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Evaluation of Serum Concentration of Copeptin, Resistin, Irisin and Some Immunogical Variables in Polycystic Ovary Syndrome Infected Patients in Kirkuk City

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Annotation: Background: Polycystic ovary syndrome is most common disorder in the endocrine system in women of fertile and reproductive age, as it is associated with irregular menstruation, indicators of insulin resistance, and androgen excess. . **Objective:** The current study was designed to evaluation of Polycystic ovary syndrome-PCOS infection effects on some variables such as Copeptin, Resistin and Irisin, Luteinizing hormone-LH, Folic stimulating hormone-FSH, Testosteron . **Methods:** The study was conducted on 50 patients infected with PCOS and 30 healthy women (uninfected), who attended the Al-Jumhuri general hospital of Kirkuk city from 15/5/2024-15/6/2024. The results : results showed a significant ($P<0.05$) increase in serum level of (Copeptin, Resistin and Irisin, LH, T.T) and a significant decrease in level of (FSH) in PCOS infected patients compered healthy women . Conclusion: Copeptin, Resistin, Irisin and some variables are important physiological and immunogical

biomarkers that can support the diagnosis of PCOS.

Keywords: polycystic ovary syndrome, Copeptin, Resistin, Irisin, Tumor necrosis factor.

Introduction

Polycystic ovary syndrome is a heterogeneous syndrome that affects women of reproductive age, with risks for heart and metabolic diseases. Obesity and insulin resistance are the most common, about 50-70%, respectively, and they are two important features of polycystic ovary syndrome, but they are not considered diagnostic criteria. Androgen excess and obesity are Insulin resistance is associated with the risk of low-grade chronic inflammation, metabolic risk, and heart disease in obese women with the syndrome, so recent research is focusing on the gradual discovery of biomarkers in metabolic changes with polycystic ovary syndrome (vonica *et al*., 2020). Polycystic ovary syndrome is widespread worldwide and poses a threat to women's health in general, as symptoms of excessive hair growth, infertility, and menstrual disorders appear, as well as metabolic problems, insulin resistance, and type 2 diabetes. The causes of the disease are still not completely clear, as there is a role for environmental and genetic factors such as glandular disorders (Hong *et al*., 2020).

Polycystic ovary syndrome develops in women by stimulating the ovaries by increasing the production of the male hormone (testosterone), either by excessive secretion of luteinizing hormone from the anterior pituitary gland and a high level of insulin in the blood due to the improvement of the ovaries for this stimulation, or it may be a decrease in the level of sex hormones associated with globulin, which leads to To increase androgen (STRAUUS., 2003).

Copeptin is a 39-amino acid glycopeptide, which consists of a signal peptide, arginine (Jochberger *et al*, 2006). Polycystic Ovarian Syndrome, a common endocrine illness, affects approximately 5 to 10% of women of reproductive age. Copeptin has significant associations with cardiometabolic parameters regardless of age or weight. (Jyotsna., 2024).

Resistin is a small protein rich in cysteine, which is secreted by mature white adipocytes. It is secreted in the form of a polypeptide and was first named by Steppan. Its levels increase in types of obesity caused by diet and genetics and decrease with the use of anti-diabetic drugs. However, it is mainly secreted by Mononuclear cells in peripheral blood (Chen., 2013 and Zou., 2005), as their levels have been associated with a high incidence of cardiovascular disease and deaths (Wang., 2020). Many studies have indicated a relationship between the hormone resistin and polycystic ovary syndrome. Studies have found that the hormone is elevated (. Hall., 2019 and Mancinelli ., 2009) or is within its normal levels (Kumar., 2011). Some studies have noted that resistin and insulin resistance are a positive relationship (Mohiyiddeen., 2010 and . Baskind., 2016), but they failed. Other studies prove this (Stamatiades., 2018 and Cahoreau., 2015).

Irisin is a hormone composed of 112 amino acids. It was discovered for the first time in 2012 by researcher Bostrom and his group and was named after the Greek goddess of the messenger, Iris (Boström., 2012). It is an adipomycin substance that is secreted mainly from skeletal muscle and adipose tissue. Small amounts of it are also produced from the testicles and liver. The pancreas, brain, and spleen (Martinez ., 2018).

Tumor necrosis factor - TNF α is one of the inflammatory cytokines that is responsible for determining the nature of the immune response (Liberale., 2021). Tumor necrosis factor is a

multifunctional cytokine that is manufactured by adipose, endothelial, and fibroblast cells (Kien., 2015) and participates in regulating immunity, reproduction, and apoptosis (Wlodarczyk et al., 2020). It plays a role in regulating the ovarian cycle, so it plays a role during the growth and development of ovarian follicles (Mahdi ., 2011).

Materials and Method

Examination of blood samples:- Serum separated from five ml of venous blood were obtained from the patients and control groups to assessed Lactoferrin, Iron, ferritin, IL-6, Zn by using the American company Monbined, by the American company . All variables were measured by ELISA.

Statistical Analysis

The process of collecting data for the samples used for the study and analyzing them statistically was done using the (SPSS) system by extracting the arithmetic mean and standard deviation. The Test was also used to analyze differences between the main and secondary groups. Significant differences were chosen for these groups under a probability level of $P \leq 0.05$.

Results

Estimation the physiological and immunological variables in the two study groups:

Table (1) shows the mean ± S.D of physiological parameter in the two study groups.

Groups / Parameter	Mean ± SD	
	Control n=30	**PCOS n=50**
LH (mlU/ml)	**7.44±1.25**	**15.45±3.12**
FSH (mlU/ml)	28.31±**3.56**	**12.49±1.45**
Testosterone (ng/ml)	**5.14±0.95**	**9**.67±1.54
Copeptin (mg/dl)	56.14±13.65	85.43±10.34
Resistin (ng/ml)	2.76±0.42	5.22±1.08
Irisin (ng/ml)	654.76±20.65	865.87±22.876
TNF-α (pg/ml)	55.4±7.32	95.33±8.35

Results of current research showed a significant elevated in (LH, Testosteron, Copeptin, Resistin, Irisin, TNF-α) and a significant decrease in the (FSH) in the serum of patients compered healthy women). at its level, the probability of $P \leq 0.05$. as in the following figures:

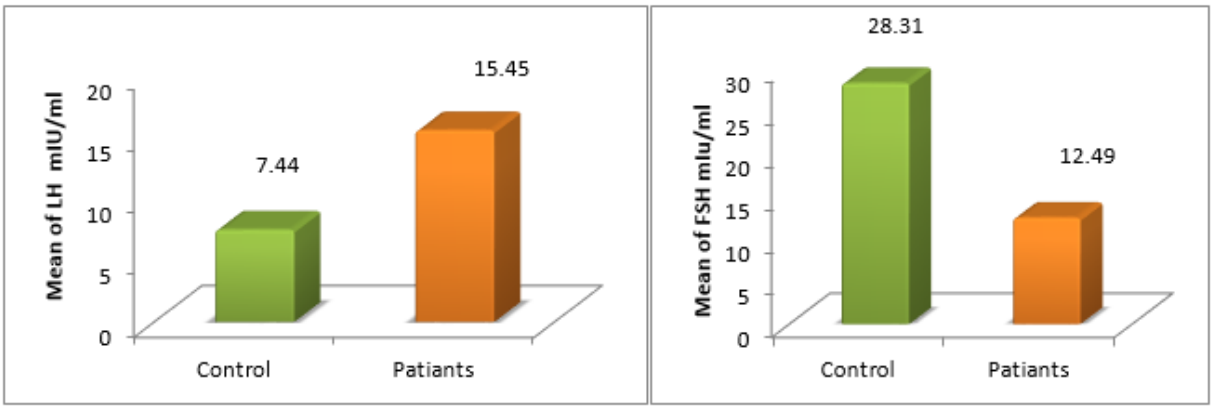

Figure (1): LH concentration in the blood serum of all groups
Figure (2): FSH concentration in the blood serum of all groups

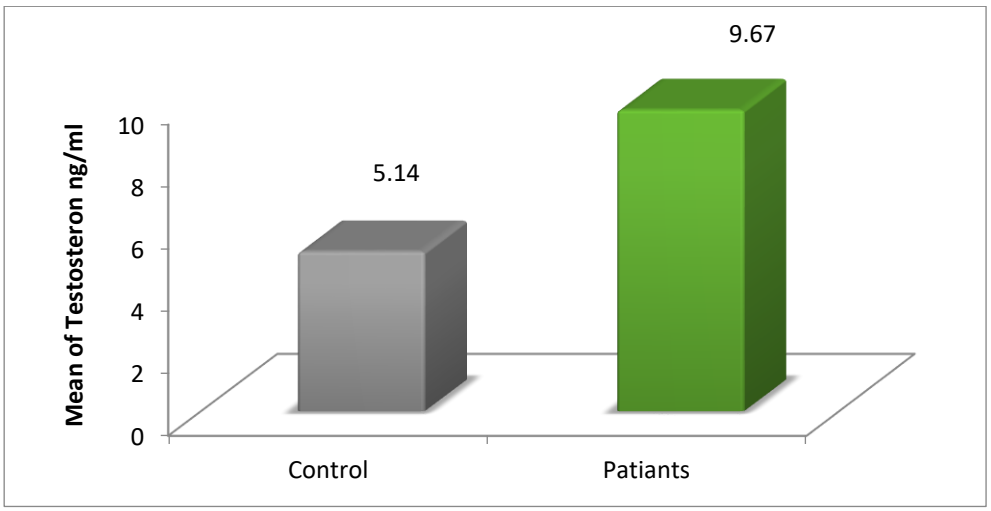

Figure (3): Testosterone concentration in the blood serum of all groups

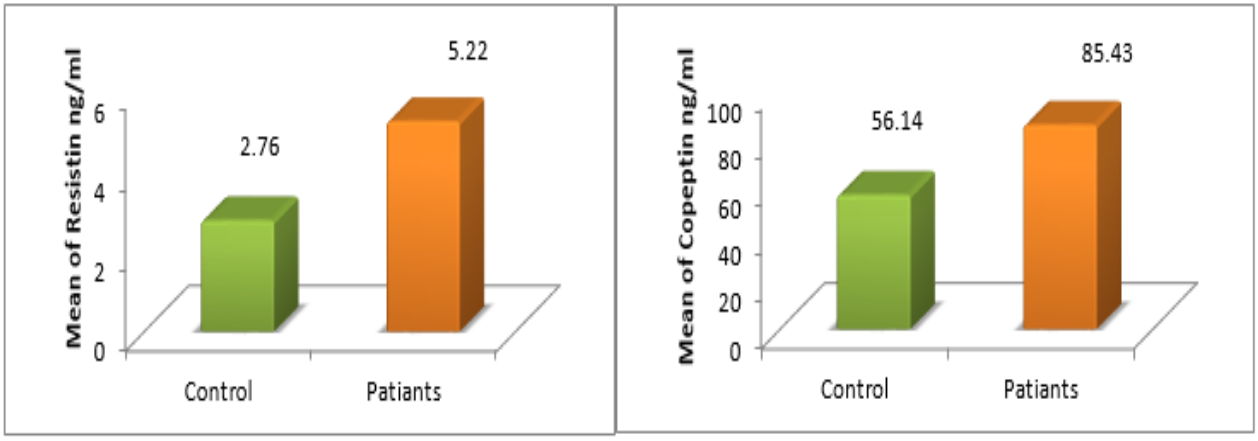

Figure (4): Resistin concentration in the blood serum of all groups
Figure (5): Copeptin concentration in the blood serum of all groups

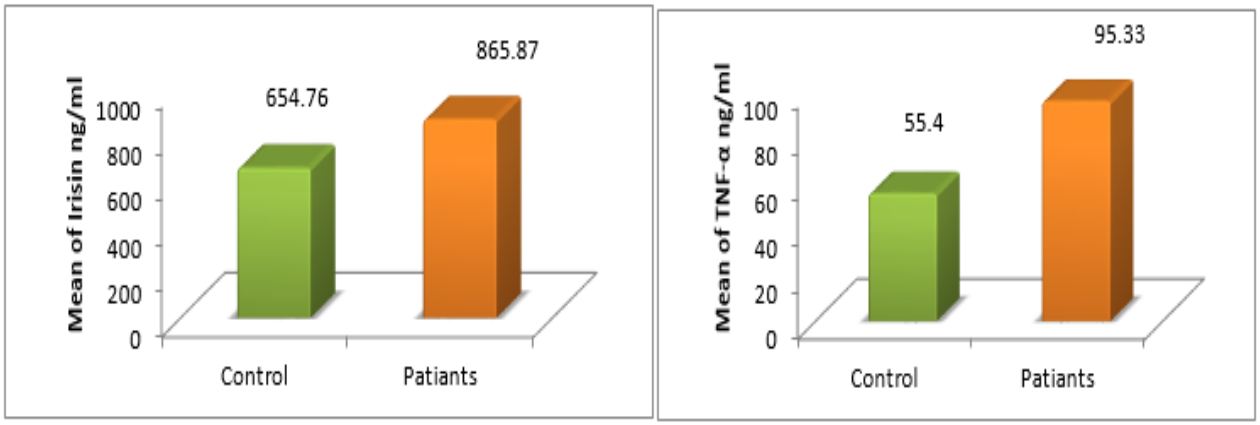

Figure (6): Irisin concentration in the blood serum of all groups
Figure (7): TNF-α concentration in the blood serum of all groups

Discussion

The results of current study are consistent with results of some studies (Hussain., 2021) (Jadav., 2020) from the message, which indicated in their study an increase in level of luteinizing hormone in blood serum of patients with polycystic ovary syndrome compared to healthy women, as it reinforces the reason for the resulting increase. It may also occur as a result of psychological stress

or an imbalance in the diet (Henríquez., 2020). An increase in the level of luteinizing hormone causes a defect in the ovulation process or the absence of ovulation in the follicular cycle, Although luteinizing hormone initiates ovulation and then stimulates the corpus luteum to create steroid hormones, a high quantity of it lowers the efficiency of aromatase and hinders the development of the oocyte. (Al-Jubouri, 2014). While Hus., 2020, indicated that the diagnosis of polycystic ovary syndrome is made with the best sensitivity and specificity with an LH/FSH ratio greater than 1 (Hasan *et al*., 2020).

On the other hand, the results of the current research indicated a decrease in concentration of follicle-stimulating hormone in blood serum of patients with PCOS compered healthy women . The slight decrease in the hormone level may be because a high prolactin concentration may inhibit FSH secretion (Eldar-Geva., 2001). also (Melmed., 2004) indicated that the decrease in the hormone level may be due to the production of adrenaline from the adrenal gland, which in turn affects the concentration of FSH from During androgen secretion.

The results of the research also indicated an elevated in testosterone in women infected with PCOS, as the results agreed with some studies (Sahlah and Aseel.,2019) indicated elevated of testosterone level, Excessive androgens are one of the most important causes of polycystic ovary syndrome. Androgens are secreted as a result of abnormal dysfunction in the ovary, and poor follicle formation is the primary effect of excess androgens that disrupt normal androgen synthesis. (Shabbir., 2023).

Also the results of this study showed an increase in levels of resistin in blood serum of women with PCOS. the results agreed with some studies (İlyas., 2009 and ahereh., 2021) who indicated a significant elevated in resistin hormone in women infected with PCOS, and on other hand, a study showed that the concentration of resistin are higher in overweight and obese females than in thin women, regardless of the occurrence of Polycystic ovary syndrome (ABBAS.,2021 and Hussein., et al.,2024), as resistin is secreted by blood cells and adipose tissue, which inhibits glucose tolerance and insulin sensitivity. Fat cells are the most important cause of insulin resistance because they reduce the number of insulin receptors, and since they secrete the hormone resistin, insulin resistance occurs, so weight loss It helps reduce insulin resistance and improve blood sugar measurement.

On the other hand, the research results indicated an increase in copeptin levels, as the result agreed with some studies (adel.,2020 and Mutaz., 2018 and Hani.,2022), which indicated an increase in copeptin levels in patients PCOS. also they studied 150 women with polycystic ovary syndrome. Copeptin levels are associated with insulin resistance, but because of low sensitivity, it cannot be considered a sign of insulin resistance. (Widecka., 2019). a study also found that there is a relationship between copeptin levels, insulin resistance, and metabolic syndrome ((Saleem., 2009). Therefore, it was found that high levels of copeptin in the blood may be an important diagnostic indicator in patients suffering from polycystic ovary syndrome. (Gruden *et al*, 2014).

Also the Serum irisin concentration were significantly rise in PCOS women compared with healthy women this result agree with (Zhang., 2018 and M.S. BOSTANCI., 2015). also we found that metformin therapy leads to lower irisin levels in women with polycystic ovary syndrome (Telagareddy., 2024). irisin could be considered as a biomarker for prognosis and therapy followup in patients with PCOS (Saba.,2023). In the current study, it was found that there was an increase in irisin levels, and this is consistent with the results (Park *et al* ., 2013), the elevated concentration of serum irisin were determined in patients with metabolic syndrome. however, it has also been suggested that the elevated irisin level may represent a state of irisin resistance(GARCÉS., 2014) .

Similar investigations have suggested that circulating irisin levels were greater in patients with PCOS than in normal healthy controls, but this link disappeared when the researchers compared them to healthy controls with the same BMI as patients with PCOS. (Mancuso., 2019 and. Kukla.,2020), Furthermore, it has been proposed that BMI, a weight status indicator, may operate as a modulator of circulating irisin alterations in PCOS patients. Furthermore, this meta-analysis found that circulating irisin was lowered in response to hyperinsulinemia in patients with PCOS,

but to a higher amount than in healthy controls, implying that people with PCOS function in this regard may be affected. (Chen.,2022).

The research results are consistent with the results of (Shorakae., 2018 and Al-Musawy., 2018), who indicated an increase in level of tumor necrosis factor in women with polycystic ovary syndrome, as the reason is attributed to inflammatory factors, as PCOS is characterized by the presence of low-grade chronic inflammation (Dadachanji.,2018 and Wedad and Mohanad.,2021) and that an increase in tumor necrosis factor in women with polycystic ovary syndrome is an indication of Immune dysfunction in affected women, as hyperandrogenism, which is a hallmark of this condition, can affect common forms in the genes that encode tumor necrosis factor and its type 2 receptors (Al-Musawy., 2018).by increasing receptors Androgen receptor mRNA- in women with polycystic ovary syndrome that stimulate glucose uptake in the fasting state by monocytes mononuclear cells, which activates the nuclear transcription factor in those cells, causing increased production of inflammatory cytokines, including tumor necrosis factor (Lainez., 2019).

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