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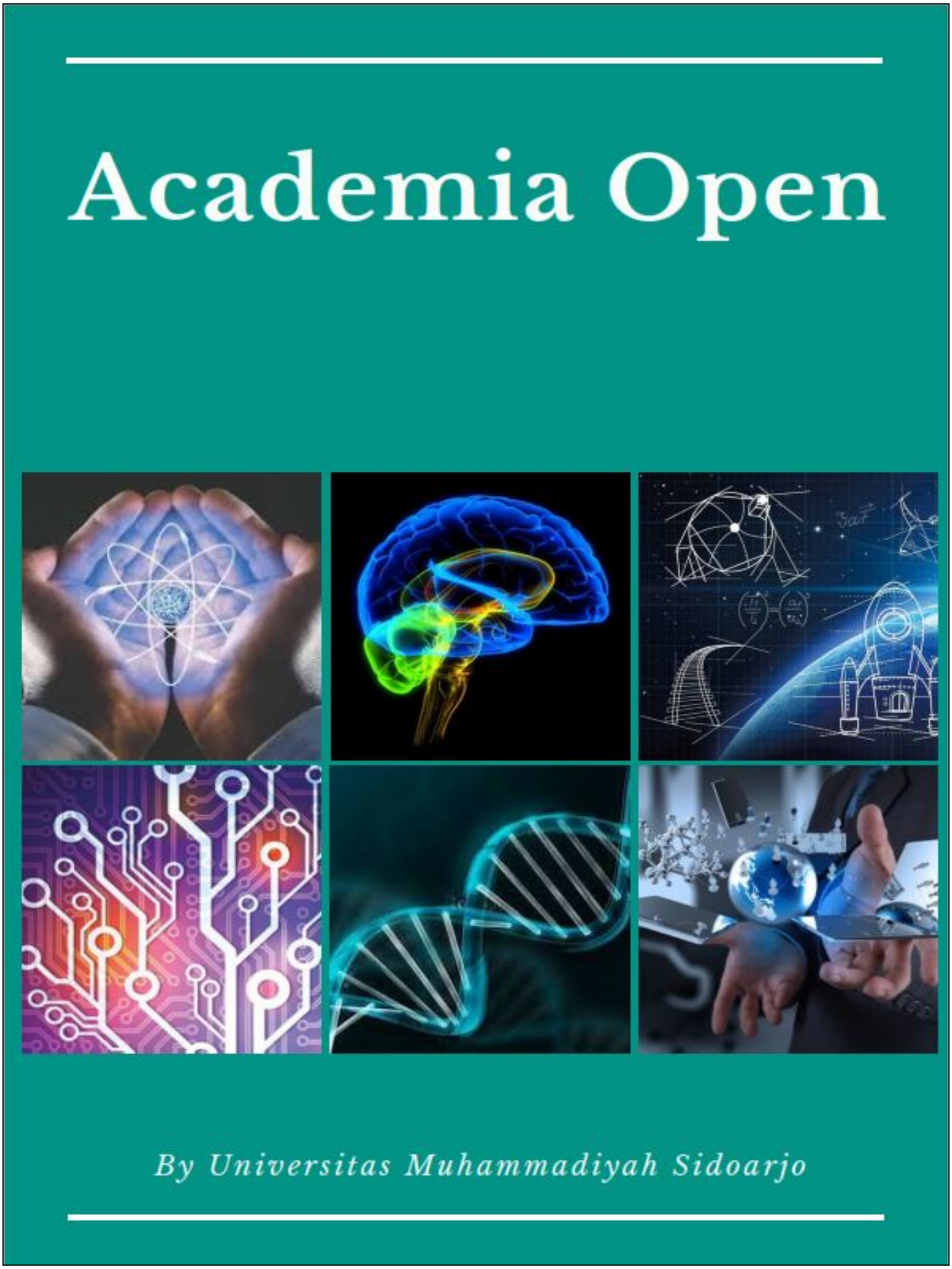


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# Hormonal Alterations in Women with Polycystic Ovarian Syndrome

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## Abstract

**General background:** Polycystic ovary syndrome (PCOS) is among the most common endocrine disorders affecting 5–10% of women of reproductive age, associated with infertility, metabolic dysfunction, and cardiovascular risk. **Specific background:** Although PCOS is widely studied, the hormonal mechanisms underlying its heterogeneity remain insufficiently clarified, particularly in Middle Eastern populations. **Knowledge gap:** Limited data exist on the hormonal alterations across age groups of women with PCOS in Iraq, where prevalence is rising. **Aims:** This study investigated hormonal parameters—LH, FSH, testosterone, prolactin, T3, and TSH—among 50 PCOS patients compared with 25 healthy controls in Ramadi. **Results:** Findings showed significantly elevated LH, testosterone, prolactin, and TSH, alongside reduced T3, with the most pronounced LH increase in women aged 36–45 years ($p < 0.05$). FSH remained unchanged overall, while clinical signs such as menstrual irregularities, obesity, hirsutism, and galactorrhea were markedly more frequent in PCOS cases. **Novelty:** This study provides age-stratified evidence linking hormonal imbalances with clinical manifestations in Iraqi women, highlighting hypothyroidism as a contributing factor. **Implications:** The results underscore the importance of routine thyroid and hormonal monitoring, genetic screening, and lifestyle interventions in managing PCOS and reducing its reproductive and metabolic complications

**Highlights:**

- PCOS patients showed significantly elevated LH, testosterone, prolactin, and TSH with reduced T3.
- Age group 36–45 years exhibited the highest hormonal imbalance, especially LH increase.
- Clinical manifestations included menstrual irregularities, obesity, hirsutism, and galactorrhea

**Keywords:** Polycystic Ovary Syndrome, Hormonal Imbalance, Luteinizing Hormone, Hypothyroidism, Infertility

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# Introduction

Polycystic ovaries syndrome (pcos) is one of the most common hormonal disorders that affect approximately (5-10%) of women of childbearing age and is characterized by the presence of small cysts filled with ovarian fluid [1].

Polycystic ovary syndrome (PCOS) is the most common and main hormonal cause in premenopausal women, which involves the reproductive system of women with health problems (WHO,2023).

PCOS can also be diagnosed with hyperandrogenism and polycystic ovaries [2].

The syndrome can be described as a multifaceted metabolic disease associated with insulin resistance and obesity [3].

A number of researchers indicated that the syndrome is accompanied by biochemical and physiological signs that pose a risk to the vascular system [4].

The syndrome is the most common cause of anovulation in infertility and is characterized by multiple clinical symptoms such as diabetes mellitus, coronary arteries diseases, hyperandrogenism, obesity, acne, and hirsutisim [7].

As for its causes, they are not precisely known, and opinions have varied in explaining its occurrence, including disorders in the hormones that stimulate the gland or a defect in the pituitary gland that results in an increase in the luteinizing hormone (LH) to the follicle stimulating hormone (FSH), or as a result of disorders in the adrenal gland [5].

As for the other opinion, it referred to the role of insulin in increasing the secretion of male hormones, especially the testosterone hormone, which results from the presence of insulin resistance [6].

The syndrome leads to dyslipidemia, cardiovascular disease and endometrial carcinoma, and affects the external appearance of women due to obesity, hirsutism and acne [7].

From the foregoing and as a result of the widespread spread of the syndrome in Iraq and Anbar Governorate, the study attempted to achieve the following objectives:

1. A study of the changes in the hormonal parameters associated with the syndrome, represented by luteinizing hormone (LH), follicle stimulating hormone (FSH), testosterone , prolactin, triiodothyronine hormone (T3) and thyroid stimulating hormone (TSH).

# Method

## A. Preparing the Patients Cases Under Study

This study was conducted in the laboratories of the Fertility and Sterility Center at the Women’s and Children’s Teaching Hospital in Ramadi from 1/1/2022 to 1/4/2022 and included follow-up of (50) patients’ cases of women with polycystic ovaries and they were compared to the control group, which included (25) samples as follows:

### 1. Pathological Samples

The pathological cases were confirmed after conducting clinical examinations and referred to them by the competent medical staff, as well as ultrasound examinations.

The pathological samples, which numbered 50, were divided into different age groups, as shown in the following table:

**[Table 1. about here]**

### 2. Sample Collection

Blood was obtained from one of the veins of the forearm of the tested and the control group with a volume of (10 ml) on the second or third day of the menstrual cycle for the purpose of measuring the hormones FSH, LH, prolactin, testosterone, TSH and T3, and in the absence of the cycle, the advanced hormonal parameters are measured on any day. The blood was separated at a speed of 3000 revolutions per minute for half an hour, then it was placed in test tubes of his wine for the purpose of measuring hormonal and biochemical parameters, and kept in deep freezing at a temperature of -3° C until use.

### 3. Hormonal Parameters

#### a. Measurement of the Concentration of Follicle-Stimulating Hormone (FSH) in the Blood Serum

The concentration of the hormone in the blood serum of women with polycystic syndrome, as well as the control group, is measured by following the accompanying steps with the FSH test kit and the imported French (Biomerieux), which consists of the following materials:

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1) FSH Strips (STR): These are ready-to-use strips consisting of 10 wells covered with a thin plate and marked with the symbol FSH; for the purpose of distinguishing it.

2) Solud phase receptacles (SPRs): They are ready to use, just like the tip used in the micropipette, except that they are marked at their wide end with the symbol (FSH) for the purpose of distinguishing them.

3) FSH control (Cl): It was prepared by adding 3 ml of distilled water and leaving it for 5-10 minutes.

4) FSH calibrator (Sl): It was prepared by adding 2 mm 3 of distilled water and left for 5-10 minutes.

5) FSH dilutant (Rl): It is ready for use.

6) Mle card: It is a ready-made card that contains the main encoded information of the titration data used in the evaluation of the test for the concentration of follicle-stimulating hormone.

The principle of measuring the concentration of follicle-stimulating hormone was based on the Enzyime immunoassay sandwich method with a final Fluorescent detection

**b. Measurement of the Concentration of Luteinizing Hormone (LH) and Thyroid Stimulating Hormone (TSH) in the Blood Serum**

The concentration of luteinizing hormone and TSH in the serum of women with PCOS syndrome, as well as the control group, were measured by following the accompanying steps with the test kit for luteinizing hormone imported from the French company Biomerieux, consisting of the following materials:

1) Strips for LH and TSH: they are ready for use, just like in the FSH strips; It consists of ten holes.

2) Solid Phosereceptacles (SPRs): They are ready-to-use, just like the SPRs of follicle-stimulating hormone, except that they are marked with Luteinizing Hormone.

3) LH Control (C1) and TSH: It was prepared by adding 3 mm 3 of distilled water and leaving it for (5-10) minutes.

4) LH Control (S1) and TSH: It was prepared by adding 2 mm 3 of distilled water and left for (5-10) minutes.

5) LH dilutant (R1) and TSH which is ready for use.

6) The MLe card: It is a ready-made card that contains the main encoded information of the calibration data used in evaluating the result of the test for the concentration of luteinizing hormone.

The principle of measuring the concentration of LH and TSH was also based on the Combines enzyme immunoassay sandwich method with a final Fluorescent detection where there is competition between the antigen present in the sample and the antigen marked with anti-LH antibodies coated with SPR1 and in the end a radioactive product is formed, the amount of this radiation was measured by the device automatically. As for the method of work, the same method used during the measurement of follicle-stimulating hormone was followed.

**c. Measurement of the Prolactin Concentration in the Blood Serum**

The concentration of prolactin in the serum of women with PCOS syndrome, as well as the control group, was measured by following the accompanying steps with the prolactin test kit imported from the French company Biomerieux consisting of the following materials:

1) Milk hormone strips: They are ready-to-use strips consisting of ten holes covered with a thin plate and marked with the symbol PRL for the purpose of distinguishing them.

2) Solid Phose receptacles (SPR): They are ready-to-use, just like the SPR of follicle-stimulating hormone and luteinizing hormone, except that they are marked with PRL.

3) PRL Control (C1): It was prepared by adding 3 mm 3 of distilled water and leaving it for (5-10) minutes.

4) PRL Calibrator (S1) : It was prepared by adding 2 mm 3 of distilled water and left for 5-10 minutes.

5) PRLdilutant (R1): It is ready for use.

6) The MLe card: It is a ready-made card that contains the main encoded information of the calibration data used in evaluating the test result for the concentration of the milk hormone.

As is the case in measuring the concentration of FSH and LH hormones, the principle of measuring milk hormone depends on the competition between the specific anti-prolactin antibodies and the antigen present in the sample. In the end, a radioactive product is formed, the amount of this radiation was measured by the device automatically.

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As for the method of work, the same steps used to measure the concentration of follicle-stimulating hormone and luteinizing hormone were followed.

**d. Measurement of the Concentration of Testosterone in the Blood Serum**

The hormone was measured in the blood serum of PCOS patients, as well as the control group, by following the accompanying steps with the test kit for testicular lipid hormone imported from the French company Biomerieux consisting of the following materials:

1) Strips: They are ready-to-use tapes consisting of ten holes.

2) Solid Phose receptacles: They are ready to use, completely similar to the tip used in the micropipette, except that they are marked at their wide end with the symbol TES for the purpose of distinguishing them.

3) TES Control (C1): It was prepared by adding 2 mm 3 of distilled water and leaving it for (5-10) minutes.

4) TES Calibrator (S1): It was prepared by adding 2 mm 3 of distilled water and left for (5-10) minutes.

5) PRLdilutant (R1): It is ready for use.

6) The MLe card: It is a ready-made card that contains the main encoded information of the calibration data used in evaluating the test result for the concentration of the testosterone hormone.

The principle of measuring testosterone hormone depends on the method of immunocompetitiveness for binding to the enzyme while investigating the final radiation formed with a final fluorescent detection. Which is done automatically by Mini Vidas device. And that the reaction medium moves periodically to and from SPRS and the solutions in the tape several times.

The sample is transported into the hole containing the conjugate which is alkaline phosphetase labeled – testosterone.

### B . Statistical Analysis

The statistical program (SPSS 10.01) version 1999 was used to analyze the results by extracting the arithmetic mean and standard deviation (SD ± Mean), and the T-test selection was also used to analyze the differences between the main and secondary groups under the probability level (0.05) Al-Rawi (1984).

## Results and Discussion

### A. Results

**1. Clinical Signs Changes in Some Clinical Signs of PCOS in Women Compared to the Control Group**

It is evident from Table (4-1) that there are many clinical signs associated with PCOS for women compared to the control group. The percentages of these signs varied, so menstrual cycle disturbance was 98.6%, which is the highest percentage in the clinical signs of patients, then the percentages of obesity, then the appearance of hirsutism and the emergence of hirsutism gradually increased. Count and secretion of milk at a lower rate and significantly higher (P<0.0) compared to the control group.

**a. Changes in Some Clinical Signs of the Syndrome for Different Ages of PCOS**

Table (2) shows that there are no significant differences in the percentage of clinical signs (hirsutism, milk production and obesity) for all age groups, while it was found that the age group (36-45) years was the only age group in which a significant increase (0.05 P) appeared. <) in the percentage of menstrual irregularities, it was (93% ± 0.99) compared to the age group (18-25) years, and the age group (26-35) years if it was 87 ± 0.85% and 83 ± 0.83%, respectively, and the same was true for To the emergence of acne, the percentage of counting decreased significantly (P<0.05) in the age group (36-45) years, as it was (46±0.0.3%) compared to the two advanced age groups.

**[Table 2. about here]**

**2 . Hormonal Changes**

**a . Changes in the Level of Follicle-Stimulating Hormone (FSH) and LH for PCOS in Women Compared to the Control Group**

From Table (3), it is clear that there was a significant (P<0.05) increase in the level of LH, which amounted to (17.4 ± .8) for women with polycystic ovaries, compared to the control group (6.04 ± 0.025). No significant differences were observed in the level of follicle stimulating hormone for women with PCOS compared to the control group.

**[Table 3. about here]**

**b. Comparison of Changes in the Level of Follicle-Stimulating Hormone (FSH) and LH for Different Ages of PCOS**

It is evident from Table (4) that the age group (36-45) is the only age group in which there was a significant increase (P<0.05) in the level of LH, reaching (17.2 ± 0.95) compared with the age group (26-35). Which amounted to (15.45 ± .65) and the age group (18-25) reached (15.15 ±0.35).

With regard to follicle stimulating hormone, there was a significant decrease (P<0.05) in its level and for the last age group, and it amounted to (.95 ± 0.25) compared with the two groups (26-35) and (18-25), and it reached (4.45 ± .45) and (4.05 ± 0.55) respectively.

**[Table 4. about here]**

**c. Changes in the Level of Testosterone Hormone and Prolactin Hormone for PCOS in Women Compared to the Control Group**

Table (5) shows a significant increase (P<0.05) in the level of testicular lipid hormone in women with polycystic ovaries, which amounted to (0.3 ± 1.41) compared to the control group (0.08 ± 0.3). From the same table, significant increases (P<0.05) were found in the level of prolactin in women with polycystic ovaries, which amounted to (0.5 ± 22.2) compared to the control group (0.4 ± 9.01).

**d. Changes in the Levels of Testicular Fat Hormone and Milk Hormone for Different Ages of PCOS in Women**

When comparing different ages in Table (4-6), it was found that there was a significant (P<0.05) increase in the level of prolactin in the last age group (36-45), reaching (25.2±0.9) compared with the other two age groups. As for the testicular fat hormone, the results did not show any significant differences in its level between the age groups under study.

**[Table 5. about here]**

**[Table 6. about here]**

**e. Hormonal Changes in the Levels of Thyroid Stimulating Hormone (TSH) and T3 Triiodide for PCOS in Women Compared to the Control Group**

The results of the table (7) showed a significant increase (P<0.05) in the level of thyroid stimulating hormone for women with polycystic ovaries, which amounted to (5.15±0.15) compared to the control group (2.55±0.35), as for the triiodide hormone, it showed the result In the same table, there was a significant decrease (P<0.05) and it was (0.8±0.2a) compared to the control group (1.7±0.3).

**f. Changes in the Levels of Thyroid-Stimulating Hormone (TSH) and Triiodothyronine (T3) at Different Ages for PCOS in Women**

Table (8) shows that there are no significant differences (P<0.05) in the level of thyroid stimulating hormone (TSH) and thyronine triiodide (T3) for all age groups.

**[Table 7. about here]**

**[Table 8. about here]**

## B. Discussion

**1. Changes in Some Clinical Signs of PCOS**

**a. The Emergence of Acne and Hirsutism**

The significant increase in the percentage of hirsutism and hirsutism may be attributed to the significant increase in the concentration of testicular fat hormone secreted by the ovary as a result of continuous stimulation by the luteinizing hormone, which increases significantly in PCOS and this was indicated by Robert L. and David A. (2016).

The increase in acne and hirsutism may be explained by the increased production of androgens secreted by the adrenal gland John Mihailidis MD etal (2017).

It may appear that type 2 diabetes has a role in increasing the percentage, and this may be due to the increase in ovarian androgen secretion, and this is what was stated [6].

Sometimes the sensitivity of hair follicles to the testicular lipid hormone as a result of some genetic factors may play a role in increasing the percentage of acne and hirsutism in PCOS.

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The increase in the hormone cortisol from the adrenergic gland may have a role in increasing the percentage of the above two criteria.

**b. Menstrual Irregularities and Infertility**

From the results of the study, it was found that there was a significant increase in the percentage of menstrual irregularities, and this may be explained on the basis of the lack of ovulation in women as a result of the continued increase in the secretion of the testicular fat hormone, the high level of estrogen and a decrease in progesterone, which leads to an increase in the thickening of the endometrium, and this is what studies have found Ryan M. Marquardt (2019)

The confusion that occurs in the ovaries as a result of the imbalance in the work of hormones in the syndrome may have a role in causing uterine bleeding, the severity of which depends on the degree of hormonal imbalance.

The rise of estrogen and low progesterone may work to increase the thickness of the lining of the uterus and may develop in the future, causing the state of hyperplasia of the lining of the uterus (Endometrium hyperplesia) and may lead in the future to the emergence of uterine cancer.

As for the high percentage of infertility in women with polycystic ovaries, it may be due to several explanations, including the presence of an imbalance in the hypothalamic-pituitary axis, which may increase the ratio of luteinizing hormone secretion to follicle-stimulating hormone (LH/FSH ratio). As a result, ovarian theca cells are stimulated to secrete higher levels of testicular lipotropic hormone, which may disrupt the growth and development of ovarian follicles [8].

The hypothalamus and the imbalance in the secretion of its gonadotropin-releasing hormones (GnRH) may have an important role in causing infertility in PCOS, and this was indicated by several researches, including Christopher R. McCartney,et al (2022).

As for the results of the current study, it found an increase in the milk hormone (hyperprolacteinemia), and this condition is associated with infertility in a section of women with polycystic ovaries because it affects the hypothalamic-pituitary axis and as a result may affect the maturation of the follicles and failure in the ovulation process.

Hypothyroidism may contribute to the infertility of women with polycystic ovaries, as it was found in the current study a decrease in the hormone triiodothyronine and an increase in the concentration of the thyroid stimulating hormone, and this may lead to an increase in the secretion of testicular fat and causing a state of infertility.

The state of infertility may be attributed to women suffering from type 2 diabetes (Diabetes Mellitus type П), which may stimulate the ovaries to secrete androgens, which may contribute to infertility.

The increase in the concentration of total cholesterol in patients with PCOS, which has been proven in the results of the current study, may play an important role in the case of infertility, because it is the main source of the formation of steroid hormones, including androgens, and this may explain the increase in the level of male hormones in patients with the syndrome and its negative effects on fertility.

**2. Hormonal Changes**

**a. Changes in the Levels of Luteinizing Hormone and Testicular Lipoprotein**

The significant increase in LH levels with no significant differences in follicle stimulating hormone can be explained on the basis of an imbalance in the hypothalamic-pituitary axis, which leads to an increase in the pulsating release of LH from the hypothalamus, so the ratio of LH to follicle stimulating hormone (LH) increases FSH: by more than 2.5 and this is what was indicated by a study [8]. Also, the increased secretion of Gonadotropin-releasing hormones (GnRH) from the hypothalamus affected the increase of LH from the pituitary gland Pedro Marques (2022)

It was found from the study that there is a direct linear relationship between the increase in luteinizing hormone and testicular fat hormone, and this may be due to several reasons, including that the increase in the ratio of LH: FSH in the syndrome increases the building of androstenedione without being converted by the enzyme (Aromatase into estrogen) but rather works The ovary converts it into the testicular fat hormone, and this is consistent with a study Judy L. Cameron (2003) Luteinizing hormone may also stimulate the growth of the adrenergic cortex, which works to increase the formation of testicular lipids, and this is what was stated [9].

The testicular lipid hormone can be increased by inhibiting the production of hepatic sex hormones binding globulin (HSBG) by inhibiting the production of hepatic sex hormones binding globulin (HSBG) and this may lead to an increase in the concentration of testicular lipid in the bloodstream of patients with the syndrome.

Hypothyroidism, which has been proven in the current study, may have a role in increasing the testicular fat hormone as a result of the decrease in globulins associated with sex hormones, and the result is an increase in the concentration of free testicular fat hormone [10].

The results of the study show that the ages (36-45) were the only ones in which there was a significant increase in the concentration of luteinizing hormone and testicular fat, and this can be explained on the basis that the incidence of these

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ages with type 2 diabetes is more than other ages, which may lead to Influence on the pituitary gland to secrete higher levels of luteinizing hormone, which in turn leads to increased secretion of testicular fat hormone.

**b. Prolactin Hormone and Milk Flow**

The increase in the concentration of milk hormone to its normal level in PCOS may be due to the increased stimulation of the cells responsible for its production in the anterior lobe of the pituitary gland called (Lactotrophes), which may lead to an increase in its secretion and its increase is always associated with milk production in women and this is what was observed in the section of women suffering from PCOS, and this is identical to what was stated [11]. As for the explanation that we reached from the results of the current study, there is a relationship between hypothyroidism and prolactin. When the secretion of T3 by the thyroid gland decreases, the hypothalamus stimulates the secretion of Thyroid releasing factor, which in turn increases the stimulation of the secretion of thyroid-stimulating hormone. It also stimulates the cells responsible for secretion of prolactin in the pituitary gland, and as a result, the secretion of prolactin increases.

High prolactin hormone is often positively correlated with infertility, obesity and diabetes mellitus, and inversely with testosterone hormone, and this was indicated by Zahra Davoudi ( 2021 ) in her study of the clinical symptoms of PCOS.

As for the results of the percentage of milk yield, it was 31.60%, which is higher than the percentage obtained by Jamil (2007) when it was 29.2%, as well as what was mentioned by et al, Coron (2008) for American women, as it was 22.6%.

And it differed from what AL-Rubaei (2006) found in his study of women with cysts in Basra governorate, which found that the milk hormone was not affected by the women, as it was at the normal level.

The results of the study agreed with the results of (2007) Collen in his study of women with polycystic ovaries in Britain, and the study showed that the percentage of infected women was 29%.

**c. Thyroid- Stimulating Hormone and Thyronine Triiodide**

The significant increase in the levels of thyroid stimulating hormone and the decrease in the levels of triiodide and thyronine can be explained on the basis of a decrease in the function of the thyroid gland to form its hormones represented by T3 and T4, and this decrease stimulates the pituitary gland to increase the secretion of the hormone (TSH) to stimulate the thyroid gland and this is consistent with many studies It has been demonstrated that T3 is low and TSH is elevated in women with PCOS [12]. Hypothyroidism in some women with ovaries may be associated with increased secretion of TRH from the hypothalamus [13].

The decrease in T3 hormone in women with the syndrome may be due to the decreased effectiveness of the thyroid gland itself to form its hormones as a result of the lack of iodine entry into the gland through iodide trapping [14].

Genetic and immune factors may play a role in the decreased activity of the thyroid gland in some women suffering from PCOS [15]. Some research has indicated the occurrence of auto immune thyroditis (AIT) diseases and the formation of high levels of antibodies in the blood serum against one or more antigens of the thyroid gland. This may reduce T3 and T4 hormone levels in polycystic syndrome Huanhuan Fan, et al (2023). The decreased activity of the thyroid gland may have a role in reducing globulin associated with sex hormones, and thus increasing the concentration of free testicular fat hormone in the blood, and this is one of the reasons leading to the occurrence of PCOS.

A study conducted on some women with polycystic ovaries explained that the decrease in T3 hormone may be due to an increase in the activity of the enzyme deiodinase, which works to break down the iodine molecule [14].

## Conclusions

1. It appeared that there was a decrease in the concentration of T3 triiodothyronine hormone, which may give evidence of hypothrodism.

2. The rise of the prolactin hormone is often positively correlated with the state of infertility and obesity and inversely with the testosterone hormone.

3. There is a direct linear relationship between the increase in luteinizing hormone and testosterone hormone.

**Recommendations**

1.Conducting a genetic study for women with the syndrome to find out the percentage of genetic transmission of the disease.

2.Do regular thyroid examinations for the affected women .

3.The need to follow the regulations of fitness and continuous exercise to reduce obesity.

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