Original Article

The Relationship between Reproductive Hormones and Metabolic Parameters in Women with Polycystic Ovary Syndrome

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Summary:

Background: Polycystic ovarian syndrome (PCOS) is a condition associated with chronic anovulation, and androgen excess. Clinically, PCOS women usually presents with menstrual irregularities, infertility, and hirsutism. Women with this syndrome are at increased risk of metabolic syndrome (MS).

Objective: To study the characteristics of the MS in women with PCOS.

Patients and Methods: This study was conducted during the period from March 2013 until the end of September 2013. A total of 50 PCOS women were studied (25 PCOS women with MS and 25 PCOS women without MS) with an age ranged from (35-45) years. Women with PCOS were referred to Medical City Hospital in Baghdad and compared with 25 healthy women as control group. Serum luteinizing hormone (LH), follicle stimulating hormone (FSH), prolactin, progesterone, testosterone, fasting serum glucose (FSG), serum triacylglycerol (TAG), and high density lipoprotein cholesterol (HDL-C) were measured for each individuals.

Results: Means of FSG, TAG, LH, prolactin, progesterone, testosterone levels, and LH/FSH ratio were significantly elevated in PCOS women than in the control group, while serum HDL-C levels were significantly lowered in PCOS women than in the control. There was a significant increase in FSG and TAG in PCOS women with MS as compared to PCOS women without MS, (P=0.0001).

While, there was a significant decrease in serum HDL-C in PCOS women with MS as compared to PCOS women without MS.2

No significant differences were found in LH, FSH, prolactin, progesterone, testosterone, LH/FSH ratio, day of menstrual cycle, and duration of infertility between PCOS women with and without MS.

Conclusions: The present study showed that PCOS women with MS had abnormalities in hormonal and lipid profile.

Key Words: Polycystic ovarian syndrome, metabolic syndrome, hormonal profile.

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Introduction:

Polycystic ovarian syndrome (PCOS) is a clinically and biochemically heterogeneous condition characterized by dermatologic, reproductive and metabolic manifestations (1), present in 12–21% of women of reproductive age, depending on the criteria used and the population assessed (2). Perpetual sequence of hormonal and metabolic aberrations in PCOS patients may commence early, even in adolescent period, and extend throughout life (3).

Metabolic abnormalities, including pre-diabetes, dyslipidemia, and metabolic syndrome (MS), have been widely studied in adult women with PCOS. Women with PCOS tend to have more than two to four times metabolic disturbances compared to those without PCOS (4). Metabolic syndrome encompasses a group of factors that together confers an increased risk of cardiovascular disease and is associated with insulin resistance and type 2 diabetes mellitus (5).

The gonadal hormonal homeostasis in PCOS women is altered. The disorder can be morphological (polycystic ovaries) or predominantly biochemical (hyperandrogenemia). Hyperandrogenism, a clinical hallmark of PCOS, can cause inhibition of follicular development, microcysts in the ovaries, anovulation, and menstrual changes (6). The other clinical features of PCOS are signs and symptoms of hyperandrogenism like hirsuitism, acne and baldness (7).

The relationship between PCOS and MS is possibly mutual. Thus, not only MS is prevalent among PCOS women, but also women with MS may commonly present the reproductive/ endocrine hallmarks of PCOS (8).

In all young women, irregular menses are common in the years immediately after menarche. Obesity has also been linked to increased androgen production and hirsutism (9). High androgen levels additionally worsen the disturbances in the lipid metabolism, it may lead to the abnormalities in lipoprotein profile by working directly at the liver through the induction of hepatic lipase activity and it decreases lipoprotein

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lipase activity in abdominal fat cells (10). Initial laboratory testing for the assessment of hirsutism should include total and/or free testosterone. Serum testosterone level is the best marker for ovarian hyperandrogenism (11).

Polycystic ovarian syndrome is a reproductive disorder because of the cysts formation in the ovaries. The increased level of luteinizing hormone (LH) and prolactin are a main diagnostic cause of this syndrome (12), and cause anovulatory infertility in women of reproductive age (13). The women with PCOS had lower concentrations of follicle stimulating hormone (FSH) and sex hormone-binding globulin while higher ovarian volume, LH to FSH ratio, free androgen index, concentrations of LH, and testosterone than the control women (14).

The aim of this study was to investigate the characteristics of metabolic abnormalities in women with PCOS.

Patients and Methods:

This study was conducted during the period from March 2013 until the end of September 2013. A total of 50 PCOS women were studied (25 PCOS women with MS and 25 PCOS women without MS) with an age ranged from (35-45) years. Women with PCOS were referred to Medical City Hospital in Baghdad and compared with 25 healthy women as control group. The separated serum was used for measurements of LH, FSH, prolactin, progesterone, testosterone, fasting serum glucose (FSG), serum triacylglycerol (TAG), and high density lipoprotein cholesterol (HDL-C). Women with PCOS were diagnosed according to the Rotterdam criteria (two out of three following criteria were sufficient for diagnosis of PCOS): (1) irregular menstruation, (2) clinical and/or biochemical signs of hyperandrogenism and (3) polycystic ovaries. All women included had polycystic ovary as judged by vaginal ultrasound, finding more than 10 follicles in each ovary of a diameter between 2 and 8 mm with an ovarian volume exceeding 6.2 ml was taken to be diagnostic (15). Irregular menstruation was defined as oligomenorrhea (< 6 menstrual periods/year) or amenorrhea (abnormal suppression or absence of menstruation for more than 6 months). All infertile women presented with infertility were subjected to special criteria: stopped any medication at least for three months before investigation, they were infertile at least one year, they had not been referred for in vitro fertilization or intrauterine insemination, the spermograms of their husbands had been reported as normal and had no any reproductive disorders, diabetes or evidence of cardiovascular disease, or infection. Metabolic syndrome was diagnosed using the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) definition (16).

Criteria for metabolic syndrome according to NCEP ATPIII definition

Risk Factor	Defining Level
Waist circumferences (WC)	>88 cm in women
Triacylglycerol (TAG)	≥150 mg/dl
High Density Lipoprotein Cholesterol (HDL-C)	<50 mg/dl in women
Blood Pressure (BP)	≥130/85 mmHg
Fasting Blood Glucose (FBG)	≥100 mg/dl

Measurements:

-Anthropometric Measurements: Body mass index (BMI) was calculated by dividing subjects weight (Kg) by their height (m^2). BMI calculated as: BMI= mass (kg)/(height (m))^2 (17).

Biochemical Assessments: Glucose was determined by using the enzymatic colorimetric method (GOD-POD) (18). Serum TAG and HDL-C were measured using an enzymatic colorimetric method (19, 20).

Serum LH, FSH, prolactin, progesterone, and testosterone were estimated by VIDAS using kits provided by Biomerieux (France). The assay principle combines an enzyme immunoassay sandwich method with a final fluorescent detection (ELFA) (21).

Statistical Analysis: The statistical package for the social science-version 17 (SPSS-17) had been used for all statistical analysis. Data were expressed as means (±SD). Student's t-test was used to test the significant differences between two means and the P value of less than 0.05 was considered to be significant.

Results:

Characteristics of PCOS and control group were summarized in table (1). There was a significant increase in BMI, WC, systolic blood pressure (SBP), diastolic blood pressure (DBP), FSG, TAG, LH, prolactin, and progesterone between PCOS women and the control group, (P=0.0001). While, there was a significant decrease in serum HDL-C between PCOS women and the control group, (P=0.0001). A significant increase was found in testosterone and LH/FSH ratio between PCOS women and the controls, (P<0.05). There was no significant difference in age, FSH, and day of menstrual cycle between PCOS women and control group.

Table (2) showed a significant increase in SBP, FSG, and TAG between PCOS women with and without MS, (P=0.0001). While, there was a significant decrease in serum HDL-C between PCOS women with and without MS. No significant differences were found in age, BMI, WC, DBP, LH, FSH, prolactin, progesterone, testosterone, LH/FSH ratio, day of

menstrual cycle, and duration of infertility between PCOS women with and without MS.

Table (1): Characteristics of PCOS and control group

Age (years)	38.27 ± 2.88	36.33 ± 0.30	0.652 NS
BMI (kg/m²)	29.63 ± 3.88	21.93± 0.59	0.0001
WC (cm)	87.34 ± 4.29	72.93 ± 1.06	0.0001
SBP (mmHg)	125.33 ± 7.74	120.0 ± 0.61	0.0001
DBP (mmHg)	84.80 ± 4.85	78.67 ± 0.67	0.0001
FSG (mg/dl)	102.80 ± 9.12	91.73 ± 1.54	0.0001
TAG (mg/dl)	142.40 ± 16.82	87.93 ± 6.92	0.0001
HDL-C (mg/dl)	44.63± 10.57	67.33 ± 1.02	0.0001
LH (IU/L)	15.16 ± 8.83	6.59 ± 1.12	0.0001
FSH (IU/L)	5.87± 3.76	7.40 ± 0.49	0.333 NS
Prolactin (µg/l)	25.86± 12.63	12.35 ± 0.82	0.0001
Progesterone (nmol/l)	7.64 ± 4.64	2.59 ± 0.47	0.0001
Testosterone (ng/ml)	2.89 ± 1.93	0.66 ± 0.03	0.045
LH/FSH ratio	2.57 ± 2.35	0.89 ± 0.09	0.045
% LH/FSH ratio: > 2 < 2	85% 15%	- 100%	-
Day of Menstrual Cycle	2.90 ± 1.12	2.53 ± 0.23	0.169 NS
Duration of infertility (years)	5.40 ± 3.61	-	-

NS: not significant.

Table (2): Comparison between PCOS with and without MS

Age (years)	39.93 ± 4.76	36.60 ± 1.61	0.684 NS
BMI (kg/m²)	30.73 ± 0.97	28.53 ± 0.98	0.571 NS
WC (cm)	88.80 ± 1.12	85.87 ± 0.98	0.751 NS
SBP (mmHg)	130.53 ± 1.24	120.13 ± 1.69	0.0001
DBP (mmHg)	86.60 ± 1.27	83.00 ± 1.08	0.411 NS
FSG (mg/dl)	110.80 ± 1.24	94.80 ± 0.89	0.0001
TAG (mg/dl)	152.60 ± 2.05	132.20 ± 4.46	0.0001
HDL-C (mg/dl)	38.67 ± 2.31	50.60 ± 2.23	0.0001
LH (IU/L)	17.85 ± 2.26	12.47 ± 2.28	0.214 NS
FSH (IU/L)	6.07 ± 0.96	5.67 ± 1.01	0.509 NS
Prolactin (µg/l)	26.30 ± 3.34	25.41 ± 3.28	0.278 NS
Progesterone (nmol/l)	8.60 ± 1.45	6.68 ± 0.85	0.306 NS
Testosterone (ng/ml)	3.59 ± 0.47	2.19 ± 0.47	0.410 NS
LH/FSH ratio	2.94 ± 0.19	2.20 ± 0.11	0.724 NS
% LH/FSH ratio: > 2 < 2	(90%) (10%)	(80%) (20%)	-
Day of Menstrual Cycle	3.20 ± 0.32	2.60 ± 0.23	0.169 NS
Duration of infertility (years)	6.20 ± 1.01	4.60 ± 0.82	0.231 NS

NS: not significant.

Discussion:

Women with PCOS may present with a wide range of symptoms. The Rotterdam criteria are the most widely accepted for diagnosis and the national guideline references these criteria. Women with PCOS have a higher risk of MS and its cardiovascular sequel (22). Women with PCOS assessed by Rotterdam criteria yet with regular cycles are metabolically less abnormal (23, 24).

Metabolic syndrome is a constellation of three main abnormalities (impaired FSG, dyslipidemia, and hypertension) which relate to a state of insulin resistance, and has been known for several decades. The same pathogenic mechanism is found in women with PCOS and in whom features of MS may also found (25). It has been indicated that age can influence both the clinical presentation and metabolic manifestations of PCOS (26). Obesity is an early step in the etiological cascade leading to full metabolic syndrome. Increased body weight in female significantly increases the risk of having MS (27). The present study has been suggested that BMI may influence the levels of reproductive hormones in PCOS women. Also, there was association between hypertension and PCOS, which is in agreement with the study of Azevedo et al. (28).

Dyslipidemia is one of the most common metabolic abnormalities in PCOS, and plays a crucial role in the incidence of MS, and is associated with increased risk of cardiovascular disease (29). All women with PCOS included in this study showed high serum FSG and TAG, while low serum HDL-C accordance to the others (30, 31). According to one explanation, associations between sex steroids and lipids are mediated by obesity and insulin resistance (32). Also, it has been shown that PCOS patients had higher levels of LH and LH/FSH ratio, while FSH was found to be low; a finding that was also reported by Saxena et al., (33). As a result of this derangement the ratio between LH and FSH levels which is normally around 2:1 and sometimes even more (2:1 or 3:1) in approximately 60% of the patients with PCOS. Similarly, some studies examined the association of metabolic parameters with LH/FSH ratio among PCOS women, and found statistically significant differences among two groups of women (34, 35), which is agree with the results obtained in this study. In addition, PCOS women had higher serum testosterone, but lower serum FSH than the control and these results were similar with what was reported by Fakhoury et al., (36).

Conclusions:

It was concluded that PCOS women with MS had higher BMI than those without MS and controls. Also there were significant differences in FSG, TAG, HDL-C, LH, prolactin, progesterone, testosterone, and LH/FSH ratio between PCOS women and the control as well as in FSG, TAG, and HDL-C between PCOS women with MS as compared to those without

MS. An elevation was found in serum LH, FSH, prolactin, progesterone, testosterone, and LH/FSH ratio in PCOS women with MS as compared to those without MS, but it was not significant.

Authors contributions :

Design of study: Dr. Hind Shakir Ahmed, Dr. Ahsan Khalil Abbas

Collection of sample: Dr. Hind Shakir Ahmed

Preparation of sample: Dr. Hind Shakir Ahmed, Dr. Ahsan Khalil Abbas

Sample measurements: Dr. Hind Shakir Ahmed, Dr. Ahsan Khalil Abbas

Statistical analysis: Dr. Ahsan Khalil Abbas

Preparation of manuscript: Dr. Hind Shakir Ahmed, Dr. Ahsan Khalil Abbas

Discussion: Dr. Hind Shakir Ahmed, Dr. Ahsan Khalil Abbas

Typing of article: Dr. Hind Shakir Ahmed

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