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Evaluation the levels of some hormones in women with polycystic ovary syndrome

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ABSTRACT

This study was conducted on 40 Samples of Patients with polycystic ovary syndrome (PCOS) after their diagnosis, The study aimed to identify the most important hormonal disorders associated with this syndrome. The study begins from October 2017 to March 2018, the age from (19-45) years. Blood samples were taken during the (2-4) days of menstrual cycle and the selected samples were compared with 20 healthy women as control group, and the following hormones were evaluated Lutenizing hormone (LH), Follicle Stimulating Hormone (FSH), Prolactin (PRL), Testosterone (Testo) and Oxytocin (OX), the study showed a high significant in the concentrations of OX, Testo and LH ($P \leq 0.01$), a high significant in the PRL concentration ($P \leq 0.05$) and a high significant in the FSH concentration ($P \leq 0.05$), the results were distributed to three groups according to BMI, age and treatment, in term BMI it was divided into three groups, BMI (18.5-24.9) (25.0-29.9) (≥ 30) kg/m² the results showed a high significant ($P \leq 0.05$) in the LH and OX concentration in group BMI (18.5-24.9) kg/m² and in both PRL and Testo in group BMI (≥ 30) kg/m². in term age, it was divided into three groups (19-26) (27-35) (36-45) years, the results showed a high significant ($P \leq 0.05$) in LH and Testo concentration at age group (36-45) years, compared to other groups, and a high significant ($P \leq 0.05$) in both PRL and OX, between three group of age, treatment it was divided into three groups of metformin, progesterone contraceptive used and non-used of the treatment. the results showed a high significant ($P \leq 0.05$) in LH, PRL, OX and Testo concentrations, and a high significant ($P \leq 0.05$) of FSH in women treated compared with non-used.

Introduction

Polycystic ovary syndrome (PCOS) is an endocrine disorder which affects 5-15% of women in reproductive aged and is characterized by anovulation or oligoovulation, hyperandrogenism and polycystic ovaries [1], The Symptoms of PCOS includes the endocrine system and reproductive signs which occur in the shape of obesity, amenorrhea or oligoamenorrhea, hirsutism, male pattern hair loss, acne and reproductive disorders, cardiovascular diseases, lipid disorders and malignancies, such as endometrial and breast cancer [2], The actual cause of PCOS is hidden and probably comes from a combination of factors such as genetic factors, exposure to high levels of androgen prenatally, epigenetic factors and environmental factors.

different environmental factors play a main role in the occurrence and treatment of PCOS, among which dietary pattern, stress smoking, and physical activity could be pointed out [3], A cyst is a water-filled sac containing the egg, that should have been normally discharged for possible fertilization. The diversion of the egg into a cyst, termed as 'functional cysts', prevent ovulation. As ovulation is blocked, it results in the 'amenorrhea' or disorder of the menstrual cycle. When multiple cysts are formalized in the ovarian follicles due to the hormonal imbalance, it is characterized as PCOS. Because of the water possess cysts, some of this can be as big 10 mm wide, the size of ovary increases, up to 10 cm wide. Non-attendance of menstrual cycle and ovulation prevent fertilization,

and conceit, thus pregnancy becomes difficult [4], The three criteria for diagnosis of PCOS are ovulation dysfunction, hyperandrogenism, and polycystic ovary [5]. This multifactorial disturbance is associated with hyperandrogenism, luteinizing hormone (LH) hypersecretion, relatively low levels of Follicle stimulating hormone FSH [6].

Study Samples :

This study was conducted at the Samarra hospital laboratories and in the external clinics in Samarra from October 2017 to March 2018. The study included 60 women aged between 19-45 years, the samples were divided into two groups:

The First group

Included 20 sample of healthy women (as a control group) after making sure that they are not infected and do not suffer from any interruption of the menstrual period or ovulation.

The second group

Included 40 sample of patients with polycystic ovaries syndrome. The incidence of the syndrome was determined depending on the appearance of at least two of the following symptoms [7].

1-Irregular menstruation.

2- Elevated clinical biochemical androgens, it is also important to note the high of the Luteinizing hormone with follicle stimulating hormone where the ratio of FSH /LH is at a rate of 1:2 or more as well as high prolactin and testosterone and clinical symptoms such as obesity and hair loss.

3-Diagnosed a number of polycystic ovaries using ultrasound waves.

Working Methods

Method of drawing blood samples

Ten milliliter of venous blood was withdrawn using a Disposable Syringe for women with PCOS and without (as control group) aged between 19-45 years. During the 2-4 days of the menstrual cycle, the blood is put in normal disposable test tubes and left to coagulate and then centrifuged using centrifuge at 4000 cycles per minute for 10 minutes to separate the serum and then withdraw the serum using the micropipette and put the serum in the test tube and then the serum was kept separated by freezing at (-20°C) until it is used in hormonal tests.

Body measurement

The length of the women was measured using a length scale in cm unit and the weight of their bodies using the balance in Kg unit. Body mass index (BMI) was calculated by $\text{weight (kg)} / \text{height}^2 \text{ (m}^2\text{)}$ [8].

Determination of serum hormones concentrations

Hormones concentrations were determined by following the steps provided with its own ready-made analysis Kit according to the instruction of the manufacturer of Elisa technology: prolactin [9], Follicle stimulating hormone [10], Luteinizing Hormone [11], Oxytocin [12], Testosterone [13].

Statistical analysis

The results obtained were analyzed using the T-test and Duncan test and statistical differences were extracted at the two levels ($P \leq 0.05$) ($P \leq 0.01$) [14].

Results and Discussion

The study showed a significant difference in concentrations of Luteinizing hormone (LH), Follicle Stimulating hormone (FSH), Prolactin (PRL), Testosterone (Testo) and Oxytocin (OX) between patients with PCOS and without (table 1).

Table (1): comparison of patients with PCOS and control for some hormones .

Parameters	mean $\pm$ SD control No = 20	mean $\pm$ SD patients No = 40	P-Value
LH (mIU/ml)	5.15 $\pm$ 1.51	10.05 $\pm$ 2.06	0.002**
FSH(mIU/ml)	5.15 $\pm$ 0.80	3.39 $\pm$ 0.47	0.04*
PRL (ng/ml)	12.12 $\pm$ 1.8	17.8 $\pm$ 1.6	0.03*
Testo(ng/ml)	0.66 $\pm$ 0.11	1.06 $\pm$ 0.32	0.015**
OX(mIU/ml)	45.4 $\pm$ 6.5	64.9 $\pm$ 9.0	0.003**

*Significant at a level ($P \leq 0.05$)

**Significant at a level ($P \leq 0.01$)

SD= Standard deviation

This study showed a high significant ($P \leq 0.01$) in the LH concentration in women with polycystic ovary syndrome, the results were (10.05 $\pm$ 2.06) (5.15 $\pm$ 1.51) mIU/ml respectively, this study was consistent with [15-16], and showed a significant decrease in the concentration of follicle stimulating hormone ($P \leq 0.05$), the results were (3.39 $\pm$ 0.47) (5.15 $\pm$ 0.80) mIU/ml, this study was consistent with [17], there are many reasons for the high and low concentrations of these hormones which may be an abnormal disorder of hypothalamus leads to increase the pulse frequency of Gonadotrophin releasing hormone (GnRH) which is characterized by being fast and growing, leading to increased secretion of LH, this increase in the pulse frequency leads to a preferential production of LH compared to the FSH, the low levels of progesterone and estrogen cause increased LH concentration. Estrogen and progesterone from the ovaries regulate a number of brain secretions of GnRH impulses, and the hidden GnRH of each pulse, the GnRH pulses slow down because of the high levels of estrogen, progesterone and vice versa [18], the current study also showed a high significant ($P \leq 0.05$) for prolactin and ($P \leq 0.01$) for testosterone, the results were (17.8 $\pm$ 1.6)(12.12 $\pm$ 1.8) (1.06 $\pm$ 0.32)(0.66 $\pm$ 0.11) ng/mL respectively. The cause of elevated prolactin in women with PCOS, may be due to estrogen which causes to raise the prolactin when it decreases. The increase in the prolactin due to the negative impact of women with PCOS on the psychological and neurological condition and causing psychological anxiety [19], or may be due to hyperinsulinemia, which causes hyperandrogens in the body which affects the secretion of prolactin causing it to increase, or may be due to disturbance in the body of patients with PCOS especially the high level of androgens which may lead to a number of neuroendocrine changes such as low level of

dopamine which is prolactin inhibitor factor .while the elevation of the testosterone due to the excessive production of androgen in the ovary, which interferes with the hypothalamus sensitivity of the negative feedback thus increases the pulse frequency of GnRH ,which leads to increased secretion of LH, and this increase stimulates the cells of the ovaries to produce more androgen, hyperinsulinemia also indirectly works to increase the free testosterone in serum by inhibiting hepatic production of sex hormone-binding globulin(SHBG) [20], the study also showed a high significant ($P \leq 0.05$) in the oxytocin concentration, the results were (64.9 ± 9.0) (45.4 ± 6.5)

mIU/ml respectively, oxytocin secretion is affected by the mechanism associated with the hypothalamus –pituitary –gonadal system and other mechanisms therefore any disorder in the hypothalamic –pituitary gland system leads to an imbalance in the concentration of this hormone, also found increase the central and peripheral oxytocin levels response to a wide range of stimuli such as fear and stress stimuli and response to several types of psychological and social stress [21].

The study showed a significant difference in concentrations of (LH, FSH, PRL, Testo and OX) for patients with pcos according to BMI values table (2)

Table (2): comparison of Body Mass index effect for patients with pcos on some hormones

Parameters	Mean± Standard deviation		
	Patients BMI(18.5-24.9)kg/m2 NO=11 Normal weigh	Patients BMI(25.0-29.9)kg/m2 NO=19 Over weight	Patients BMI(≥ 30)kg/m2 NO=10 Obese
LH(mIU/ml)	a 14.06±1.29	b 10.12±1.42	c 6.01±1.28
FSH(mIU/ml)	b 2.09±0.81	b 3.04±0.85	a 5.04±0.30
PRL(ng/ml)	c 11.21±1.63	b 17.23±1.50	a 24.98±1.96
Testo(ng/ml)	b 0.82±0.03	b 0.91±0.02	a 1.45±0.27
OX(mIU/ml)	a 73.9±2.1	b 60.8±3.5	b 59.9±1.9

*the different letters horizontal mean there are a significant difference at a level ($P \leq 0.05$)

The results presents a significant decrease ($P \leq 0.05$) in LH concentration with increasing of BMI value on the three group, in which the levels were (6.01 ± 1.28) (10.12 ± 1.42) (14.06 ± 1.29) mIU/ml in groups with BMI (≥ 30) (25.0-29.9) (18.5-24.9) kg/m2, this study is consistente with [22], there are several explanations given about the effect of weight gain on LH ,Insulin has been identified as a major regulator of energy through its brain actions it also plays a role in regulating neural control over reproduction by influencing the secretion of GnRH, increase insulin resistance associated with obesity in obese women may interfere with sex hormone –binding globulin in the liver leading to a lack of activation of estrogen and this in turn leads to the continual presence of non-anti-estrogen in the peripheral tissue in addition, obesity -related hyperinsulin increases the activity of aromatase by promoting and accelerating the conversion of the testosterone in the blood to estrogen, high estrogen contributes to reduced sensitivity and inhibition of reflexes on the hypothalamic –pituitary axis, this mechanisms leads to a calming LH response to stimulate GnRH [23], While for FSH, the result indicate that the level of hormone significantly elevated ($P \leq 0.05$) at group with BMI (≥ 30)kg/m2 [obese group] as compared with group (BMI 18.5-24.9 and 25-29.9) kg/m2 ,with no significant change between normal weight and overweight groups, in which the levels were (5.04 ± 0.30) (3.04 ± 0.85) (2.09 ± 0.81) mIU/ml, this

increase may be due to a high concentration of testosterone [24], the study also found a significant increase ($P \leq 0.05$) in prolactin concentration with increasing of BMI value on the three groups, in which the levels were (11.21 ± 1.63) (17.23 ± 1.50) (24.98 ± 1.96) ng/ml, in groups with BMI value (18.5-24.9) (25.0-29.9) (≥ 30)kg/m2 ,this study consistence with [24],the high level of prolactin in obese women may be linked to the BMI, according to many studies that have observed high levels of prolactin in obese women which supported that the level of PRL linked to positively with obesity [25],while for testosterone ,the result indicated that the level of hormone significantly elevated ($P \leq 0.05$) at group with BMI (≥ 30)kg/m2,[obese group] as compared with group (BMI 18.5-24.9 and 25.0-29.9)kg/m2, with no significant change between normal weight and overweight groups, in which the levels were (1.45 ± 0.27) (0.91 ± 0.02) (0.82 ± 0.03) ng/ml, the study consistence with [26], obesity is associated with increased total testosterone and reduced sex-hormone binding globulin (SHBG) which leads to a high free testosterone in blood, obesity plays a role in functional and reproductive changes, which is one of the most important features of pcos ,the adipose tissue has the ability to manufacture effective androgens in the body, the more obesity increases the level of androgen, which due to the transformation of cholesterol in a series of metabolic processes into the surrounding testosterone, which is another source of

this hormone in addition to the ovaries, While for oxytocin, indicate that the level of hormone significantly elevated ($P \leq 0.05$) at group with BMI (18.5-24.9) kg/m² [normal weight] as compared with group (25.0-29.9 and ≥ 30) kg/m², with no significant change between overweight and obese groups, in which levels were (73.9 $\pm$ 2.1) (60.8 $\pm$ 3.5) (59.9 $\pm$ 1.9)

mIU/ml, this study consistence with [27], the level of oxytocin in the serum is inversely proportional with the BMI, Oxytocin helps to regulate body weight by reducing appetite and accelerate metabolism [28]. The study showed a significant difference in concentrations of (LH,FSH, PRL, Testo and OX) for patients women with pcos in age group table (3).

Table (3): comparison between concentration of some hormones for patients with pcos according to age groups

Parameters	Mean $\pm$ Standard deviation		
	Patients(19-26)year NO=10	Patients (27-35)year NO=20	Patients (36-45)year NO=10
LH (mIU/ml)	b 7.0 $\pm$ 1.0	b 7.5 $\pm$ 1.1	a 15.6 $\pm$ 1.5
FSH(mIU/ml)	b 2.5 $\pm$ 0.6	b 2.7 $\pm$ 0.8	a 5.0 $\pm$ 0.1
PRL (ng/ml)	c 11.0 $\pm$ 1.3	b 18.0 $\pm$ 1.2	a 24.6 $\pm$ 3.8
Testo(ng/ml)	b 0.8 $\pm$ 0.1	b 0.9 $\pm$ 0.3	a 1.5 $\pm$ 0.2
OX(mIU/ml)	a 76.1 $\pm$ 8.5	b 63.6 $\pm$ 3.1	c 54.9 $\pm$ 1.5

*the different letters horizontal mean there are a significant difference at a level ($P \leq 0.05$)

The results indicate that the level of LH significantly elevated ($P \leq 0.05$) at group with age (36-45) year, as compared with groups (19-26)(27-35) years, with no significant change between age groups (19-26)(27-35) years, in which the levels were (15.6 $\pm$ 1.5) (7.5 $\pm$ 1.1) (7.0 $\pm$ 1.0) mIU/ml, this study is consistent with [29], which suggests that the concentration of LH increases with age until menopause, which causes pituitary disorder and this increases level of LH, the reason for the high LH may due to the low levels of estrogen and progesterone [30], While for FSH, the result indicates that the level of hormone significantly elevated ($P \leq 0.05$) at group with age (36-45) year as compared with groups (19-26)(27-35)years, with no significant change between groups (19-26)(27-35) years, in which the levels were (5.0 $\pm$ 0.1) (2.7 $\pm$ 0.8) (2.5 $\pm$ 0.6) mIU/ml, this increase may be due to low concentrations of estrogen and progesterone[30], whereas the results showed a significant increase ($P \leq 0.05$) in PRL concentration with age on the three groups (19-26) (27-35) (36-45) years, in which the levels were (11.0 $\pm$ 1.3) (18.0 $\pm$ 1.2) (24.6 $\pm$ 3.8) ng/ml, this study is consistent with [26], with age, increases

the production of prolactin receptors, Estrogen also promotes the growth of prolactin –producing cells, stimulates the production of prolactin directly and suppresses the production of dopamine[19], While for testosterone the result indicate that the level of hormone significantly elevated ($P \leq 0.05$) at group whit age (36-45) years as compared with groups (19-26) (27-35) years, with no significant change between groups (19-26) (27-35)years, in which the levels were (1.5 $\pm$ 0.2) (0.9 $\pm$ 0.3)(0.8 $\pm$ 0.1) ng/ml, the reason for this due to the low level of female hormones with age, leading to the rise of male hormone [31], The results showed a significant decrease ($P \leq 0.05$) in oxytocin concentration with age on the three groups (19-26)(27-35)(36-45) years, in which the levels were (76.1 $\pm$ 8.5) (63.6 $\pm$ 3.1) (54.9 $\pm$ 1.5) mIU/ml, oxytocin concentration decreases with age, studies have shown that the low estrogen levels reduce the levels of oxytocin in the serum [23].

The study showed a significant difference ($P \leq 0.05$) between the patients with pcos used metformin and progesterone contraceptives compared with patients without treatment table (4).

Table (4): comparison of the effect of the use of treatment among patients with pcos used for treatment and non-treatment for the concentration of some hormones

Parameters	Mean $\pm$ Standard deviation		
	Patients user metformin NO=15	Patients users progesterone contraceptives NO=15	Patients with out treatment NO=10
LH(mIU/ml)	b 8.6 $\pm$ 0.8	b 9.1 $\pm$ 0.4	a 12.5 $\pm$ 1.8
FSH(mIU/ml)	a 3.7 $\pm$ 0.7	a 4.0 $\pm$ 0.9	b 2.2 $\pm$ 0.5
PRL (ng/ml)	b 14.2 $\pm$ 0.3	b 15.7 $\pm$ 0.6	a 23.7 $\pm$ 0.4
Testo (ng/ml)	b 0.9 $\pm$ 0.2	b 0.8 $\pm$ 0.1	a 1.5 $\pm$ 0.2
OX (mIU/ml)	b 56.0 $\pm$ 3.8	b 65.9 $\pm$ 3.7	a 72.8 $\pm$ 3.0

*the different letters horizontal mean there are a significant difference at a level ($P \leq 0.05$)

The study illustrated a significant decrease ($P \leq 0.05$) in patients with pcos which they used metformin and progesterone contraception compared with Patients without any treatment in the concentration of LH, PRL, Testo and OX ,while showed a high significant ($P \leq 0.05$) in FSH concentration. the results were (8.6 ± 0.8) (9.1 ± 0.4) (12.5 ± 1.8) mIU/ml, (14.2 ± 0.3) (15.7 ± 0.6) (23.7 ± 0.4) ng/ml, (0.9 ± 0.2) (0.8 ± 0.1) (1.5 ± 0.2) ng/ml, (56.0 ± 3.8) (65.9 ± 3.7) (72.8 ± 3.0) mIU/ml, (3.7 ± 0.7) (4.0 ± 0.9) (2.2 ± 0.5) mIU/ml, respectively, metformin reduces the rate of insulin hormone and then reduces the rate of androgen hormone, which leads to the regularity of hormones and regularity of the menstrual cycle, progesterone contraceptives contain estrogen and progesterone and lead to lower androgen production and regulation of

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تقييم مستويات بعض الهرمونات لدى النساء المصابات بمتلازمة المبايض المتعددة الأكياس

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² قسم الكيمياء ، كلية العلوم ، جامعة تكريت ، تكريت ، العراق

الملخص

اجريت هذه الدراسة على 40 عينة من المريضات بمتلازمة المبايض المتعددة الأكياس بعد أن تم تشخيصهن. هدفت هذه الدراسة على تحديد اهم الاضطرابات الهرمونية التي ترافق هذه المتلازمة, بدأت الدراسة من تشرين الأول 2017 ولغاية آذار 2018, تراوحت اعمارهن بين (19-45) سنة, تم اخذ عينات الدم خلال (2-4) من أيام الدورة الشهرية, وقرنت العينات المدروسة مع 20 امرأة سليمة كمجموعة سيطرة, تم من خلال الدراسة الحالية تقدير تراكيز الهرمونات الأتية (الهرمون اللوتيني, الهرمون المحفز للجريب, هرمون البرولاكتين, هرمون الشحمون الخصوي و هرمون الأوكسيتوسين), وقد أظهرت النتائج ارتفاعاً معنوياً في تراكيز كل من هرمون الأوكسيتوسين والشحمون الخصوي واللوتيني بمستوى ($P \leq 0.01$) وارتفاعاً معنوياً في تركيز هرمون البرولاكتين بمستوى ($P \leq 0.05$) وانخفاضاً معنوياً في تركيز الهرمون المحفز للجريب بمستوى ($P \leq 0.05$) , كما قسمت النتائج الى ثلاث مجموعات حسب مؤشر كتلة الجسم BMI والعمر والعلاج , بالنسبة لمؤشر كتلة الجسم فقد قسمت الى ثلاث مجموعات kg/m² (18.5-24.9) (25.0-29.9) ($BMI \geq 30$) وقد أظهرت النتائج ارتفاعاً معنوياً بمستوى ($P \leq 0.05$) في مجموعة BMI (24.9-18.5) في تركيز كل من هرمون LH وOX وارتفاعاً معنوياً بمستوى ($P \leq 0.05$) في تركيز كل من PRL, Testo, FSH ,وبالنسبة للعمر قسمت الى ثلاث فئات (19-26) (27-35) (36-45) سنة واظهرت النتائج ارتفاعاً معنوياً بمستوى ($P \leq 0.05$) في تراكيز كل من LH و Testo في الفئة العمرية (36-45) سنة وارتفاعاً معنوياً بمستوى ($P \leq 0.05$) في تركيز PRL وOX بين الفئات, اما بالنسبة للعلاج قسمت الى ثلاث مجموعات مستخدمات للميتفورمين والمستخدمات لموانع الحمل البروجسترونية وغير المستخدمات للعلاج, اظهرت النتائج انخفاضاً معنوياً بمستوى ($P \leq 0.05$) في تركيز كل من Testo, LH, OX, PRL وارتفاعاً معنوياً بمستوى ($P \leq 0.05$) في تركيز FSH في النساء المستخدمات للعلاج مقارنة مع غير المستخدمات.