SCIENTIFIC EVENTS GATE

The International Innovations Journal of Applied Science

Journal homepage: https://iijas.eventsgate.org/iijas

ISSN: 3009-1853 (Online)

Investigation of some fertility indicators in Iraqi women with polycystic ovary syndrome

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ARTICLE INFO

Article history:
Received 10 Jun. 2024
Revised 2 Jul. 2024,
Accepted 6 Jul. 2024,
Available online 15 Jul. 2024

Keywords:
polycystic ovarian syndrome
biochemical tests
sex hormones
thyroid hormones
leptin

ABSTRACT

Polycystic ovary syndrome (PCOS) is a complex, heterogeneous, multigenic disorder in women of childbearing age with multiple consequences. The exact mechanism of PCOS is not yet fully understood; There are several factors have a role such as genetic, environmental, nutritional, metabolic and other interactions Therefore, the existing study designed to estimate the levels of some biochemical tests and the sex hormones that have a role in PCOS progress. 100 Iraqi women were agreed to participate in the current study, divided into two groups included 50 clinically diagnosed with PCOS women that compared with 50 healthy women without PCOS as a control group (CTRL). The results showed different significant differences of the studied parameters between the PCOS and the CTRL. There was a significant increased level of FBG, HbA1c, insulin resistant, TG and LDL in the PCOS group in comparison to the CTRL, while a significant decreased level of HDL was appeared in PCOS group in comparison to the CTRL. Regarding the results of sex hormones, there were significant increased levels of LH, FSH, testosterone, estradiol hormones in the PCOS group in comparison to the CTRL. In addition, the results of thyroid hormones appeared a significant increased level of T3 hormone in the PCOS group in comparison to the CTRL. Also, the results of leptin hormone showed a significant increased level in the PCOS group in comparison to the CTRL. In conclusion, there was a significant relationship between FBG, HbA1c, insulin resistant, TG, LDL, HDL, LH, FSH and T3 parameters with PCOS.

1. Introduction

Polycystic ovary syndrome (PCOS) is a complex, inhomogeneous, multigenic disease in women of childbearing age with multiple consequences. The exact mechanism of PCOS is not yet fully understood; There are several factors have a role such as genetic, environmental, nutritional, metabolic and other interactions (Heidarzadehpilehrood *et al.*, 2022). The syndrome prevalence varies ranging from 4 to 20% in women of procreative age. (Heidarzadehpilehrood *et al.*, 2022). The exact mechanism of PCOS is not yet fully understood; There are genetic, environmental, nutritional, metabolic and other interactions. PCOS begins at the beginning of life. So, it is one of the ancient diseases that has continued throughout human evolution. Women with PCOS suffer from various conditions over the pregnancy period, including miscarriage, premature birth, intrauterine death, or stillbirth. Also, they exposed to a significant increase in the risk of progressing insulin resistance, an imbalance in

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the levels of Blood lipids, impaired glucose tolerance and type 2 diabetic mellitus are considered clinically and health-related because they are very common. (Yakıt and Aslan, 2024; Du *et al*., 2023; Heidarzadehpilehrood *et al*., 2022; Visser, 2021; Firoozabadi *et al*., 2020; Pundir *et al*. 2020; Ye *et al*., 2018). Also, Women with PCOS also suffer from weight gain, and thus weight gain leads to an exacerbation of the syndrome's phenotype. PCOS classically characterized by hyperandrogenism and oligoanovulation (Aşık and Ede Çintesun, 2023).

In addition to the role of sex hormones that affects women of reproductive age (Xing *et al*., 2022). Multiple biochemical pathways have been identified that may be a cause of PCOS, and many genes have been tested for these pathways, including genes involved in the biosynthesis of steroid hormones, metabolism, The functions of reproductive and gonadal hormones extend beyond just reproduction. These hormones also impact various other physiological processes, including the regulation of energy balance, insulin secretion, obesity and more (Stener-Victorin *et al*., 2020; Stener-Victorin and Deng, 2021; Heidarzadehpilehrood *et al*., 2022). PCOS is a common hormonal situation that affects women of procreative age. It commonly starts through adolescence, but the symptoms may differ over time. Hormonal abnormality, irregular periods, leftover androgen levels, and cysts formation in the ovaries might result from PCOS, women with PCOS have heightened levels of a luteinizing hormone (LH) which is the hormone responsible for ovulation (Dumesic *et al*., 2020; Dobbie *et al*., 2023), and lower levels of a follicle-stimulating hormone (FSH) which is a hormone necessary for pubertal development and the function of a woman's ovaries (Dobbie *et al*., 2023; Whooten *et al*., 2023). Also, women with PCOS suffering from a deficiency in the production of estrogen and an excess of androgens, as hyperandrogenism is one of the most prominent symptoms (Zeng *et al*., 2020; Dobbie *et al*., 2023). Because of these hormonal imbalances, women with PCOS often suffer from irregular ovulation and irregular menstrual cycles (Dobbie *et al*., 2023).

The PCOS etiology is still poorly understood, several studies indicating that it is a complex, polygenic disorder with ovarian hyperandrogenism, one of the main clinical characteristics of this syndrome (Dobbie *et al*., 2023). Multiple biochemical pathways have been identified that may be a cause of polycystic ovary syndrome (Heidarzadehpilehrood *et al*., 2022).

Many genes have been tested for these pathways, including genes involved in the biosynthesis of steroid hormones, metabolism, the reproductive and gonadal hormones action included the regulation of obesity, energy, insulin action and secretion, and many others (De Leo *et al*., 2016; Heidarzadehpilehrood *et al*., 2022).

Therefore, the present study aimed to estimate the levels of the biochemical tests and the sex hormones that have a role in the development of PCOS. One hundred Iraqi women were agreed to participate in the current study, divided into two groups, the first group included 50 clinically diagnosed with PCOS women that compared with 50 healthy women without PCOS as a control group.

2. Methodology

2.1. Collection of blood samples

This study was conducted on 100 women who visited the gynecology department at Maysan Hospital for Childhood and Maternity in Amara District, Maysan Provence, Iraq. The study group consists of 50 women who were diagnosed with polycystic ovary syndrome by a specialist, their age range was between 18 – 40 years, and 50 apparently healthy women in a similar age group for the PCOS group considered as a control group (CTRL), most of them were married and had several children. A declaration was obtained from each participant agreeing to participate in the study, and scientific research ethics approval was obtained from the University of Baghdad, College of Science, under the number CSEC/1223/0128.

For both study groups, 5 milliliters of venous blood were drawn. The blood sample was separated into two portionss. The first part, 3 milliliters, was placed in gel tubes and the blood was permitted to coagulate, and then the serum was separated using the centrifugation for 10 minutes at 3000 rpm, the serum was stored in a 1.5 ml Eppendorf tube at a temperature of - 20 C° until the biochemical and hormonal tests are conducted. The remaining part (2 ml) was placed in an EDTA tube and left on a mixer for several minutes to prevent any coagulation, then the Hemoglobin A1 c (HbA1c) test was performed for all samples. Fasting blood glucose (FBS), insulin resistant, lipid profile, renal function and liver function tests were estimated automatically through Roche Cobas c111 autoanalyzer (Roche company, Germany). Furthermore, to measuring the levels of several sex hormonal tests such as LH, FSH, testosterone, prolactin, progesterone, estradiol and thyroid function test (T3, T4 and TSH) automatically through using Roche e411 autoanalyzer (Roche company, Germany). While the level of leptin hormone was estimated via using the commercial ELISA kit (Cloud-Clone Corp., USA).

2.2. Statistical analysis

The IBM SPSS version 27.0 was used to analyze the data of the current study. The normality, homogeneity of variance, and randomization were estimated to determine the type of the current data and to choose the correct statistical analysis. The mean and standard deviation (SD) were calculated for the parametric data, independent student t-test was used to calculate the probability. In addition, the frequencies and percentages were calculated for the non-parametric data, Pearson's chi-square was employed to compute the probability of the non-parametric data. The probability was significant when it was less than 0.05.

3. Results and discussion

3.1. Sampling

This study was conducted on 100 women who visited the gynaecology department at Maysan Hospital for Childhood and Maternity in Amara District, Maysan Provence, Iraq. The study group consists of 50 women who were diagnosed with PCOS by a specialist with age means 30.56 ± 8.42 years, and 50 healthy women with age means 29.62 ± 7.62 years, and no significant difference was appeared for the age of the two group (Table 1).

The socio-demographical data of the studied groups in Table 1 showed that 90% of the PCOS group and 94% of the healthy controls were married. Also, 80% of the PCOS group and the healthy controls have no abortion. In addition, 52% of the PCOS group was diagnosed after marriage, and 72% of the PCOS group have a family history, and 78% of the PCOS group have chronic diseases such as bowel celiac disease, diabetic mellitus, rheumatoid arthritis, systemic lupus erythematosus, and etc. All the PCOS group (100.0%) were depended on the fast food in their diet.

Table 1: Socio-demographical data of the studied groups

Socio-demographical data		PCOS group (n= 50)	CTRL group (n= 50)	Probability
Age means ± SD (Years)		30.56 ± 8.42	29.62 ± 7.62	P > 0.05
Social status frequency (%)	Single	5 (10.0)	3 (6.0)	P > 0.05
	Married	45 (90.0)	47 (94.0)	
Abortion times frequency (%)	None	40 (80.0)	50 (100.0)	P < 0.05
	One time	3 (6.0)	0 (0.0)	
	Two times	5 (10.0)	0 (0.0)	
	Third times and more	2 (4.0)	0 (0.0)	
PCOS diagnosis frequency (%)	Before marriage	24 (48.0)	-	Uncountable
	After marriage	26 (52.0)	-	
Family history frequency (%)	Yes	14 (28.0)	0 (0.0)	P < 0.001
	No	36 (72.0)	50 (100.0)	
Chronic diseases frequency (%)	Yes	11 (22.0)	0 (0.0)	P < 0.001
	No	39 (78.0)	50 (100.0)	
Fast food frequency (%)	Yes	50 (100.0)	0 (0.0)	P < 0.001
	No	0 (0.0)	50 (100.0)	

3.2. Biochemical tests

3.2.1. Blood glucose, hemoglobin A1c, insulin resistant, renal function and lipid profile tests

The results in Table 2 showed the variant significant differences for the biochemical tests between the PCOS and the CTRL groups. There was a significant increased level mean of FBG, HbA1c, insulin resistant in the PCOS group from the CTRL. While the results showed non-significant variances in the levels of blood urea (BU) and serum creatinine tests between the compared groups. The same result appeared in the cholesterol level, but significant heightened of serum triglyceride (TG) levels and the low-density lipoprotein (LDL) levels were appeared in the PCOS group from the CTRL, while a significantly decrease level of high-density lipoprotein (HDL) was appeared in the PCOS group from the CTRL (Table 2).

Table 2: Blood glucose, HbA1c, insulin resistant test, renal function test, and lipid profile levels

Biochemical tests mean ± SD	PCOS group (n= 50)	CTRL group (n= 50)	Probability
FBG (mg/dl)	172.34 ± 62.72	90.86 ± 16.11	P < 0.001
HbA1c (%)	6.10 ± 1.39	5.30 ± 0.50	P < 0.001
Insulin resistant test (ng/ml)	4.54 ± 2.93	2.11 ± 1.86	P < 0.001
BU (mg/dl)	26.54 ± 8.34	24.28 ± 8.83	P > 0.05
S. creatinine (mg/dl)	1.0 ± 0.48	1.12 ± 0.44	P > 0.05
S. Chol (mg/dl)	192.70 ± 65.80	179.46 ± 47.83	P > 0.05
S. TG (mg/dl)	201.26 ± 98.23	124.62 ± 24.67	P < 0.001
S. HDL (mg/dl)	23.14 ± 11.80	50.16 ± 10.31	P < 0.001
S. LDL (mg/dl)	74.22 ± 43.81	31.96 ± 7.53	P < 0.001

FBG: fasting blood glucose, HbA1c: hemoglobin A1c, BU: blood urea, S. creatinine: serum creatinine, S. Chol: serum cholesterol, S. TG: serum triglyceride, S. HDL: serum high density lipoprotein, S. LDL: serum low density lipoprotein

3.2.2. Liver function test

The results in Table 3 showed different non-significant differences of the liver function test in the PCOS group from the CTRL. The results showed a decreased non-significant level of AST in the PCOS group from the CTRL. While for ALT and ALP, the results showed non-significant increased levels in the PCOS group from the CTRL (Table 3).

Table 3: Liver function test levels

Parameters mean ± SD	PCOS group (n= 50)	CTRL group (n= 50)	Probability
AST (mg/dl)	22.10 ± 6.15	24.30 ± 9.50	P > 0.05
ALT (mg/dl)	58.38 ± 17.98	22.06 ± 6.77	P > 0.05
ALP (mg/dl)	69.18 ± 28.24	60.60 ± 33.97	P > 0.05

AST: Aspartate transaminase, ALT: Alanine transaminase, ALP: alkaline phosphatase

The present results of the blood glucose, HbA1c, insulin resistant, renal function, and lipid profile levels showed different significance. It appeared highly significant in the PCOS group compared to the CTRL group for the blood glucose, HbA1c, insulin resistant, S. HDL, and S. LDL tests. While it appeared highly non-significant in the PCOS group in comparison to the CTRL for BU, S. Chol, S. TG, and liver function tests. In contrast the level of s. creatinine appeared a non-significantly lowered in the PCOS group from the CTRL. The present results agreed with other earlier studies (Rezaee *et al*., 2016; Lerchbaum *et al*., 2013; Numbi *et al*., 2019; Rostami Dovom *et al*., 2022).

While the results of renal function test were disagreed with previous studies indicated an association between PCOS and kidney diseases development (Du *et al*., 2023; El-Eshmawy *et al*., 2022; Rostami Dovom *et al*., 2022).

Although the PCOS considered a common endocrine disorder that affects the procreative-age women. Interestingly, the patients also exhibit several metabolic disorders include insulin resistant, obesity and dyslipidemia. These overlapping features suggest an elevated risk for cardiovascular disease (Lin *et al*., 2024; Liao *et al*., 2021 and Julie, 2003).

3.2.3. Sex hormone

The results of sex hormone illustrated in Table 4, showed different significant differences, there were significant increased levels of FSH, LH, testosterone, estradiol hormone in the PCOS group from the CTRL. While, there was non-significant difference for prolactin level in the PCOS group from the CTRL (Table 4).

Table 4: Sex hormones levels

Sex hormones levels mean ± SD	PCOS group (n= 50)	CTRL group (n= 50)	Probability
LH (ng/ml)	13.69 ± 2.13	5.46 ± 0.91	P < 0.001
FSH (ng/ml)	12.25 ± 1.49	7.53 ± 0.80	P < 0.001
Prolactin (ng/ml)	21.42 ± 1.48	19.74 ± 1.44	P > 0.05
Testosterone (ng/ml)	0.99 ± 0.25	0.38 ± 0.08	P < 0.05
Progesterone (ng/ml)	62.90 ± 7.32	12.40 ± 1.80	P < 0.001
Estradiol (ng/ml)	74.52 ± 10.34	6.0 ± 0.69	P < 0.001

Also, the present results appeared significant increased levels of sex hormones except prolactin in the PCOS group in comparison to the CTRL, it appeared a non-significantly increased in the PCOS group from the CTRL. In PCOS patients, there sex hormones were elevated, but prolactin level remains relatively unchanged, because PCOS doesn't directly causing hyperprolactinemia (Darenskaya *et al*., 2024; Williams *et al*., 2023; Atalyan *et al*., 2021 and Williams *et al*., 2016).

Previous studies indicated a relationship between the PCOS development and the levels of LH, FSH and estradiol hormones (El-Eshmawy *et al*., 2022). PCOS patients have several metabolic disorders appeared resulting from the sex hormonal disorders (Mansour *et al*., 2023 and Xing *et al*., 2022). In addition, our results of the sex hormones were agreed with the study of Gungor and Gungor (2023), who reported a significant increase levels of sex hormones and the AMH in the PCOS patients. In addition, Xing *et al*. (2022) reported about the association between the sex hormones disorders and the levels of blood glucose, lipid profile and liver function tests.

3.2.4. Thyroid hormones

In addition, different significant differences appeared in the results of thyroid hormones between the PCOS group and the CTRL were showed in Table 5. There was a significant increased level of T3 hormone in the PCOS group from the CTRL, while there was non-significant decreased level of T4 and TSH hormones in the PCOS group from the CTRL (Table 5).

Table 5: Thyroid hormone levels

Thyroid hormones levels mean ± SD	PCOS group (n= 50)	CTRL group (n= 50)	Probability
T3 nmol/L	1.20 ± 0.64	0.91 ± 0.07	P < 0.05
T4 nmol/L	92.92 ± 28.53	99.34 ± 31.28	P > 0.05
TSH nmol/L	2.28 ± 1.28	2.33 ± 1.64	P > 0.05

The results of thyroid function were agreed with the results of previous investigations indicated a significant increase in the levels of thyroid hormones in the PCOS patients although the role of thyroid hormones still unclear (Fan *et al*., 2023 and Kirkegaard *et al*., 2024).

3.2.5. Leptin hormone

The results of leptin hormone showed a significant increased level in the PCOS group in comparison to the CTRL (Table 6).

Table 6: Leptin hormone levels

Leptin hormone level mean ± SD (ng)	PCOS group (n= 50)	CTRL group (n= 50)	Probability
	34.16 ± 5.46	13.73 ± 1.09	P < 0.001

Our results appeared a significant increase level of leptin hormone in the PCOS group in comparison to the CTRL, these results were agreed with another previous study indicated a significant association between the increase level of leptin hormone and concluded that leptin hormone is a significant indicator for the diagnosis and treatment of PCOS (Peng *et al*., 2022). Also, Sharif (2022) concluded a significant association between leptin hormone and each of BMI and insulin resistant in hyperinsulinemia PCOS patients. In addition, there was a significant correlation between leptin hormone and some sex hormone in PCOS patients (Ramanand *et al*., 2017 and Fathy Mohamed *et al*., 2021).

4. Conclusions

In conclusion, there was a significant relationship between FBG, HbA1c, insulin resistant, TG, LDL, HDL, LH, FSH and T3 parameters with PCOS.

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