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Hormonal Profile Changes as A predictive Marker for Polycystic Ovary Syndrome and Infertility in Women

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P A P E R I N F O

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A B S T R A C T

Background: This study aims to examine the role of hormones that are important for controlling female reproductive processes: the follicle-stimulating hormone (FSH), Sex binding globulin (SBHG), luteinizing hormone (LH), testosterone (T) and free testosterone (FT) levels as a prognostic marker among polycystic ovary syndrome (PCOS) patients, and their relationship with obesity.

Design and Methods: This study included one hundred samples of Iraqi patients aged between (25 and 40) years. A healthy BMI level is around (20-24.9) kg/m2, and around (25-29.9) kg/m2 is overweight. Then, when BMI is more than (30kg / m2), the woman is considered fat. The groups are collected from the Obstetrician and Gynecologist" in Karbala Hospital from December 2023 to March 2024. BMI, waist-to-hip ratio (WHR), LH, FSH, TT, FT, and SHBG levels were evaluated in each subject.

Results: A significant increase in LH (P=0.0001), FSH levels (p=0.05), LH/FSH ratio (P=0.0001), TT (p=0.025), and FT (p=0.0001) in PCOS patients compared to the control group. However, the SHBG level (p=0.0001) in PCOS patients compared to the control group was significantly diminished.

1. INTRODUCTION

The suffering environment of Iraq from acts of desecration is due to the wars that Iraq witnessed since 1990 and after 2003. This resulted in a large number of injuries and deaths due to radioactive materials and destructive chemicals. These calamities led to either infertility or cancer. Infertility is a disease. The reproductive system usually is defined as the failure clinically to chieve pregnancy after more than one year of uniform without protection sexual coition. In the last few years, infertility has been increased .[1]

In reproductive system the uterus is a most substantial organs and structures; this vacant muscular organ has a pear-shaped organ located between lower intestine and bladder. Uterus is composed from two parts, body and cervix; cervix is the lower portion of the uterus. The opening os is the vessel opening, which opens into the vagina and helps in the flowing out of the menstrual blood from the uterus to the vagina and leads to the uterus into two fallopian tubes. Alongside to this is ovary, which closes all stages of the tube. Ovary known is the egg-producing organ as contains 200,000 to 400,000 follicles. Figure 1 [2].

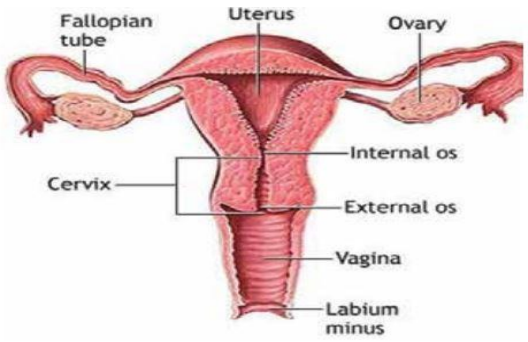

Figure 1. The reproductive system of women [2]

Infertile Women (IW) is defined as the way of a disturbance affecting contraceptive methods despite intercourse and without regular using of any means of despite the happening of pregnancy at least for six months [3]. Sanitize It was a general disturbance with an emotional impact effectiveness On the structural

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generative, described through the clinical pregnancy to the Inability of a The two partners after one year or more of regular Without protection sexual coition [4]. Because of the fight in Iraq around 2003, deaths with a large numbers of injuries because of the destructive chemicals and radioactive materials. The environment of Iraqi suffering from execution of opposition. People, which have endured of these overwhelming events as, well [2]. Failure to conceive a healthy baby after a year of continuous, Not protected sexual activity known as infertility. The World Health Organization (WHO) reports that this disorder is estimated to impact 1 in 6 persons worldwide and is acknowledged as a major reproductive health issue [5]. Numerous causes, including as medical disorders, environmental variables, and psychological ones, can lead to infertility. Due of the ongoing hostilities that have negatively harmed the ecosystem and public health, infertility rates in Iraq are especially alarming [6]. Healthcare services have been disrupted as a result of the ongoing unrest, which may make it more difficult for people to receive essential fertility treatments and reproductive health information. Additionally, as mental health is a major factor in the results of reproductive health, the psychological stress brought on by conflict might make infertility problems worse [7].

Infertility rates can also be influenced by environmental variables, such as pollution exposure and lifestyle changes [8]. Consequently, tackling infertility in Iraq necessitates a comprehensive strategy that takes into account the interaction of biological, environmental, and psychological elements, especially in light of the population's ongoing struggles [9]. Insulin resistance (IR) and type 2 diabetes mellitus (T2DM) are more likely to strike infertile women, especially if they are overweight or fat. The hormonal abnormalities and metabolic dysfunctions that frequently accompany infertility are primarily to blame for this association. One significant risk factor of T2DM is IR when a body's cells become less receptive to insulin [10]. Research shows that fat women have higher rates of IR than women who are not obese, which can increase the risk of developing DM and other metabolic problems [11]. Furthermore, this elevated risk is further compounded by the hormonal disorders linked to infertility, such as those observed in PCOS. IR, unpredictable menstrual periods, and high testosterone levels make PCOS the most common hormonal condition affecting women in their reproductive years [12]. The most widespread endocrine defect affecting women of Childbearing age is PCOS, which is closely attached to metabolic syndrome, insulin resistance, cardiovascular disease, and future risk of developing diabetes. In addition to having a higher risk of T2DM, PCOS in women also has a markedly increased risk of cardiovascular disorders, such as heart attacks and strokes [13]. For women who are experiencing infertility, the combination of obesity, insulin resistance, and hormone abnormalities produces a complex health landscape that requires close monitoring and management of their general health. Different studies have reported an increase in the number of follicle cells in PCOS patients. The Impaired susceptibility to apoptosis in mature follicular cells leads to high abnormal follicle development. Responsibility is attributed to the tendency of cysts on ovaries in patients with infertility [1]. This study aims to highlight the role of hormones that are important for controlling the reproductive processes of females: follicle-stimulating hormone (FSH), Sex hormone binding globulin (SHBG), testosterone, free testosterone, and luteinizing hormone (LH), levels as a prognostic marker among women with PCOS and their relation with obesity, infertility, and other symptoms of the disease in the city of Karbala.

2. MATERIAL AND METHODS

This study was conducted during the period from (Dec.2023 to Mar.2024). A case-control study was designed; 100 individuals, 50 patients, and 50 healthy subjects were the control group, aged from (20) to (45) years. The diagnosis is based on the numerous surveys of PCOS biomarkers, presentation long-established by UTS, clinical history, and Normal level BMI is between (20-24.9) kg/m2. However, the overweight is around (25-29.9) kg/m2. Women who have a BMI ≥ 30kg / m2 are treated as obese. Groups are collected from the Obstetricians and Gynecologists" in Karbala Hospital.

3. STATISTICAL ANALYSIS

Data analysis was performed Using the Statistical Package for the Social Sciences (SPSS) version (23.0 with results expressed as (mean ± standard deviation) SD [14].

3. RESULTS AND DISCUSSION

The clinical features of PCOS patients with infertile women are demonstrated in Table 1.

The Elevation in LH is a repeated PCOS symptom, while it isnot needed for diagnosis. LH enhances ovarian androgen production, ovulation induction, luteinization, and primary agent participation in hyperandrogenism in patients with PCOS. LH enhances the androgens primarily in the ovarian theca cells, where LH receptors are located [11]. High levels of LH concentrations show a relation with further severe kinds of PCOS. Preceding research confirms the positive relationship between ovarian volume and follicle number and high concentrations of LH in women with PCOS, which is linked together with the most serious menstrual disorder and a high probability of Inability to conceive. The PCOS

women with hypersecretion of LH also reflect the severity conditions [15].

A relative deficiency in FSH impairs follicular development [16]. It impairs estrogen and FSH synthesis due to increased LH pulse frequency so that ovulation and follicle growth are inhibited, contributing to the formation of polycystic ovaries in women [13]. Steadily quick (GnRH) pulsing, Which favors pituitary LH over synthesis of FSH and leads to an increase in the LH level and, therefore, varied LH / FSH ratios identical to PCOS, is believed to be a feature of the neuroendocrine condition. The development in the Follicular is restrained by lowering the level of FSH, with high LH levels enhancing ovarian androgen production [14]. FSH is produced by the hypothalamus in the pituitary gland, which causes a difference in hormonal levels in affected women.[15]

The Rotterdam Agreement approved that, to diagnose hyperandrogenism in PCOS women, the circulatory FT tests should be used instead of serum TT [16]. One of the most common causes of women's infertility is PCOS [20]. The blood level of TT is directly related to the rise in LH levels [17]. This study agrees with Das et al. (2014) that both groups have a positive association between serum PCOS, age, BMI, and WHR [18]. Mean LH, BMI, and LH/ FSH ratio were elevated in the PCOS population. Also this study is showing the strength correlation between risk of PCOS and SHBG levels in reproductive aged females. A low level of serum SHBG associated with the complexity and long-term prediction of PCOS has a vital role in causing the disease [19]. The SHBG concentration in PCOS-infertile women is usually low because these women have risen androgen levels and ordinarily present with compensatory IR and HA. Moreover, androgens and insulin inhibit the synthesis and secretion of SHBG in the liver.

The association between SHBG and BMI levels in both groups is negative, as linear regression analysis shows. It has recently been recognized that PCOS does not only appear as a classic phenotype associated with obesity. The same applies to women who are underweight or have a normal body. In women of normal or underweight with PCOS [20]. Resistance of Insulin associated with PCOS upgrade with suitable treatment of the disease. Nevertheless, relationships between insulin–BMI, SHBG– SHBG–BMI, and insulin were investigated in a previous study [21]. Similar correlations in both PCOS groups in insulin BMI, BMI, and SHBG. with increased BMI and decreased SHBG levels, fasting insulin levels elevated with higher BMI. These connections were researched previously. However, the finding is that the insulin levels of SHBG did not show reverse linear relevance in women with PCOS with normal weight of the body. Thus, this leads us to conclude that SHBG is not compatible with describing the metabolism of carbohydrates and changes in levels of serum insulin in normal/slim weight women PCOS [22].

TABLE 1. The features of the 50 patients with (PCOS) infertile women and 50 control women

Variables	Groups		
	PCOS infertile women Patients group, No= 50 (Mean±SD)	Healthy group. No= 50 (Mean±SD)	P-Value
Age (25-40) Years	20.21± 5.67	20.34± 7.16	0.125
BMI(kg/m²)	19.66 ± 1.19	13.62 ± 1.04	0.002
18.9-24.9:BMI	10(12%)	90(100%)	
BMI:25-29.9	25.(38%)	-	
BMI:≥30	25(50%)	-	
WHR	1.08± 0.06	0.34± 0.05	0.001
Female infertility No (%)	33(66%)	-	-

TABLE 2. Biochemical Parameters registered in healthy groups and patients

Parameter	(Mean±SD) PCOS infertile women (n= 50)	(Mean±SD) Healthy group. No= 50	P-Value
LH (m.IU/mL)	13.02±3.16	4.95±2.18	0.0001
FSH (m.IU/mL)	6.37±3.01	5.29±2.43	0.05

FSH/LH	2.28±0.69	0.804±0.23	0.0001
TT (ng/mL)	2.49±0.92	1.01±0.37	0.025
FT (p g /mL)	13.14±2.03	3.14±3.05	0.0001
SHBG (ng/mL)	51.72±5.34	22.45±33.64	0.0001

TABLE 3. The Correlation of SHBG level in serum with biochemical parameters and anthropometric in PCOS infertile women group

Biochemical parameters	r = Correlation	P-Value
LH (m.IU/mL)	-0.204	0.073
FSH (m.IU/mL)	-0.226	0.065
LH/FSH	-0.194	0.109
TT (ng/mL)	-0.129	0.183
FT (ng/mL)	-0.317	0.001
BMI (Kg/m2)	-0.291	0.035
Age (Years)	-0.411	0.001

4. CONCLUSION

Prophecy biomarkers are used to diagnose patients at risk of getting early damage, so it is necessary to monitor and target therapy protocol carefully. In general, SHBG is considered to be an interesting biochemical marker for patient classification and diagnosis of PCOS women at risk of organ damage during (the 25-40) years of the disease. A low level of serum SHBG is associated with the complexity and long-term prediction of PCOS, which plays a vital role in its pathogenesis. This study discusses the connection between SHBG, PCOS, and hormonal levels.

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Arabic Abstract

خلفية الدراسة: تهدف هذه الدراسة إلى فحص دور الهرمونات المهمة في التحكم في العمليات التناسلية الأنثوية: هرمون تحفيز الجريب (FSH)، وهرمون ربط الجنس (SBHG)، وهرمون اللوتين (LH)، وهرمون التستوستيرون (T) ومستويات التستوستيرون الحر (FT) كمؤشر تشخيصي بين مرضى متلازمة تكيس المبايض (PCOS)، وعلاقتهن بالسمنة.

التصميم والطرق: شملت هذه الدراسة مائة عينة من المرضى العراقيين الذين تتراوح أعمارهم بين (25 و 40) عامًا. يبلغ مستوى مؤشر كتلة الجسم (BMI) الصحي حوالي (20-24.9) كجم / م 2، وحوالي (25-29.9) كجم / م 2 يكون زيادة الوزن. ثم عندما يكون مؤشر كتلة الجسم أكثر من (30 كجم / م 2)، تعتبر المرأة بدينة.

تم جمع المجموعات من "قسم أمراض النساء والولادة" في مستشفى كربلاء من ديسمبر 2023 إلى مارس 2024. تم تقييم مؤشر كتلة الجسم ونسبة محيط الخصر إلى الورك (WHR) ومستويات LH و FSH و TT و FT و SHBG في كل موضوع.

النتائج: لوحظ زيادة كبيرة في مستويات (P = 0.0001) LH و (p = 0.05) FSH ونسبة (P = 0.0001) LH / FSH و (p = 0.025) TT و (p = 0.0001) FT لدى مرضى PCOS مقارنة بالمجموعة الضابطة. ومع ذلك ، انخفض مستوى (p = 0.0001) SHBG بشكل كبير لدى مرضى PCOS مقارنة بالمجموعة الضابطة.