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Hormonal Disorders Associated with Polycystic Ovaries Syndrome (PCOS)

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Annotation: This study was carried out to look at the hormonal conditions linked to polycystic ovarian syndrome (PCOS) in women living in Thi-Qar Province. 70 samples of women with PCOS who have received a medical diagnosis were included in the research. obtained from outpatient clinics for the period from December 2022 to June 2023, their ages ranged from 20-41 years. Along with 40 samples of healthy women of identical age acting as a control group, the effect of (age, body mass index, marital status, blood group) and its relationship to PCOS was studied.

The study showed that the age group most susceptible to PCOS is the second age group (31-41) years, while the percentage decreased in the first age group (20-30) years. According to the results of the current study, a rise in body mass index (BMI) is closely correlated with a higher incidence of polycystic ovaries. The study concluded that there is a relationship between PCOS and blood groups. The highest incidence of the disease was in women of blood group (O), while the percentage decreased to a minimum in women of blood group (AB). Additionally, it was shown that married

women were more likely than unmarried women to have PCOS.

In comparison to the control group, women with PCOS had significantly higher concentrations of the hormones LH, FSH, Prolactin, Testosterone, and TSH, according to the study's findings (P 0.05). When compared to the control group, the progesterone and estradiol levels in the PCOS patient group were considerably lower (P 0.05).

1. Introduction

One of the most common hormonal and genetic disorders in women is polycystic ovary syndrome (PCOS), as it was described for the first time by Stein and Leventhal in 1935. The incidence of the syndrome is estimated at about (15-20%) of women in the world of childbearing age (12 – 45) years (El Hayek *et al.*, 2016 ; Bulsara *et al.*, 2021), It is regarded as the most important factor in women's infertility., whether it is primary or secondary infertility, that the syndrome of polycystic ovaries is a clinically heterogeneous condition in affected women, as it occurs in the vast majority of societies, environmental and genetic factors have a significant impact on the pathogenesis of PCOS, but the main reason for its occurrence Not known precisely (Ibáñez *et al.*,2017; Motlagh Asghari *et al.*, 2022).

There are many clinical and biochemical manifestations associated with this syndrome, including hyperandrogenesis, such as Testosterone hormone, from the normal limit, which often causes infertility, anovulatory and hirsutism. (Kanbour and Dobs , 2022), In addition to insulin resistance (IR) and increased insulin, as 70% of women with this syndrome are exposed to insulin resistance that develops into type 2 diabetes. The disease also causes other long-term complications, mainly resulting from obesity, such as hypertension and chronic cardiovascular diseases. CVD (Witchel *et al.*, 2019; Mumusoglu *et al*., 2020), Recurrent pregnancy loss (RPL), stroke, endometrial carcinoma, ovarian cancer, and breast cancer (Kazerooni *et al*., 2013).

The exact cause of PCOS is not known. However, given that heredity significantly contributes to the development of this illness, it is assumed that it has a genetic basis. Studies have shown that there are 100 candidate genes that contribute to the development of its pathogenesis, includes the CYP19, CYP11A, CYP21, and CYP17 genes that produce steroid hormones, the TPA, PTI-1, TNF-α genes that cause chronic inflammation, and the genes that promote insulin resistance, such as FSHR, INSR and IL-6 genes (li *et al.*, 2014; Kumar *et al*., 2022) . Polycystic ovary syndrome is defined as a complex, genetically heterogeneous disorder characterized by hyperandrogenesis, oligoamenhorrea or amenhorrea, hirsutism, and acne (Liu *et al.*, 2021; Motlagh Asghari *et al.*, 2022).

The ovaries of women with PCOS have a large number of cysts containing immature eggs, the size of which ranges from 2-9 mm, as in each menstrual cycle, a cyst grows to form a mature egg, whose size ranges from 18-22 mm, but what happens here is that a large number of cysts grow simultaneously Then all of them stop growing in the middle of the road, so none of them reach the appropriate size, and ovulation does not occur, and the cysts appear as pearl necklace beads, with an increase in the size of the ovary when ultrasound imaging (Ashraf *et al* ., 2019 ; Mumusoglu and

Yildiz, 2020).

1.1. Aim of the study

Due to the huge increase in the number of women with polycystic ovarian syndrome (PCOS), the following goals were set for this study:

- Investigating the effects of: age, body mass index, marital status and blood group on the incidence of PCOS.
- Examining the impact of PCOS infection on the hormones prolactin, luteinizing hormone (LH), estrogen, progesterone, testosterone, and thyroid-stimulating hormone (TSH) to investigate the disease's hormonal complications.

2. Materials and Methods:

- **Subjects**

Blood samples from PCOS-affected women were collected from Thi-Qar Governorate's private outpatient medical laboratories. The study included 70 female patients diagnosed by the specialist doctor, who were compared with 40 healthy women, whose ages ranged between (20-41 years), for the period from December 2022 to June 2023. Women who were treated with medication and those with other diseases were excluded. A questionnaire was used. It was prepared to study the effect of age, height, weight, marital status, and blood group.

- **Blood collection**

Five milliliters (5 ml) of blood were drawn from each sample and put into sterile, EDTA-free test tubes where they were left to stand for 20 minutes at room temperature before being centrifuged at a speed of 3000 rpm for the same amount of time. Until the hormone concentration is determined, keep the serum at a temperature of (-20) °C.

2.1. Finding the incidence of PCOS by age group:

According to the following law:

(category number/total number)*100

- Group I : (20-30) years
- Group II: (31-41) years

2.2. Finding the percentage of PCOS by blood group:

- (A, B, AB, O) blood groups

2.3. Finding the incidence of PCOS according to marital status:

- Group I : married
- Group II: single

2.4. Finding the incidence of PCOS by body mass index (BMI)

According to the following law: (Girgin ,2018).

BMI = Weight (kg) / Height (m^2).

- Group I: BMI (18.5-24.9) normal weight.
- Group II: BMI (25-29.9) overweight.
- Group III: BMI (30-34.9) obesity.

2.5. Hormonal study of women with PCOS:

Follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin, estrogen, progesterone, testosterone, and thyroid stimulating hormone (TSH) measurements were made on the third day of

the menstrual cycle using the Enzyme Linked Fluorescent Assay technology (EIFA) with the Bio Merieux (Mini VIDAS) device.

2.6. Statistical analysis:

The data were statistically analyzed using SPSS for Windows, version 23, the statistical tool for social sciences. Analysis of variance (ANOVA) and t-test are used. Means and standard deviations (SD) were obtained in order to assess the significant of the differences at the significance level (p 0.05).

3. Results:

3.1. The relationship of polycystic ovary syndrome with age:

The current study showed that the incidence of polycystic ovaries among women reached its maximum in the second age group (31-41) years, when it was (62.4%), while the percentage decreased in the first age group (20-30) years, when it was (37.6%), Figure (1).

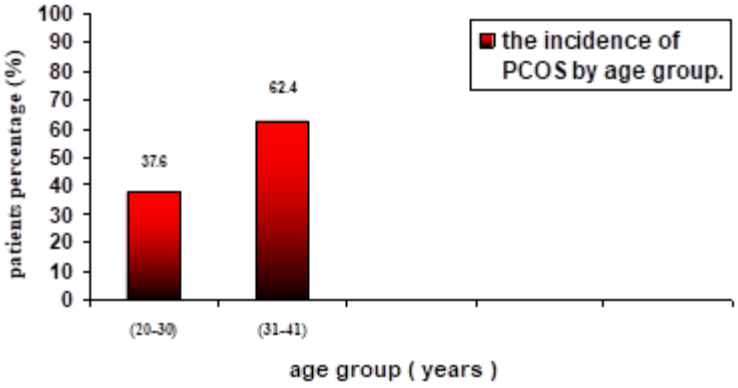

Figure (1): The prevalence of polycystic ovarian syndrome by age group.

3.2. The relationship of polycystic ovaries syndrome with body mass index (BMI):

The findings of the present study clearly showed a link between the rise in body mass index (BMI) and high prevalence of PCOS, the incidence rate was (50% in the third group of BMI (30-34.9) Class 1 obesity and (39%) in the second group of BMI (25). -29.9) overweight, while the infection rate decreased to the lowest level (11%) in the first BMI group for BMI (18.5-24.9)) normal weight, Figure (2).

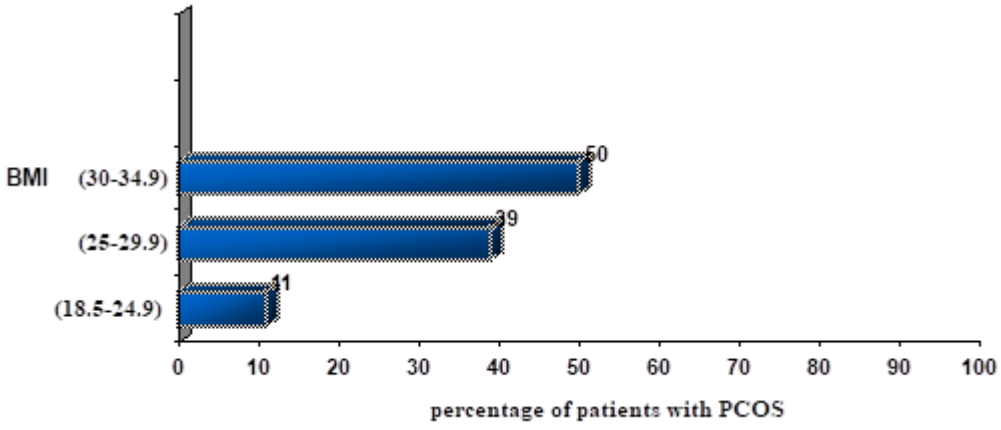

Figure (2): The incidence of PCOS according to BMI.

3.3. The relationship of polycystic ovary syndrome with the blood group:

The current study showed a relationship between the incidence of polycystic ovary syndrome and blood groups, as the highest incidence of PCOS was (49%) in women of the (O) blood group, while the percentage decreased to its minimum (9%) in women of the blood group (AB) Figure (3).

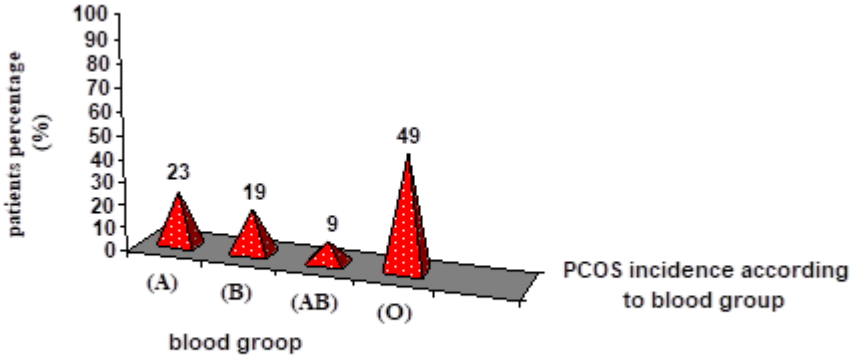

Figure (3): The incidence of PCOS according to blood groop.

3.4. Relationship of polycystic ovary syndrome with marital status:

The current study recorded that the incidence of polycystic ovary syndrome among married women was high, reaching (73.5%), compared with only (26.5%) for single women, Figure (4).

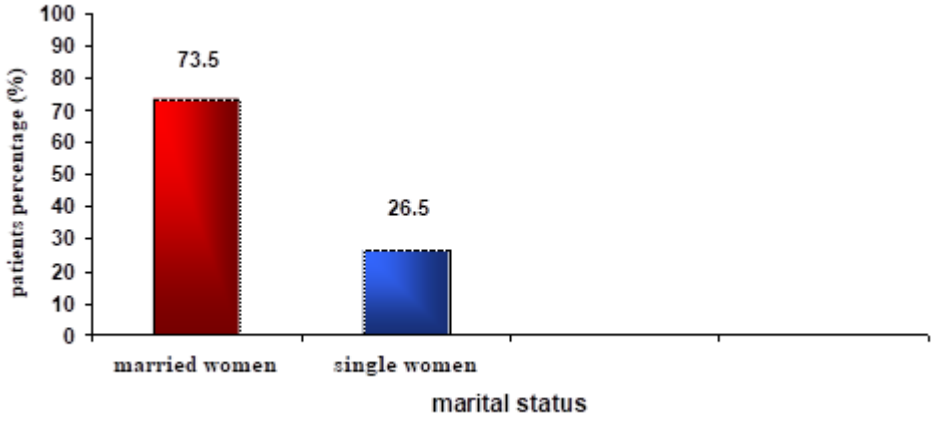

Figure (4): The incidence of PCOS according to marital status.

3.4. Effect of polycystic ovary syndrome on hormonal parameters:

Compared to the control group, PCOS patients had significantly higher levels of the hormones LH, FSH, Prolactin, Testosterone, and TSH, as shown in Table 1 of the study's findings. Furthermore, as compared with the control group, PCOS patients' progesterone and estradiol concentrations were significantly lower (P 0.05), according to the data.

Table (1): Effect of polycystic ovary syndrome (PCOS) on hormonal parameters.

(2) PCOS group Mean ± SD	**(1) Control group** Mean ± SD	**studied parameters**
15.84 ± 2.84 [a]	6.72 ± 1.54 [b]	LH (µlU/ml)
5.23 ± 1.05 [a]	4.18 ± 0.85 [b]	FSH (µlU/ml)
12.33 ± 1.64 [b]	34.61 ± 5.22 [a]	Progesterone (ng/ml)
85.81 ± 12.41 [b]	162.42 ± 38.25 [a]	Estradiol (pg/ml)
18.12 ± 3.38 [a]	9.21 ± 1.33 [b]	Prolactin (ng/ml)
33.26 ± 7.12 [a]	11.52 ± 4.19 [b]	Testosterone (pg/ml)
3.17 ± 0.62 [a]	2.06 ± 0.21 [b]	TSH (µlU/ml)
70	40	number of samples

The letters (a,b) stand for substantial differences, (SD) for standard deviation, (P > 0.05): no significant difference, and (p 0.05): are significant. The identical letters (a,a) don't differ much.

4. Discussion:

4.1. The relationship of polycystic ovary syndrome with age:

Polycystic ovary syndrome prevalence among women shown in figure (1) reached its peak in the second age group (31-41) years, while the percentage decreased to its minimum in the first age group (20-30) years. The reason for this may be due to a change in hormones or because of the diet, as most women with advancing age have an increase in weight, and the reason may be attributed to the delay in diagnosing the disease to advanced stages (Laura, 2018).

On the other hand, the pathogenesis of PCOS is complex and linked to several factors, including an increase in genes contributing to insulin resistance, compensatory hyperinsulinemia, chronic infections, defects in the formation of ovarian steroids, and an imbalance in adrenal androgen production. All these factors contribute to pathological events that often increase in the second age group (Ashraf *et al* ., 2019; Bulsara *et al.*,2021).

4.2. The relationship of polycystic ovaries syndrome with body mass index (BMI):

Figure 2 from the current study demonstrated the significant prevalence of polycystic ovarian syndrome (PCOS). is directly proportional to the increase in body mass index (BMI), as the incidence reached a maximum (50%) in the third group of BMI (Class 1 obesity), while the incidence gradually decreased to (39% in the second group for BMI (overweight) until it reached its minimum level (11%) in the first BMI group (normal weight). This study is consistent with many studies indicating that weight gain and high body mass are among the most important distinguishing external signs that indicate of having polycystic ovary syndrome the reason for this may be due to the presence of a decrease in the thyroid hormones T3 & T4 (Romitti *et al.*,2019), which are responsible for regulating the metabolic processes in the body, which in turn affects energy production and the rate of burning calories in the body, and thus the basic metabolic rate in the body decreases thus, weight gain due to a decrease in the metabolic rate in most cases, and the high TSH hormone in this study is the best evidence of a decrease in thyroid hormones (George and Kaiser ,2018; Mandy,2020).

On the other hand, the cause may be due to hyperandrogenism of the adrenal cortex as a result of excessive secretion of cortisol, as well as androgens produced by the action of luteinizing hormone in the ovaries (Chen *et al.*,2021), this is evident through the increase in the concentration of Testosterone in this study, in addition, obesity may occur as a result of insulin resistance and compensatory hyperinsulinemia, which stimulates the ovaries to form testosterone (Ding *et al.*, 2021), insulin filters sugar from the blood to be used by the cells and converts it into glycogen in the liver and muscles or converts it into fatty acids, which makes the cells obese, while some studies attribute the cause of obesity to a high concentration of total cholesterol and triglycerides (Sin *et al.*,2011; Barber *et al.*,2019).

4.3. The relationship of polycystic ovary syndrome with the blood group:

The results of the current investigation indicated a connection between PCOS incidence and blood group, as the highest incidence of PCOS was (49%) in women of blood group (O), while the percentage decreased to a minimum (9%) in women of blood group (AB), the reason for this may be attributed to the fact that genetic genes contributing to pathological events may be more frequent in blood group (O) than they are in other groups, especially group (AB), in addition to the fact that the (O) group constitutes the largest proportion among the rest of the groups, unlike the rare (AB) blood group (Mandy 2020) .

4.4. Relationship of polycystic ovary syndrome with marital status:

The current study recorded that the percentage of polycystic ovaries among married women was higher, reaching 73.5%), while the percentage was 26.5%) only for single women, as married women are more susceptible to PCOS than unmarried women, due to a change or disorder in female hormones, as well as an increase in androgens (Ashraf, *et al* ., 2019). Hyperandrogenism, or elevated

levels of free testosterone, is caused by the adrenals and ovaries producing too much androgen, which is a key hormone in the pathophysiology of PCOS (Kanbour and Dobs, 2022).

Gonadotrophin hormones are released from the pituitary gland in response to the hypothalamus's production of GnRH. LH receptor is activated by luteinizing hormone (LH), which then increases androgen production in ovarian theca cells. FSH receptor in ovarian granulosa cells is also stimulated by follicle-stimulating hormone (FSH), which results in the conversion of androgens into estrogens, helping in follicle development (Bulsara et al., 2021). It is believed that dysregulation of the neuroendocrine system is the cause of the hypothalamic-pituitary-ovarian (HPO) axis's imbalance. This imbalance then results in an excess of gonadotropin, and as GnRH levels rise, LH production outpaces FSH production, significantly increasing the LH:FSH ratio in PCOS (Walters *et al.*,2018; Robert,2018).

4.5. Effect of polycystic ovary syndrome on hormonal parameters:

4.5.1. Luteinizing Hormone and Follicle Stimulating Hormone

According to Table 1 of the study's results, PCOS patients had considerably greater levels of the gonadal hormones follicle stimulating hormone (FSH) and luteinizing hormone (LH) than the control women, in addition to that the increase in LH was almost three times greater than FSH The reason may be attributed to a defect in the hypothalamic pituitary axis, which causes an increase in the LH / FSH ratio, and thus stimulates the ovaries to secrete higher levels of testosterone, which causes an imbalance in the growth and development of the ovarian follicles (Walters *et al.*,2018).

The reason for the rise in LH may be due to the rise in androgens, as the process of producing androgens from estrone may increase the sensitivity of the pituitary gland to GnRH from the hypothalamus, as well as its effective action in increasing the sensitivity of gonadotrophin hormones to their receptors on cell surfaces, which contributes to the pathogenesis of PCOS and thus an increase in the concentration of LH (Ashraf *et al* ., 2019; William 2021).

On the other hand, the reason for the high FSH concentration may be due to the decrease in estrogen, through its connection to the amount of the estrogen hormone, the FSH hormone has a significant impact on the activity of the aromatase enzyme, as the reduction of the estrogen level leads to stimulation of the production of FSH by negative feedback (Walters *et al.*,2018), this explains the higher FSH concentration in PCOS women.

Aromatase inhibitors (AIs) have been described as ovulatory stimulators due to their selective action in preventing the conversion of androgens to estrogens in ovarian follicles, which is thought to lower the creation of follicles necessary for optimal ovulation in women with PCOS. This leads to the establishment of a positive feedback cycle with estrogens of the HPO axis, which in turns triggers the endogenous release of GnRH, encourages FSH production, and stimulates follicle growth (Casper and Mitwally, 2011; Badawy and Elnashar, 2011).

4.5.2. Progesterone Hormone

According to the current study's findings, Progesterone levels in the PCOS group were found to be considerably lower than those in the control group (P 0.05), and this is consistent with the results of other studies that indicated a decrease in the concentration of progesterone in PCOS, which occurs due to the conversion of progesterone into androgen before ovulation, and thus the failure to ovulation prevents the formation of the corpus luteum and thus reduces the production of progesterone, as progesterone is formed mainly from the corpus luteum in the ovaries as well as the adrenal cortex (Sabrina, 2019; Kanbour and Dobs, 2022).

On the other hand, the decrease in progesterone may be attributed to the excessive increase in LH causing anovulation (Arduc *et al.,* 2015), which explains the decrease in progesterone concentration in PCOS women. In addition, progesterone may be reduced by the effect of stress and psychological anxiety associated with PCOS (Tabrizi *et al.,* 2022). Also, the rise in the milk hormone may prevent ovulation and thus may cause a decrease in progesterone (Elgellaie *et al.,* 2021).

4.5.3. Estradiol Hormone

According to the results of the current study, women with PCOS had substantially lower levels of estradiol than those in the control group (P 0.05). and this difference might be explained by an excessive increase in LH, which results in a lack of ovulation and a lack of formation of the corpus luteum that secretes this hormone. On the other hand, the rise in testosterone concentration is another reason for the decrease in estrogen, because the latter is secreted from the mature follicles at the same time. The rise in testosterone In PCOS women, it inhibits the maturation and development of ovarian follicles (Walters *et al.,* 2018; Kanbour and Dobs,2022).

In addition, the high level of LH inhibits the activity of the aromatase enzyme and inhibits the growth of the oocyte, as the aromatase enzyme stimulates the conversion of androgens (testosterone and androstenedione) into estrogens (estradiol and estrone), therefore, suppressing this enzyme due to the excessive rise of the LH hormone causes hyperandrogens and low estrogens, because of this hormonal disorder, ovulation does not occur (Zhang *et al.*,2012; Arduc *et al.,* 2015), and this explains the decrease in estrogen and progesterone levels and the increase in testosterone levels in PCOS patients. On the other hand, the cause for the drop in estrogen might be explained by the rise in prolactin, as the latter inhibits the activity of the aromatase enzyme, thus preventing the conversion of androgens into estrogens (Casper and Mitwally, 2011).

On the other hand, high TSH may be a cause of decreased estrogen, as it leads to increased secretion of testosterone. Therefore, TSH alters the metabolism of estrogen and lowers the amount of Sex Hormone Binding Globulin (SHBG), which transports androgens and estrogens to the target tissue (Dahiya *et al.*,2012).

4.5.4. Prolactin Hormone

Contrasted with the control group, the findings showed that prolactin hormone concentration was higher in women with PCOS. The reason may be due to psychological disorders and stress for PCOS women, and severe anxiety because the concentration of prolactin increases in the bloodstream due to stress resulting from the deterioration of the health status (Palubska *et al.*,2017; Elgellaie *et al.*,2021).

On the other hand, the reason for this may be attributed to an imbalance in hormones and a decrease in the levels of thyroid hormones T3 and T4, which lead to an increase in the secretion of the thyroid stimulating hormone (TSH), and this works directly to stimulate the secretion of prolactin (Wang JF, *et al.,* 2017; Nath *et al.,* 2019), therefore, it is necessary to do an analysis of TSH thyroid functions, because its deficiency causes an increase in prolactin hormone and irregular menstruation (Yamini, 2018).

4.5.5. Testosterone Hormone

Through the findings, it was shown that PCOS women's testosterone levels were higher than those of the control group. The reason may be attributed to obesity, as studies indicated that weight gain and a high body mass index are among the most important distinguishing signs that indicate infection with PCOS, and that obesity plays a major role. In the functional and reproductive changes that are linked to each other, which is one of the most important characteristics of PCOS syndrome, the adipose tissue has the ability to manufacture effective androgens in the body, with the increase in obesity, the level of androgen hormone increases, due to the conversion of cholesterol by a series of metabolic processes to the peripheral testosterone, which is another source of this hormone, and this explains the high concentration of testosterone (Lerchbaum *et al.,* 2014; Abdelazim *et al.,* 2020).

On the other hand, the cause may be due to insulin action, directly or indirectly. Although PCOS women suffer from insulin resistance, ovarian steroids show hypersensitivity to insulin, as the latter works synergistically with LH hormone to enhance androgen production by insulin receptors (Ding *et al.,* 2021). In addition, compensatory hyperinsulinemia affects non-ovarian sites such as the liver,

adrenal gland, and pituitary gland, and insulin inhibits the production of hepatic globulin associated with the sex hormone (SHBG), and thus androgens increase (Bulsara *et al.,* 2021).

In addition, the cause may be increased stress, as stress works to increase the secretion of Corticotropin-Releasing Hormone (CRH), which increases the release of Adrenocorticotrophic Hormone (ACTH), which affects the adrenal cortex to secrete androgens (Dissen *et al.,* 2009), as androgens increase as a result of excessive secretion of cortisol (Tsilchorozidou *et al.,* 2003). Hypothyroidism is also a cause of high testosterone because the high concentration of TSH reduces the production of SHBG in the liver, and thus the concentration of free testosterone increases (Dahiya *et al.,* 2012).

4.5.6. Thyroid Stimulating Hormone

Considering the findings of the recent study, women with PCOS had considerably higher TSH levels than women in the control group. Low levels of the thyroid hormones T3 and T4 in PCOS women with hypothyroidism may be the cause of this discrepancy, which are known to cause infertility. TSH production is enhanced via a negative feedback mechanism when T3 and T4 levels are low (Wang *et al.,* 2017; Romitti *et al.,* 2018).

The cause may be attributed to obesity and insulin resistance. Obesity affects thyroid function. People who are overweight tend to have abnormal activation of the thyroid axis, which leads to elevated TSH levels, obesity is often associated with insulin resistance, which can also effect on thyroid function, as insulin resistance impairs the ability of thyroid hormone to enter cells and exert its metabolic influence (Benetti-Pinto *et al.,* 2017; Liu *et al.,* 2018).

5. Conclusions and Recommendation

5.1. Conclusions:

- Polycystic ovary syndrome (PCOS) is more common as women become older.
- The rise in body mass index is closely correlated with PCOS percentage.
- There is a relationship between the incidence of PCOS and blood group.
- Married women are more likely to have PCOS than single women.
- There is an increase in the concentration of Testosterone, Prolactin, LH, FSH and TSH in PCOS patients.
- A drop in PCOS women's levels of the hormones progesterone and estradiol.

5.2. Recommendation:

- Studying the relationship of polycystic ovary syndrom (PCOS) with uterine, ovarian and breast cancer.
- Studying the effectiveness of some medicinal plant extracts in treating (PCOS).
- Researching the benefits of exercise in the management of (PCOS).
- Molecular study on the most frequent causative genes in (PCOS) patients.
- A comparative study of the treatments used to treat (PCOS) to determine the best one.
- Determine the causative agents of (PCOS), the risk factors, and the most important methods of prevention.

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