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Comparison of hormonal levels between infertile PCOS and non-PCOS females

Neamat Abdulkadhim Obaida [1,*], Ahmed Noori Mousa [2] and Ali Sultan Maala Alshammari [3]

[1] *Department of Infertility and Assisted Reproductive Techniques, Kamal Alsamarai Teaching Hospital, Iraq, Baghdad.*
[2] *Department of Biochemistry, Al-Kindi Teaching Hospital, Iraq, Baghdad.*
[3] *Department of Microbiology, Al-Kindi Teaching Hospital, Iraq, Baghdad.*

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Abstract

Background: Polycystic ovary syndrome (PCOS) is a complex condition characterized by elevated androgen levels, menstrual irregularities cystic ovaries. Other clinical features include obesity, acne, amenorrhea, excessive hair growth, and infertility. PCOS has been linked to insulin resistance and obesity and many patients with PCOS have insulin resistance and hyper-insulinemia, which play a significant role in the pathogenesis of PCOS

Method: This study was conducted during the period starting from November 2022 to May 2023. One hundred infertile female patients aged range 18–46 years.

Women complaining from infertility included in this study were divided into 2 groups:

- Group I: PCOS group, including 42 females diagnosed with PCOS.
- Group II: Non-PCOS group, involving 58 females with either male factors or unexplained causes of infertility.

Results: BMI was significantly higher among PCOS females (28.61 ± 1.06 vs.25.62 ± 1.65; p=0.046), there was significantly higher LH levels (6.12 ± 0.12 vs. 4.59 ± 0.31; p=004), LH/FSH ratio (1.20 ± 0.12 vs. 0.78 ± 0.05; p=0.001) and significantly lower FSH levels among PCOS patients (5.62 ± 0.62 vs. 6.67 ± 0.58; p=0.043). There were also no significant correlations among PCOS women between BMI with LH, FSH, LH/FSH ratio, E2, prolactin and testosterone hormones

Keyword: Polycystic ovary syndrome; Infertility; Hyper-insulinemia; Insulin resistance

1. Introduction

Polycystic ovary syndrome (PCOS) is a complex condition characterized by elevated androgen levels, menstrual irregularities, and/or small cysts on one or both ovaries. (1). Research suggests that 5% to 10% of females 18 to 44 years of age are affected by PCOS, making it the most common endocrine abnormality among women of reproductive age in the U.S (2). PCOS affects approximately million women of childbearing age in the U.S. Costs to the U.S. Health care systems for the identification and management of PCOS were costed approximately $4 billion per year (3).

Women seeking help from health care professionals to resolve issues of obesity, acne, amenorrhea, excessive hair growth, and infertility often receive a diagnosis of PCOS. Women with PCOS have higher rates of endometrial cancer, cardiovascular disease, dyslipidemia, and type II diabetes mellitus (3). Although PCOS is a common endocrine disorder, the pathogenesis and etiology and of this disease is still not completely understood (4). However, studies suggested that the combination of environmental and genetic factors have been shown to play a significant role in the pathogenesis of

* Corresponding author: Neamat Abdulkadhim Obaida

PCOS, in addition to the effect of socio-economic status and unhealthy behavior; including lack of exercise, smoking, poor diet , and obesity which has a high co-morbidity rate in PCOS(5) .

PCOS can be described as an oligogenic disorder in which the interaction of a number of genetic and environmental factors determine the heterogeneous, clinical, and biochemical phenotype. Although the genetic etiology of PCOS remains unknown, a family history of PCOS is relatively common; however, familial links to PCOS are unclear (6). Environmental factors implicated in PCOS (e.g., obesity) can be exacerbated by poor dietary choices and physical inactivity; infectious agents and toxins may also play a role. The reproductive and metabolic features of PCOS are sometimes reversible with lifestyle modifications such as weight loss and exercise (6). Although the cause of PCOS is unknown the pathophysiology of PCOS involves primary defects in the hypothalamic–pituitary axis, insulin secretion and action, and ovarian function (4).

PCOS has been linked to insulin resistance and obesity (7) and about more than half of patients with PCOS have insulin resistance and hyper-insulinemia, which play a significant role in the pathogenesis of PCOS, not only by affecting the reproductive abnormalities of PCOS, but also by amplifying metabolic defects (8) . This increased insulin levels contribute to or cause the abnormalities seen in the hypothalamic-pituitary-ovarian axis which lead to increases gonadotropin releasing hormone pulse frequency, LH over FSH dominance (9). As a result, this hyper-insulinemia may contribute to a hyper androgenic state by increasing of theca cells production of androgen and influencing hepatic production of sex hormone binding globulin, result in higher concentrations of free androgens (10). Therefore, these findings have led to the development of an important therapeutic strategy for patients with PCOS based on insulin-sensitizing drugs, such as metformin (11).

Therapeutic interventions are designed to reduce insulin levels and ovarian androgen production, ultimately correcting sex hormone–binding globulin (SHBG) levels. This increase in SHBG levels can be used to effectively manage the symptoms of PCOS (12, 13).

2. Subjects, Materials and Methods

This study was conducted during the period starting from November 2022 to May 2023. One hundred infertile female patients aged range 18–46 years.

The patients were recruited from the infertility clinic in High Institute of Infertility Diagnosis and Assisted Reproductive Technologies at Al- Nahrain University center all undergoing controlled ovarian stimulation for IVF /ICSI treatment. Women complaining from infertility included in this study were divided into 2 groups:

- Group I: PCOS group, including 42 patients diagnosed with PCOS.
- Group II: Non-PCOS group, including 58 patients in which the cause of infertility either male factors or unexplained causes of infertility.

Hormonal assay: Blood for FSH , LH ,E2 ,prolactin and testosterone where drawn in the early follicular phase i.e. 1-5 days from the beginning of the menstrual cycle .The blood then centrifuged and the supernatant and stored in deep freezer to be measured later. FSH, LH, E2, testosterone and prolactin hormones were measured by immunofluorescence assay.

2.1. Statistical analysis

The data were analyzed using Statistical Package for Social Sciences (SPSS) version 23.0. Mean and standard error of the mean were used to describe the data and the groups were compared by independent sample t test and Chi square. The degree of association between continuous variables was calculated by Pearson's correlation coefficient (r) and the results were considered to be statistically significant when p value equal or less than 0.05.

3. Results

Body mass index (BMI) was significantly higher among PCOS females (28.61 ± 1.06 vs. 25.62 ± 1.65; p=0.046); however: there were no significant differences between PCOS and non-PCOS females concerning their mean age (27.58 ± 1.18 vs. 30.29 ± 1.63; p=0.052), body mass indices ranking (p=0.102), duration of infertility (p=0.839) and types of infertility (p=0.479) as demonstrated in table 1.

Table 1 Comparison of demographic features between PCOS and non- PCOS females

Demographic features		**PCOS Females n.=42**	**Non-PCOS females n.=58**	***p* value**
Age (years)		27.58 ± 1.18	30.29 ± 1.63	0.052 NS
BMI (Kg/m^2)		28.61 ± 1.06	25.62 ± 1.65	0.046 S
BMI ranking n.(%)	Normal weight	6 (14.2 %)	17 (29.3 %)	0.102 NS
	Overweight	17 (40.5 %)	22 (37.9 %)	
	Obese	19 (45.3 %)	19 (32.8 %)	
Duration of infertility (years)		8.62 ± 1.20	8.05 ± 0.87	0.839 NS
Type of infertility n.(%)	Primary	31 (73.8 %)	39 (67.2 %)	0.479 NS
	Secondary	11 (26.2 %)	19 (32.8 %)	
NS: Not significant (p > 0.05); BMI: Body mass index				

Comparisons of hormonal levels between PCOS and non-PCOS females were demonstrated in table 2, accordingly there was significantly higher LH levels (6.12 ± 0.12 vs. 4.59 ± 0.31; *p*=004) and LH/FSH ratio (1.20 ± 0.12 vs. 0.78 ± 0.05; *p*=0.001); on the contrary there was significantly lower FSH levels among PCOS patients (5.62 ± 0.62 vs. 6.67 ± 0.58; *p*=0.043); however there were no significant differences concerning estradiol (E2) levels (*p*=0.170), prolactin levels (*p*=0.552) and testosterone levels (*p*=0.101).

Table 2 Comparison of hormonal levels between PCOS and non-PCOS females

Hormones (Mean ± SE)	**PCOS females n.=42**	**Non-PCOS females n.=58**	***p* value**
LH (mIU/ml)	6.12 ± 0.12	4.59 ± 0.31	0.004 S
FSH (mIU/ml)	5.62 ± 0.62	6.67 ± 0.58	0.043 S
LH/FSH ratio	1.20 ± 0.12	0.78 ± 0.05	0.001 S
E2 (pg/ ml)	52.57 ± 9.2	38.5 ± 8.9	0.170 NS
Prolactin (ng/ml)	19.96 ± 2.78	19.49 ± 1.65	0.552 NS
Testosterone (ng/dl)	53.52 ± 2.81	48.91 ± 1.23	0.101 NS

SE: Standard error; LH: Luteinizing hormone; FSH: Follicle stimulating hormone; E2: Estradiol; NS: Not significant (p > 0.05)

There were also insignificant negative correlations between BMI with LH, FSH and LH/FSH ratio; on the other hand there was a positive insignificant correlations with E2, prolactin and testosterone hormones among PCOS women (Table 3).

Table 3 Correlations between BMI and hormonal levels among PCOS patients

Hormones	**Pearson's correlation coefficient (r)**	***p* value**
LH (mIU/ml)	-0.151	0.410 NS
FSH (mIU/ml)	-0.153	0.403 NS
LH/FSH ratio	-0.214	0.239 NS
E2 (pg/ ml)	0.229	0.207 NS
Prolactin (ng/ml)	0.188	0.302 NS
Testosterone (ng/dl)	0.017	0.927 NS

NS: Not significant (p> 0.05)

4. Discussion

In recent study PCOS females had significantly higher mean body mass indices and this result was agreed with Wijeyaratne et al and many other studies, our higher incidence of over-weight and obese may be linked to the lack of exercise and related to an increasing trend in the proportion of women with the metabolic syndrome (14).

Several studies supported that the investigators are not sure that higher BMI, LH, FSH and LH/FSH ratio necessarily indicate a greater incidence of PCOs features. For example, Sharquie KE et al (15) concluded that, LH/FSH ratio has little effect in diagnosing polycystic ovarian syndrome. Dinka et al (15) reported that no significant association was showed between the body mass indices, clinical features and hormonal parameters.

LH/FSH ratio is a ratio between two gonadotropin hormones; LH and FSH. These two hormones are secreted by the B-cells of the anterior pituitary under the influence of the hypothalamic GnRH. In females (16), LH act on the theca cells of the ovary to cause androgen production from cholesterol, while FSH regulates function of granulose cells that causes the conversion of the androgens to estrogens by aromatase enzyme (17).

A delicate balance of LH and FSH is required for early follicular development. In normal females LH/FSH ratio in early follicular phase is normally 1 (18). If LH levels are too high, theca cells produced large amount of androgens causing follicular atresia, both the absolute level of circulating LH as well as its ratio to FSH is significantly elevated in PCOS women (19).The increase in intraovarian androgens believed to play a significant role in an ovulatory process (17). When any an ovulatory state exists for a period of time affected women developed bilaterally enlarged polycystic ovaries -a hall mark of PCOS patient and a finding present in more than 80% of PCOS (19).

These results are also consistent with findings of Hsu et al.(20), in which they evaluated 251 PCOS women in specific days of menstrual cycle and found that 70% of such women have elevated LH/FSH ratio >1 (20). Therefore they also concluded that the LH-FSH ratio is a valuable diagnostic tool in evaluating women with PCOS and an LH-FSH ratio of >1 may be used as a decision threshold (20).

Banaszewska et al. (21) reported abnormal LH/FSH ratio when it is greater than 2 and 4.5% of PCOS women having an elevated ratio. However they have shown that the mean LH/FSH ratio was not statistically significant difference between the PCOS and non PCO in his study (21). Another investigation in Saudi also has been reported that regardless of the age and weight factors, Saudi patients with PCOS have higher levels of LH/FSH; but have lower levels of FSH compared to controls (Fakhoury et al., 22). Kiddy et al. (23) found an inverse correlation of FSH with BMI in obese PCOS. While Yanira et al (21) revealed an inverse correlation between LH and BMI in PCOS, but Insler et al (22) determined a significantly higher level LH in non- obese PCOS women compared with obese PCOS subjects. However, we found no significant associations between LH, FSH, and LH/FSH ratio with BMI of the PCOs women.

5. Conclusion

Therapeutic interventions are designed to reduce insulin levels and ovarian androgen production, ultimately correcting sex hormone–binding globulin (SHBG) levels. This increase in SHBG levels can be used to effectively manage the symptoms of PCOS

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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