Relationship of Polycystic Ovaries with some Hormones

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ABSTRACT
The study aims to determine the relationship of polycystic ovaries with LH, FSH, Prolactin, Testosterone, Estrogen, T4, T3 hormones, fertility, hirsutism and acne. The sample was divided into two groups; the first group includes 200 women with polycystic ovaries and the second group is the control group which includes 25 healthy women.The results showed a significant decrease ($P \leq 0.01$) in FSH and T3 in the first group compared with control group and a significant increase(($p \leq 0.05$), ($P \leq 0.01$)) in LH, Prolactin, Testosterone, Estrogen, T4 compared with control groups and 40 % of 134 married women did not get pregnant after (1-7) years of marriage , 5 % are suffered abortion without giving birth any child and among the 200 infected women with PCOS There were %26 of them suffering from hirsutism and acne and %32 suffering from hirsutism only and %11 acne only. There is relationship between the concentration of LH, FSH, Prolactin, Testosterone, Estrogen, Thyroxin, hirsutism and acne with development of PCOS and its impact on fertility.

1. Introduction

polycystic syndrome ovarian (PCOS) is disorder in the endocrine glands. It causes abnormal secretion of hormones and textural changes in the ovary [1]. The reason may be hereditary or non-genetic, 5-20% of women in reproductive age of worldwide suffered from it [2] [3]. polycystic syndrome ovarian is characterized by Hyperandrogenism, the presence of multiple ovarian cysts, lack of ovulation [4]. described firstly by Stein and Levinthal in 1935 [5]. The severity of its symptoms varies from mild to severe among the most common signs of PCOS are hirsutism (excessive hair growth on the face, chest, abdomen, upper thighs, back, or buttocks, affecting 70% of women with PCOS) and acne (Which appears after adolescence and does not respond to standard treatment), metabolic disorders, difficulty conceiving, oily skin [6] [7]. hair thinning and loss from the head [8], anovulatory dysfunction and menstrual disorders [9] [10]. PCOS is considered the most common cause of infertility in women [1]. because it leads to the lack of ovulation [11]. It is believed that insulin resistance and exposure to Hyperandrogenism, increased Luteinizing hormone (LH) compared to the secretion of follicle-stimulating hormone (FSH) causes PCOS [2]. The pathophysiology of polycystic ovary syndrome includes a congenital ovarian which affected by internal variables such as the axis and hyperinsulinemia also the level of androgen synthesis which have a negative effect on follicular formation and oocyte development. It also affected by neuroendocrine disorders, including increased secretion of gonadotrophin-releasing hormone (GnRH) and successive bursts of its secretion, resulting in excessive secretion of LH, which causes a continuous imbalance in gonadotrophin secretion due to the disturbance occurring in this axis and the irregularity of the feedback mechanism that controls the secretion of hormones [12]. According to several studies, genetic variants associated with ovarian steroidogenesis may be the reason. Although there is such a high incidence, the pathophysiology of the syndrome is still not completely clear [13]. There are three sets of criteria that are used to diagnose PCOS by the National Institutes of Health (NIH) in 1990, Rotterdam in 2003, AE-PCOS Society criteria 2009 and the 2003 Rotterdam criteria are the ones that support the diagnosis of PCOS, It requires the availability of two of the three criteria: clinical or biochemical hyperandrogenism, weak or no ovulation, and polycystic ovary morphology The most common criteria currently [14].

Aim of study: The study was designed to research the relationship of polycystic ovaries with LH, FSH, Prolactin, Testosterone, Estrogen, T4, T3 hormones, fertility, hirsutism and acne.

2. Method and materials

study design

The sample was divided into two groups, The first included 200 women suffering from polycystic

ovary syndrome, including 66 non-married and 134 married women aged between 13-45 years old who were visiting the hospital for the period from 28June to 15 October 2023. They were diagnosed based on the presence of 2 out of 3 diagnostic signs of polycystic ovary syndrome, hyperandrogenism, acne, hirsutism, lack of ovulation or its absence, the presence of 10-12 ovarian cysts or more, and an increase in the size of ovaries were examined by ultrasound imaging [4]. The second group was the control group, which included 25 a healthy woman who did not suffer from any disease.

Measurement of hormone concentrations

Both hormones (LH, FSH, prolactin, testosterone, estrogen, T4, T3) were measured by Cobas e 411 device (ROCHE, Germany)

Statistical Analysis

The Statistical Analysis System- SAS (2018) was used to detect the effect of difference groups (patients and control) in study parameters. T-test was used to significantly compare between means in this study.

3. Results and discussion

Relationship of polycystic Ovaries with LH, FSH and prolactin concentration

The results showed that there is a significant increase in LH and prolactin concentration and a significant decrease in FSH of PCOS woman when compared with healthy group ((P≤0.05), (P≤0.01)) (Table 1).

Table 1

	Hormones (Mean ± Stander Error)		
Study Groups	**FSH (mIU\Ml)**	**LH (mIU\Ml)**	**Prolactin (ng/mL)**
PCOS woman	3.42 ± 0.31	8.74 ± 0.56	20.84 ± 0.95
Control	5.99 ± 0.44	4.69 ± 0.27	10.97 ± 0.41
T-test	1.132 **	1.317 **	2.181 **
P-value	0.0002	0.0001	0.0001

****** High Significant (P≤0.01)

This concentrations discrepancy of these hormones in affected women compared with the control group that can be due to several reasons related to the PCOS complexity, especially the high concentration of LH compared to a low concentration of FSH is one of the reasons of PCOS development. Because the LH, FSH control on the growth and development of follicles and the ovulation, both hormones are important as sex hormones that have a role in the reproductive process [2]. The increase concentration of LH and decrease of FSH despite it secrete from the same gland related to that the secretion of FSH is regulated by a negative feedback mechanism which depend on estrogen. Inhibin concentration and the estrogen has a positive feedback response for LH release from pituitary [15].

The reason behind increase of LH concentration and decrease of FSH may be due to feedback mechanism which refer to the increase of estrogen concentration stimulated the LH secretion (positive feedback mechanism). It explained in the results (a significant increase in estrogen concentration) while the decrease of FSH it is possible due to the suppression of its secretion by inhibin. As explained by [16], or by increase of prolactin concentration as explained by the results [17]. On the other hand [18] revealed to the continuous treatment of PCOS leads to decrease of inhibin level which causes increase in FSH concentration. It is possible the increase in prolactin and luteinizing hormone and the Isame gland (pituitary gland) under the influence of GnRH from hypothalamus. So, any factors effected on these glands may be causes imbalance in the secretion of these hormones. Baskind and Balen [12]; Barber *et al*. [19] explained that the increase of prolactin and luteinizing hormone production compared with FSH as a result from infection of pituitary gland with adenocarcinoma tumors which on its

function, level production and injuries physical in the head can affect it due to the lack of blood flow and the lack of oxygen that reaches it, which leads to lethargy or increased pressure on it and thus dysfunction of its secretion [20] [21], and psychological distress also eating disorders, psychological stress, excessive physical exercise may be causes dysfunction of pituitary gland and effect on hormonal secretion [22], the reasons of prolactin increase may be related to increase of LH secretion which causes decrease in dopamine which in turn causes increase in prolactin production [23] [24], and Prolactin may act as a "co-gonadotropin" and regulated of follicle formation by altering the function of granulosa FSH receptors [25], some of studies showed that the increase of estrogen which stimulated by LH causes increase in prolactin secretion [26]. which agree with results of the current study, The effect of estrogen in cells which secret the prolactin may be related to prolactinoma galactorrhea [27]. Also, gene mutations may have a role in the secretion and function of the hypothalamus, or make it resistant to feedback. Thereby increasing the secretion GnRH from hypothalamus [28], and the Lower concentration of FSH it is possible due to the suppression of its secretion by inhibin, being a regulator FSH [16]. [29] [30] [31] found that the concentration of prolactin was high PCOS in women compared to the control group which agree with the results of current study. It is possible to consider it a diagnostic sign of PCOS and some this increase was associated with an increase in visceral fat mass while the results did not coincide with the results of [32]. It considered that the hormone prolactin has nothing to do with PCOS which cannot be considered a diagnostic marker among affected women compared to the control group, while Filho *et al*. [33] revealed to, that it has nothing to do with PCOS and may have other causes.

There is a relationship between underactive thyroid and increased prolactin secretion because the stimulated secretion of thyrotropin increases the secretion of thyrotropin from the hypothalamus. In order to compensate for the deficiency of thyroid hormones, it was found that it increases the stimulation of prolactin secretion in an incomprehensible way [34].

Relationship of polycystic ovaries with steroid hormones concentration

The results showed that there is a significant increase in Testosterone and Estrogen concentration in woman with PCOS when compared with healthy group ((P≤0.05), (P≤0.01)) (Table 2).

Table 2

	Hormones (Mean ± Stander Error)	
Study Groups	**Testosterone (ng/mL)**	**Estrogen (Pg/mL)**
PCOS woman	0.332 ±0.05	975.00 ±6.39
Control	0.201 ±0.02	100.76 ±1.54
T-test	0.114 *	13.833 **
P-value	0.0269	0.0001

* Significant (P≤0.05), ** High Significant (P≤0.01).

In women, High Testosterone is a common with PCOS. one of its reasons is attributed to hyperandrogenism and evidenced by hirsutism, acne, or blood tests [2].Therefore, hyperandrogenism can be considered one of the prominent signs of PCOS. In agreement with [35]; and [36], it can cause the cessation of the cavernous follicle development and the occurrence of follicular atresia which leads to the interruption or cessation of ovulation. As showed by [37] [38]. An increase of testosterone concentration in blood because decrease of sex hormone-binding globulin (SHBG). the production of SHBGAs Decline leads the effect of hyperinsulinemia resulting from poor cell tolerance to glucose and increased insulin resistance. The most infected women have a high mass index and insulin resistance where the high concentrations of insulin effect on liver and reduce the production of SHBG. This leads to an increase in free testosterone, the increase of insulin concentration also causes the increase of testosterone synthesis that directly produced by theca cells in the ovary as a result of insulin binding to receptors insulin-like growth factor I (IGF-I) [39] [40]. While assume [41] , pointed out that the Hyperandrogenism is a result for a genetic defect in DNA of theca cells that leads to increase

androgen synthesis and Diamanti [42] ; Nestler *et al*. [37], explained the increase of testosterone as a result of increased secretion from theca cells in the ovary or increased production by the adrenal gland. It also rises as a result of increased concentration of luteinizing hormone and increased stimulation the ovary to produce more testosterone. The results of this study pointed out increase of LH in the infected women, it is corresponding with [43] [15]. whom discovered LH plays a vital role in androgen production from theca cells. Women with PCOS had significantly higher estrogen levels than those in the control group. It was a high-level estrogen hormone that could be linked to follicular growth suppression and problems with ovulation. It is in line with the findings of [44] [45]who observed that women with PCOS had elevated estrogen concentrations and that estrogen inhibited follicle meiosis anthers. Because high estrogen levels have been linked to increased expression of estrogen receptors, including G protein-coupled estrogen receptor 1 (GPER), this inhibits follicle growth through its receptor in granulosa cells. This rise can be connected to the suppression of the growth of antral follicles. Whereas Yu *et al*. [46] discovered that impacted women possess. This shows that the increase in estrogen concentration could be due to the conversion of excess androgen in adipose tissue to estrogen. Additionally, it lends credence to the theory that elevated luteinizing hormone levels increase ovarian testosterone production and that the impacted women had greater testosterone concentrations. These results confirm the findings of [47] [48] that excess testosterone in peripheral fat or adipose tissue is converted to estrogen by Aromatase. he high concentration of estrogen may be attributed to the effect of the increase in the concentration of luteinizing hormone LH, which is associated with estrogen by the mechanism of positive feedback, and the results of our study showed a significant increase in the concentration of luteinizing hormone LH, as Etrusco *et al.* [49] showed that hyperandrogenism causes an imbalance in the secretion of GnRH and thus increases the production of luteinizing hormone LH from the gonads, which in turn stimulates the cells of Thika and increases their production of androgens, and on the other hand stimulates granulocytes and increases their production of estrogen.

The Relationship between T4, T3 concentration with polycystic ovaries

The study's findings demonstrated that, in comparison to the control group, women with PCOS had significantly higher concentrations of thyroid (T4) and lower concentrations of triiodothyronine (T3) (P≤0.01) (Table 3)

Table 3

	Hormones (Mean ± Stander Error)	
Study Groups	**T4 (nmol/L)**	**T3 (ng/mL)**
PCOS woman	121.54 ±1.47	1.293 ±0.15
Control	107.28 ±1.19	1.894 ±0.10
T-test	3.979 **	0.394 **
P-value	0.0001	0.0049

* High Significant (P≤0.01)

It might be proof of low conversion of T4 to T3, which results from a decrease of activity in type 2 deiodinases (D2) in bodily tissues and insufficient generation of T3. A negative feedback mechanism involving the secretion of Thyrotropin-Releasing Hormone (TRH) from the hypothalamus is responsible for the low concentration of T3. This low concentration induced the pituitary gland to secrete Thyroid-Stimulating Hormone (TSH), which effects in the release of T4. According to Koenig *et al*. [50] ; Dyess *et al*. [51]; Schneider *et al*. [52] the researcher observed a high T4 in women with PCOS. [51] [52] and Galton *et al*. [53] shows that T3 Found in nerve cells and often produced fromT4 by type 2 deiodinases (D2)in glial cells as Dyess *et al*. [51] suggest that effect T3 on the hypothalamic paraventricular nucleus (PVN) is direct. It increases the sensitivity of TRH which producing by neurons as response to decrease levels of thyroid hormones. Schneider *et al*. [52], concluded that in spite of Finding a high Concentrations from T4 in D2 knockout mice also there are an abnormal increasing of

which indicated on resistance to thyroid hormone as causes to decrease production of T3 because loss of D2 activity in all target tissues due to targeted inactivation of the selenodeiodinase gene Dio2. Many thyroid disorders have been associated with PCOS Such as Hashimoto's thyroiditis (HT), Graves' disease (GD) [54], where Hu *et al.* [55], found that there is a strong correlation between HT and infection with PCOS. Sumbul and Khanam [56]; and notice there is a link between infection with subclinical hypothyroidism (SCH)And PCOS. While there are a few studies that indicate a relationship between GD and PCOS [57]; and [58]. In his study show that thyroid hormones interfere with gonadotropin By affecting the granule cells directly and modifying FSH/LH and estrogen secretion Its deficiency leads to Reducing metabolic clearance rates of androstenedione and estrone and increase conversion Androstinon into testosterone and aromatization into estradiol by reducing sex hormone binding globulin levels Which leads to exacerbation of the infection PCOS. Intracellular T_3 and T_4 is dependent not only on the local variation in the activity of the deiodinases D1, D2 and D3, but also on the ability of the cell to transport thyroid hormone [59].

The relationship between poor fertility or infertility with polycystic infected

A sample of impacted PCOS-afflicted ladies Out of the 134 married women in our sample, 40% never got the chance to conceive even though they were married for 1–7 years, and 5% had an abortion without having a kid. 27% of respondents had children but experienced abortions occasionally. Just 28% of them were able to conceive without experiencing a loss or delayed pregnancy (Table 4).

Table 4

Cases	**Without child**	**Births without abortion**	**Births with abortion**	**abortion**
Rate	40%	28%	27%	5%

Poor fertility, infertility, and delayed pregnancy are always linked to PCOS [1] [60], due to the accompanying hormonal abnormalities. We can attribute the delay in pregnancy, infertility, and poor fertility experienced by PCOS patients in our study to a number of factors, such as: high prolactin concentration, which causes infertility and delayed pregnancy in infected women, which is in line with [29] [61], or menopause and lack of ovulation due to hormonal imbalances and high LH concentration compared to FSH [11]. According to [12], there is a direct link between PCOS-related infertility and elevated LH levels [62]. Both of [54]; and [56], pointed out that both hypothyroidism and hyperthyroidism may be causes Menstrual disturbance and decreased fertility when infected with PCOS, And functional anovulation (Functional hypothalamic amenorrhea (FHA)). It is one of the forms of anovulation that has no specific organic causes. It is one of the three factors that must be present in a woman to be diagnosed PCOS [63]; and [14].

The relationship between Hirsutism and Acne with polycystic infected

Among the 200 infected women with PCOS There were %58 suffering from hirsutism including %26 of them with acne and %32 without it and %37 suffering from acne including of them with 26% with hirsutism and %11 without it (Table 5)

Table 5

Clinical symptom	**Hirsutism only**	**Hirsutism and Acne**	**Acne only**
Rate	%32	%26	%11
Clinical symptom	**Hirsutism**	**Acne**	
Rate	%58	%37	

The reason behind appearance of both hirsutism is due to hyperandrogenism in affected women. As these women are the most prominent signs consider as indicator for hyperandrogenism in affected women with PCOS. This agree with the results of this study (increase the testosterone concentration in woman with PCOS), while the 31% who were with out of hirsutism and acne, even though there was an although from increase of testosterone concentration. It is not necessary for there to be a response in the sebaceous glands or hair follicle to hyperandrogenism to judge the presence of hyperandrogenism in them, and this agree with [64]; [65]; and [66]. The reason behind Acne may be due to increase of

LH, prolactin, testosterone and decrease of follicle stimulating hormone and showed in the results of this study and agree with [67] who revealed that the Women with PCOS suffer from severe to moderate acne they have a high level of Luteinizing hormone, Prolactin and Testosterone compared to down follicle stimulating hormone.

Conclusion

There are relationship between the concentration of LH, FSH, Prolactin, Testosterone, Estrogens, Thyroxin, hirsutism and acne with development of PCOS and its impact on fertility.

Recommendation

Studying the histological effects of polycystic ovary disease, its relationship with other hormones, and the necessity of periodic examination of hormones in women

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