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Correlation of Body Mass Index and Some Hormones (Estradiol, Luteinizing, Follicle Stimulating Hormones) with Polycystic Ovary Syndrome among Young Females [20 to 35 Years]

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Polycystic Ovary Syndrome (PCOS) is the most common heterogenous complex endocrine disorder. It is affecting approximately 15 % of the women in their reproductive age. The exact cause of the PCOS is unknown, but genetic factors, environmental and endocrine factors playsa important role in the etiology of PCOS.This study was conducted between first November 2018 and May 2019 in the laboratories of the Institute of Genetic Engineering and Biotechnology for Postgraduate Studies – University of Baghdad, and the sample collected from various laboratories in Baghdad.The study included (50) women with Polycystic Ovary Syndromeand (50) women apparently healthy control fromu nmarried Iraqi women between (20-35) years old and take the weight and length to get the Body Mass Index, the result showed slightly increased in Body Mass Index(Non-significant) between two groups and get the full data from every patients by questioner form.The analysis of hormones 17B - Estradiol, Luteinizing hormone, Follicle stimulating hormone, Tri-iodothtronine, Thyroxin and Thyroid stimulating hormonecarried out by using IMMULITE 2000 systems random excess device, the results show high significant differences in the levels of serum Estradiol and Luteinizing hormonebetween two groups (P<0.01) and no significant difference in level of serumFollicle stimulating hormone.The findings also indicate a slight rise in serum concentrationsThyroid stimulating hormoneand non-significant between two groups and significant decrease in the level of serum Thyroxin(P<0.01) between women with Polycystic Ovary Syndrome and control group. The results showed significant positive correlation between 17B - Estradiol andLuteinizing hormone which gave correlation coefficient 0.67 (p-value <0.01) and negative correlation with Thyroxin which gave correlation coefficient -0.23 (p-value <0.01), while other hormones Follicle stimulating hormone, Tri-iodothtronineand Thyroid stimulating hormone no significant difference in patient with Polycystic Ovary Syndrome and apparently healthy control.Within the limitation of this study we can conclude: the concentrations of estrogen showed a elevated rise against ordinary checks in Polycystic Ovary Syndrome instances. High concentrations of androgens in peripherally converted Polycystic Ovary Syndrometo estrogens may contribute to their enhanced concentration.

Keywords: Body Mass Index; Estradiol(E2); Follicle Stimulating Hormone (FSH); Luteinizing Hormone (LH); Polycystic Ovary Syndrome; Tri-iodothtronine (T3).

Polycystic ovary syndrome "PCOS" is observed as a heterogeneous androgen excess disorder with a variable degree of hormonal and metabolic abnormalities.[1]Estrogens are a group of compounds named for their importance in both menstrual and estrous reproductive cycles. They

are primary female sex hormones.[2] Estrogens are one class of steroid hormones that includes estrone(E1),17a-estradiol (17a-E2), 17ß-estradiol (17ß-E2) and estriol (E3).[3]

In women with the polycystic ovary syndrome, chronic anovulation is an important consequence of abnormal secretion of estrogen. Serum concentrations of estradiol (both total and free) lie within the normal ranges for the early follicular and mid-follicular phases of the cycle, [4]but the pattern of secretion differs from that in the normal menstrual cycle because there is no preovulatory or midluteal increase in estradiol concentrations. Furthermore, the action of estradiol on the hypothalamic–pituitary axis and on the endometrium is unopposed because of a lack of cyclical progesterone secretion.[5,6] These effects may be compounded in obese subjectsby increased serum concentrations of estrogen arising from the extra glandular conversion of androgens by adipose tissue.[7] Both acyclical estrogen production and progesterone deficiency contribute to the mechanism of hyper secretion of LH.[8] The effects of unopposed estrogen on the endometrium include episodes of unscheduled and heavy uterine bleeding and an increased risk, in the long term, of endometrial carcinoma.[9]

The Aim of the Study

Finding the effect of Estrogen hormone in Iraqi female with PCOS and to determine the association between estrogen and various clinical and laboratory parameters PCOS.

MATERIALS AND METHODS

The total numbers of samples are 100 practicing person include 50 sample from women with PCOS and 50 samples from Healthy control. This study has included two groups. Fifty Iraqi female with PCOS patients and fifty healthy control female have been collected venous blood samples (5 ml) from each women of both PCOS and healthy control. The serum obtained by putting the blood samples in a clean dryglasses gel tube and allowed to clot at 37 ºC for 30 minutes before centrifugation. The tubes centrifuged at 6000 rpm for 5 minutes, serum was collected and kept in freezer until used for immunological test and hormonal assay.

Body Mass Index (BMI)

The BMI is a diagnostic tool for both obesity and protein-energy malnutrition.10 Body mass index has been figured by dividing weight in kilograms by height in meters squared.BMI = Mass (Kg) / height (m) 2

Laboratory Method for Thyroid Function and Prolactin Assessment

Detailed assessment of thyroid function was done for all the enrolled subjects. Five ml venous blood samples (5 ml) was taken from each women of both PCOS and healthy control, The serum obtained by putting the blood samples in a clean dryglasses gel tube and allowed to clot at 37 ºC for 30 minutes before centrifugation. The tubes centrifuged at 6000 rpm for 5 minutes, serum was collected and preserved at -20oC and then serum levels of Luteinizing hormone (LH), Follicle-stimulating hormone (FSH), 17ß-Estradiol (E2), total Tri-iodothtronine (T3), total Thyroxin (T4) and rapid Thyroid stimulating hormone (TSH) were measured in all enrolled subjects by using a enzyme immunoassay competition method with a final fluorescent detector (ELFA) on mini Kits from Siemens company, Germany.

The standard range for adult T3 was 1.2-4.14 nmol/l. Female T4 it was 65.0-165nmol/l. TSH concentration ranging from 0.4-4.0 microIU/l to Euthyroid were regarded normal.LH concentration in the follicular stage varying from 1.7-15microIU/ml. These valuesare in compliance with Siemens, Germany's commercially accessible kits.

Statistical Analysis

The Statistical Analysis System[11] program was used to effect of difference groups in study parameters. T- test was used to significant compare between means. Estimate of correlation coefficient between variables in this study.

Probability value

"P" is level of significance ofan occurrence of an event.

$P > 0.05$ Non significant

$P < 0.05$ Significant

$P<0.01$ NS: Non-Significant.

RESULTS AND DISCUSSION

Table (1 and 2) showed increased in BMI in patients compared to control group (26.93 ± 0.63 vs.25.61 ± 0.63 respectively;Non-significant). Al-Shattawi*et al*.[12] found that women with PCOS showed high significant increased ($P< 0.01$) in BMI

compared to healthy control, this is result because of the choice of age group and social status.

PCOS women have excess of androgens which may lead to high visceral and subcutaneous fat and dysregulation of appetite, so obesity is more frequently seen in women with PCOS.[13] The Iraqi society suffered from many psychological difficulties that affect women's behavior which leads to disturb the female hormonal system that might be lead to PCOS.[14]

BMI and PCOS have a specific role in ovarian activity. Overactive ovaries leads to the accumulation of oocytes, which indicate increase probability of PCOS with overweight woman, this obesity and excess weight, occur as a result of change of metabolism which can lead to involution.[15] Obesity linked to insulin resistance[16] and E2 hormone in fatty tissue inhibits the secretion of FSH making obesity pathological factor.[17]

The results were listed in table (2). Female with PCOS showed significant increase in E2 and LH compared to healthy (267.34 ± 16.28 vs. 146.28 ± 14.01 and 19.28 ± 1.68 vs. 6.20 ±0.33, respectively; P<0.01), and slightly increased in FSH level (10.08 ± 1.64 vs7.60 ± 0.34 respectively;Non-significant). These findings are close to the study done by Elslimani*et al*.,[18]

High levels of androgens in PCOS peripherally converted to estrogens may lead to their increased concentration. High levels of estrogen in PCOS patients have also been reported in other studies.[19]

Because of the heterogeneity of this disorder, there are most likely multiple underlying pathophysiologic mechanisms. Pathogenesis of PCOS is explaining as alteration in gonadotropin-releasing hormone secretion results in increased LH secretion. An alteration in insulin secretion and insulin action results in hyperinsulinemia and insulin resistance. A defect in androgen synthesis that results in increased ovarian androgen production.[20]

Table 1. Compare between patients and control in Body Mass Index (BMI)

Gender	No	Mean ± SE (kg/m^2)
Patients	50	27.72 ± 0.63 a
Control	50	25.61 ± 0.63 b
T-Test	—-	1.780 *
P-value	—-	0.0205

Means having with the different letters in same column differed significantly, * (P<0.05).

Table 2. Compare between patients and control in LH, FSH and E2 hormones

Group	Mean ± SE		
	LH (mlU/mL)	FSH (mlU/mL)	E2 (pmol/L)
Patients(No. =50)	19.28 ± 1.68 a	10.08 ± 1.64 a	267.34 ± 16.28 a
Control(No. =50)	6.20 ±0.33 b	7.60 ± 0.34 a	146.28 ± 14.01 b
T-Test	3.406 **	3.3331 NS	42.625 **
P-value	0.0001	0.1430	0.0001

Means having with the different letters in same column differed significantly, ** (P<0.01), NS: Non-Significant.

Table 3. Compare between patients and control in T3, T4 and TSHHormones

Group	Mean ± SE		
	T3 (nmol/L)	T4 (nmol/L)	TSH (mLU/ml)
Patients(No. =50)	1.777 ± 0.04 a	102.92 ± 1.21 b	2.182 ± 0.08 a
Control(No. =50)	1.711 ± 0.05 a	108.92 ± 1.40 a	2.05 ± 0.16 a
T-Test	0.1218 NS	3.677 **	0.352 NS
P-value	0.286	0.0016	0.459

Means having with the different letters in same column differed significantly, ** (P<0.01), NS: Non-Significant.

Table 4. Correlation coefficients between E2 and other of Hormones in patients

Hormones	Correlation coefficients with E2	P-value
E2 & LH	0.69	0.0001 **
E2 & FSH	0.15	0.136 NS
E2 &T3	0.07	0.484 NS
E2 & T4	-0.03	0.718 NS
E2 & TSH	0.08	0.401 NS

** ($P<0.01$), NS: Non-Significant.

Secretion of androgens by ovaries and adrenals is responsive to their respective trophic hormones (LH, ACTH).[21] Where as altered physiology is that theca cells secrete high levels of androgens to an intrinsic activation of steroidogenesis (intraglandular paracrine and autocrine mechanism) even in the absence of trophic factors in polycystic ovary syndrome women.[22]

Secretion of progesterone by corpus luteum can help to regulate the concentration of LH versus high level of FSH which has an important role to mature of follicles for next bleeding. In contrast PCOS woman, abnormality of LH associated with less response for progesterone and defect in the frequency of FSH, this leads to a high ratio of LH/FSH.

The results were listed in table (3). Female with PCOS showed slightly increase in TSH compared to healthy control (2.182 ± 0.08 vs.2.05 ± 0.16 respectively, Non-significant) and significant decreased in total thyroxin (T4) level (102.92 ± 1.21vs.108.92 ± 1.40 respectively; $P<0.01$) this due alteration in thyroid function particularly hypothyroidism and can cause ovulatory dysfunction while the serum triiodothyronine (T3) showed slightly increase (1.777 ± 0.04 vs. 1.711 ± 0.05 respectively, Non-significant) this due to hyperthyroidism.

The PCOS patients showed significant increase in TSH and slightly decreased in thyroxin level while the serum triiodothyronine (T3) showed no significant difference compared to healthy group.18 Also another study found that there were a significant elevation of TSH, T3 and T4 in serum of overweight PCOS women compared with healthy women.[23]

Al-Shattawi,24found that both TSH and T3 have significant difference between patient and healthy group. These results due to differences in the number of samples and selection of age group and social status.

From these results, we can conclude that values of estrogen controls to that of PCOS cases showed slight increase in levels of estrogen. High levels of androgens in PCOS peripherally converted to estrogens may lead to their increased concentration. High levels of estrogen in PCOS patients have also been reported in other studies.[19]

Sinha *et al*.,[25] concluded that elevated incidence of thyroid infections in PCOS patients thus points to the significance of early correction of hypothyroidism in the management of PCOS-related infertility. Both of the thyroid gland and the ovary are part of the endocrine system, most of the cases that suffering from thyroid disorder "hypothyroidism" and mostly of women with polycystic ovary syndrome are to get hypothyroidism[26], this may be due to insufficient secretion of thyroid hormone resulting from dysfunction of hypothalamic-pituitary ovarian axis.[27] A disorder of the thyroid gland system leads to decrease in sex binding globulin hormone "SBGH" which in turn increases the testosterone also, non-regularity of menstrual cycle helps to impair ovulation.[28]

Table (4) shown that the correlation coefficients between estrogen, LH, FSH and thyroid hormones. There were significant positive correlation between E2 and LH and negative correlation with T4. While other hormones FSH, T3 and TSH no significant difference in patient with PCOS and apparently healthy control.

PCOS is associated with low level of follicle stimulating hormone (FSH) and high level of LH. In parallel, high level of LH triggers the secretion of estrogen, testosterone and dihydroepiandrosteronesulphate (DHES). This ultimately leads to development of cyst in the ovary.[29] LH is produced in the pituitary gland and it is works in conjunction with FSH, the rise in estrogen tells the pituitary gland to stop producing FSH and to start making more LH. The shift to LH causes the egg to be released from the ovary, a process called "ovulation".

Generally, higher than normal levels of LH in a woman may mean the ovaries are absent

or not functioning. In a young woman, high levels may mean that puberty is early.[30]

This study concluded thatpolycystic ovary syndromecan be considered as a complex, heterogeneous metabolic syndrome triggered by the interact effect of genetic and environmental factors.Pathogenesis of PCOS is explaining as alteration in gonadotropin-releasing hormone secretion results in increased luteinizing hormone (LH) secretion.Estrogen levels showed high increase in PCOS cases against normal controls. High levels of androgens in PCOS peripherally converted to estrogens may lead to their increased concentration.

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