82.2%) of PCOS patients were with oligomenorrhea and (17.8%) with eumenorrhea , while other study (29) showed that 100% of PCOS patients were with oligomenorrhea.

The present study showed that all women with PCOS were infertile which is in agreement with that of Balen et al.(30) who reported that obesity was also associated with an increased rate of infertility, 46% patients who were with primary infertility and 26% with secondary infertility had a BMI >30kg/m2. Azziz *et al.* (31) had shown that 100% of patients with PCOS suffered from ovulatory dysfunction, which reduces their overall fecund ability. However, not all patients with PCOS are absolutely infertile, as many of women with PCOS found to ovulate intermittently.

High level of LH has been considered to be the cause of the excess testosterone secretion in PCOS women and. Increased body weight is associated with adipose-related aromatization of androgen to estrogen. This exert positive feedback on hypothalamus, resulting in increased LH secretion more than FSH secretion and elevated LH/FSH ratio. increased body weight is associated with adipose-related aromatization of androgen to estrogen. This exert positive feedback on hypothalamus, resulting in increased LH secretion more than FSH secretion and elevated LH/FSH ratio.

High serum LH and testosterone levels were found to be associated with hirsutism, infertility and menstrual cycle dysfunction.

The results of LH and FSH levels in the present study were in agreement with the results of Yesilada et al.(24) and Cascella et al.(32) who reported that the level of serum LH was significantly higher in PCOS group than in the control, whereas the level of FSH did not change significantly.

The LH/FSH ratio was higher in PCOS group than in control group and this results was in agreement with the results of Topcu et al. (33) and Welt et al. (34) who found that PCOS group had significantly higher LH/FSH ratio than the control group. In the present study, twenty seven patients (33.8%) had abnormal LH/FSH ratio while fifty three (66.2%) were with normal ratio . In another studies, Kalro et al.(35) stated that in women with PCOS,55-75% have a high LH/FSH ratio.

Testosterone level in PCOS patients was significantly elevated when compared with the control group.

This was in agreement with some studies as Yesilada et al. (24) and Topcu et al. (33) who reported that the PCOS group had significantly higher serum level of total testosterone.

Testosterone level was elevated (more than 0.9 ng/ml) in 34 (42.5%) of patients with PCOS compared with that reported by Chang *et al.* (36)in which androgen levels were elevated in 60-80 % of PCOS patients.

The data of this work found that the mean of serum testosterone level was elevated in obese and overweight as compared to the lean PCOS patients. This was coincided with the findings of Pasquali (37) indicated that elevated androgens, such as dehydroepiandrosterone sulfate and testosterone, is associated with obesity. Kirschner et al.(6) showed that abdominal obesity commonly seen with PCOS, have higher free androgen levels compared to weight matched controls. Rebuffe - Scrive *et al.* (10) reported that testosterone is known to facilitate lipolysis and providing increased free fatty acids concentrations. Jonard et al.(17)reported that the intra-ovarian hyperandrogenism promotes excessive early follicular growth and that further progression cannot proceed normally because of hyperinsulinemia and/or other metabolic influence linked to obesity. Jonard and Dewailly(38) found that women with PCOS, ovarian volume seems to be under greater influence by hyperandrogenemia. Hyperinsulinemia or obesity might share the common pathway of hyperandrogenemia to affect the size of the antral follicle pool and ovarian volume.

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