



Evaluation of Vascular Endothelial Growth Factor, Irisin, Copeptin Levels and Some Biochemical Factors in Patients With Polycystic Ovary Syndrome in Samarra City

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Abstract. This study was conducted in the laboratories of Samarra Teaching Hospital and some private laboratories in the city of Samarra in salah aldiyn Governorate for a period from 1/8/2024 to 1/9/2024, where the study included (50) samples of women of reproductive age, ranging in age from (20-40) years, and were distributed into two groups: Patient group: (30) samples were from female patients with PCOS, Control group: (20) samples of healthy women. The pathological cases of women suffering from PCOS were confirmed after conducting clinical examinations and referring them to the specialist doctor and performing an ultrasound examination. after that, blood was taken from both groups (patients and healthy women) and separated using a centrifuge. Then the sex hormones Luting hormone -LH, Folic stimulating hormone-FSH, and some biochemical variables, which included (Vascular endothelial growth factor-VEGF , Irisin, Copeptin). The results of the this study showed a significant rise in each of the hormones (LH, FSH, Testosterone ,Copeptin, VEGF) and a significant low in (Irisin) in the blood serum of women infected with PCOS compered a healthy women , with a probability of $P \leq 0.05$.

Keywords: Polycystic ovary syndrome , Vascular endothelial growth factor, Irisin , Copeptin

1. INTRODUCTION

Polycystic Ovarian Syndrome (PCOS), originally called Stein-Levanthal Syndrome: It is known as the most common endocrine disorder. As it affects the reproductive age group, women with this disease are characterized by an increase in the secretion of androgen and gonadotropin, and it affects up to 13% of women of reproductive age ⁽¹⁾. PCOS represents a complex, multifactorial disorder caused by some environmental factors as well as genetic, hormonal, and metabolic background ⁽²⁾ and is characterized by chronic lack or absence of anovulation (anovulation, infertility, dysfunctional uterine bleeding), and an excess of androgens (hirsutism and acne), and the presence of polycystic ovaries ⁽³⁾.

Vascular endothelial growth factor - VEGF, a hormone of glycoprotein nature is the most active antigenic factor, which can maintain the differential state of vascular endothelial cells and improve microvascular permeability, and plays a regulatory role in the development of diseases ^(4, 5). Among them is polycystic ovary syndrome ⁽⁶⁻⁸⁾. In addition, overexpression of the VEGF gene plays an important diagnostic role in the progression of PCOS ⁽⁹⁾.

Copeptin is a glycopeptide consisting of 39 amino acids and is the terminal portion of pre-provasopressin, which is the precursor to the protein or peptide, and consists of the signal peptide, arginine vasopressin, and neurophysin or neurophysin II. Copeptin is more stable under physiological conditions than AVP itself. Pre-pro vasopressin is cleaved into copeptin

and vasopressin within the posterior pituitary gland ⁽¹⁰⁾. Copeptin has been found to be a good marker for insulin resistance, as insulin resistance and obesity are linked to copeptin levels in the bloodstream, and thus it has an important role in the metabolic response and subsequent development of diseases in patients with polycystic ovary syndrome ⁽¹¹⁾.

Irisin is an adipomyokine substance that is mainly secreted from skeletal muscle and subcutaneous adipose tissue ⁽¹²⁾. It has also been found that it is secreted from adipose cells, as it controls metabolism by increasing the stimulation of gene expression of the Betatrophin hormone present in adipose cells, which is also responsible for controlling metabolism ⁽¹³⁾.

2. RESEARCH METHODS

Collection of blood

This study was conducted in the laboratories of Samarra Teaching Hospital and some private laboratories in the city of samarra in salah aldiyn Governorate for a period from 1/8/2024 to 1/9/2024, where the study included (50) samples of women of reproductive age, ranging in age from (20-40) years, and were distributed into two groups:

- **Patient group:** (30) samples were from female patients with PCOS.
- **Healthy group:** (20) samples were from uninfected (healthy) women.

The biochemical conditions of the women with PCOS were confirmed after conducting clinical examinations and referring them to the specialist doctor and performing an ultrasound examination. After that, blood was taken from both groups (patients and healthy people) and separated using a centrifuge, then the level of their biochemical variables was measured and at their level Probability $P \leq 0.05$.

Estimation the concentration of VEGF , Irisin and Copeptin in blood serum

The concentration of (VEGF,Irisin,Copeptin) in blood serum was estimated according to several kits prepared by Elabscience the American company.

Estimation the concentration of Sex hormones in blood serum:

The concentration of (LH , FSH, Testosterone) was measured using a hormone device (minividas) and following the ready-made steps indicated in a dedicated analysis kit, and it differs from one device to another and according to its manufacturer ^(14,15).

Statistical Analysis

The data used in the current study were analyzed statistically using the SPSS system through the sample arithmetic mean $\pm$ S.D. between patients and healthy are below the probability level of $P \geq 0.05$.

3. RESULTS AND DISCUSSION

Results

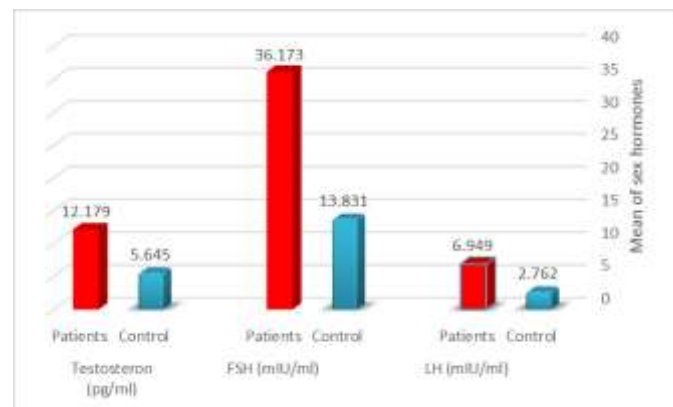
Assessment of sex hormones and biochemical parameter in all groups:

Table (1) shows the mean $\pm$ S.D of sex hormones , VEGF, Copeptin, Irisin in the patients and healthy.

$P \leq 0.05$

Parameters	Mean $\pm$ SD		p-value
	Control	Patients	
FSH (mIU/ml)	13.831 $\pm$ 3.798	36.173 $\pm$ 10.201	<0.0001*
LH(mIU/ml)	2.762 $\pm$ 0.952	6.949 $\pm$ 2.849	<0.0001*
Testosteron(pg/ml)	5.645 $\pm$ 1.223	12.179 $\pm$ 2.295	<0.0001*
VEGF (pg/ml)	122.313 $\pm$ 29.745	360.803 $\pm$ 105.906	<0.0001*
Copeptin (pg/ml)	211.068 $\pm$ 80.819	419.930 $\pm$ 118.889	<0.0001*
Irisin(pg/ml)	355.820 $\pm$ 93.587	169.751 $\pm$ 56.904	<0.0001*

The results of this study showed a significant rise in the (LH, FSH , Testosterone , VEGF, Copeptin) and a significant reduce in (Irisin) in the sera of women with PCOS compared healthy women). at $P \leq 0.05$. as in the following fig (1,2).



Fig(1):- Concentration of sex hormones in all groups

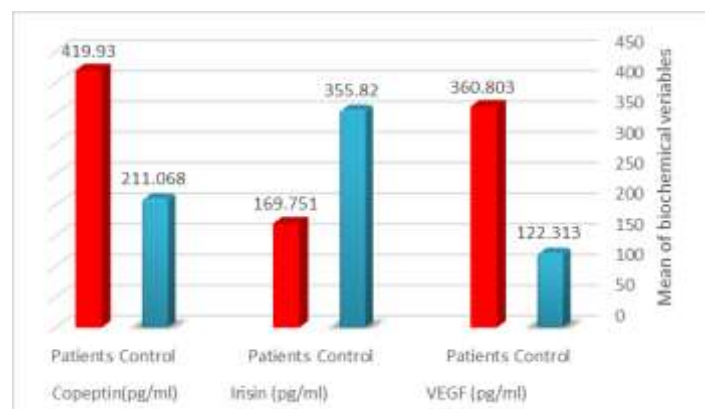


Fig (2):- Concentration of VEGF, Irisin, Copeptin in all groups

Area under the ROC curve (AUC)

The results showed the analysis of biochemical variables of FSH (AUC=0.983, $p<0.0001$), LH (AUC= 0.944, $p<0.0001$), Testosterone (AUC=0.991, $p<0.0001$), Irisin (AUC=0.970, $p<0.0001$), Copeptin (AUC=0.949, $p<0.0001$), VEGF (AUC=0.988, $p<0.0001$) were significant biomarker in predicting the risk of PCOS as showed (table 2, fig3).

Table (2):- shows Area under the curve for the biochemical variables of the studied samples

Parameters	AUC	Cut off	Sensitivity %	Specificity %	Accuracy	P-value
FSH	0.983	>22.104	90.91	100.00	0.9091	<0.0001
LH	0.944	>3.782	83.87	91.30	0.7518	<0.0001
Testosterone	0.991	>7.905	93.94	100.00	0.9394	<0.0001
Irisin	0.970	≤229.796	93.55	95.83	0.8938	<0.0001
Copeptin	0.949	>278.502	97.06	87.50	0.8456	<0.0001
VEGF	0.988	>180.987	93.75	100.00	0.9375	<0.0001

It is noted from the results of the current research that the parameters used in the current study may be an important diagnostic tool for diagnosing the extent of development of polycystic ovary syndrome, and this is what was observed through the sensitivity and specificity values, as the sex hormones, VEGF, irisin and copeptin have diagnostic significance and high sensitivity towards the disease.

Discussion

PCOS is one of the diseases that contain a group of symptoms represented by a hormonal imbalance that can affect females and girls of childbearing age. Females with polycystic ovary syndrome usually have an absence or decrease in ovulation, which leads to a difference in the regularity of the menstrual cycle. High androgen in the body, such as the presence of excess body or facial hair and a deep voice .

Also of the this study showed an elevated in luteinizing hormone in the group of patients with PCOS among to the control group, as the results of this research were consistent with the results of, and the reason for the elevated is If the LH hormone does not reach its highest level on day 14 of the menstrual cycle, ovulation does not occur, which causes egg cysts in the ovary and delayed pregnancy and menstruation.

The most common clinical symptom in affected women is an increase in the LH/FSH ratio., the LH concentration is higher than the FSH concentration, which leads to rise androgen production in the ovary and ovulation failure It was found that a cutoff value of more than 1.0 is the most diagnosis in PCOS in terms of sensitivity and specificity.

The FSH hormone also showed a significant increase. The reason for the increase is due to the growth of the ovarian follicles located on the right and left sides of the female reproductive system, which is under the control of the hormones FSH and LH. The ovarian

response is when the level of the FSH hormone reaches the required level, and the FSH level is variable during the experimental phase. This is due to follicle growth and sensitivity to stimulating nutrients. Therefore, high levels of sex hormones lead to the absence of ovulation and hormonal disturbance, as the pituitary gland and hypothalamus are the ones that regulate the main organs of the endocrine glands.

Also the results of the current research showed increase in the testosterone in patients groups compared healthy women. This result was consistent with the findings of, who demonstrated in their study that there was a significant increase in the concentration of testosterone.

The reason of high concentration of testosterone, impaired folliculogenesis is the primary effect of excess androgens that disrupt normal androgen synthesis. In the early gonadal phase, excess androgens promote the growth of primordial follicles and an increase in antral follicles.

Also the results of the current research showed that a significant elevated in the concentration of VEGF between patients groups and healthy women. Previous studies have shown that VEGF gene polymorphisms are associated with the risk of PCOS.

4. CONCLUSION

It is known that high VEGF levels are closely linked to the pathogenesis of PCOS. Higher concentrations of it lead to a greater number of active granular lutein cells, and high secretion of GLCs. In addition, expression of VEGF in PCOS patients leads to an increase in microvascular permeability, thus leading to androgen-producing ovarian dysplasia. Therefore, it may play a role in the pathogenesis of PCOS, It was found that VEGF may be related to endometrial receptivity. The level of VEGF expression directly reflects the volume of blood flow in the uterus. Therefore, VEGF may have a specific effect on endometrial vascular endothelial cells, and thus be able to promote the proliferation and migration of VEGF and rise vascular permeability. Therefore, it may play an important role in endometrial neovascularization.

On the other hand, the result showed a significant elevated in copeptin level in patients compared healthy women Therefore, copeptin plays an important role in causing polycystic ovary syndrome. So the results of the this study is agree with who showed a high concentration of copeptin in patients with PCOS, as the relationship between copeptin and patients with polycystic ovary syndrome is still unknown, as it shows that high levels of copeptin in blood serum may provide Important prognostic information in patients with PCOS The reason of high

concentration of copeptin may be secondary to rise hepatic T.G synthesis due to glucocorticoids, glucagon and epinephrine released under stress The results also showed a significant reduced in the level of irisin in patients compared to healthy people. Irisin is a secreted protein involved in the regulation of insulin sensitivity and has been implicated in polycystic ovary syndrome. A study showed that blood irisin concentration were significantly higher in PCOS compared to normal women. This is not consistent with the results of the current research. High levels of irisin in the blood were also found in women who are overweight and have higher ovarian cysts than those of normal weight. Therefore, it may contribute to the development of insulin resistance in patients.

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