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EVALUATION OF SERUM IL1B AND RESISTIN LEVELS IN WOMEN WITH PCOS

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The research from the thesis of the first researcher *

Article history:		Abstract:		
Received: Accepted: Published:	February 8 th 2022 March 8 th 2022 April 24 th 2022	The goal of this research is to evaluate the levels of IL-1 β and resistin in polycystic ovary women, as well as their relationship to obesity. From January 2021 to June 2021, blood samples from 50 patients with PCOS (22 single and 28 married) and 15 women as control were collected from private laboratories in Tikrit, Iraq, for the estimation of serum levels of IL1 β , resistin and the evaluation the levels of Testosterone, Follicle-stimulating hormone (FSH), Estradiol (E2) and luteinizing hormone (LH) by using the enzymelinked immunosorbent assay (ELISA) The results revealed that in PCOS women, blood levels of IL1 β and resistin are significantly higher (P<0.001) than in healthy controls. In addition, LH, FSH, and TSH levels all increased significantly (P<0.05).		

Keywords:: IL-1β, Resistin, PCOS, Obesity

INTRODUCTION:

Poly Cystic Ovarian Syndrome one of the most important endocrine disorders, characterized by irregularities, hirsutism menstrual obesity, hyperinsulinemia, and resistance to insulin (Legro et al., 2004). PCOS is a is a complicated condition and enigmatic in which various factors of lifestyle play a major role in the development of it (Piltonen et al. 2016; Merkin al. et 2016)

Inflammatory cytokines play a significant role in PCOS development. There was compelling evidence that lowgrade inflammation and cytokines play a major role in PCOS (Riley et al. 2016). PCOS is consider a proinflammatory condition that is characterized by elevated in levels of many inflammatory cytokines that are correlated with resistance of insulin. Also studies have been found obesity can be associated with PCOS (Barcelloset al., 2015) IL-1β is cytokine produced in most times from macrophagesas a proinflammatory cytokine, and physiologically active IL-1\beta is created via caspase1 activation via the NLRP3 inflammasome cleavage of pro-IL-1b (Sims and Smith., 2010). In addition to being linked to the improvement of obesity-related to insulin resistance, IL-1ß reduces the sensitivity of insulin in fat tissue (adipose) by inhibiting the signal of insulin

transcription (Jager et al., 2010). In human adipocytes, inhibiting IL-1β activity, synthesis or it receptors improves the signaling of insulin and it action. This is accompanied with a decrease the profile of macrophage-stimulated proinflammatory . At the tissue and systemic levels, IL-1\beta may be effective for preventing IR that related to obesity at systematic levels (Chen Bing ,2015). Adipose tissue serves as a multifunctional endocrine tissue which expresses and secreted bioactive peptides called "adipokines," which can have local or systemic effects (Kershaw and Flier 2004). Insulin, adrenaline, noradrenaline, and cortisone are hormones that work on adipocytes to regulate their function (Lehr et al. 2012). A metabolic condition occurs when adipokine secretion is disrupted (Kershaw and Flier 2004).

Resistin is an adipocytokine released by adipose tissue that has been linked to insulin resistance (IR) and obesity. A 94-amino-acid polypeptide released as a tiny cysteine-rich protein Steppan et al. (2001) discovered it while researching the PPARg effects agonists on homeostasis of glucose. (Kim et al. 2001) found this adipokine, and it's have inhibitor effect on adipocytes development, as well as its relationship with insulin resistance, have made it a possible to link between diabetes mellitus and obesity. Regardless of PCOS or control status, another study found that levels of serum resistin were higher in overweight and obese



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women in compare with lean participants (Escobar-Morreale et al. 2006).

METHODS:

From January to June 2021, a total of 50 PCOS patients (22 single and 28 married) between the ages of 17-45 were chosen from private laboratories in Tikrit, Iraq. Using the Rotterdam ESHRE/ASRM criteria in diagnosing PCOS, which characterize by oligoovulation and/or anovulation, biochemical evidence of hyperandrogen. (Heinrich et al., 1990). Simultaneously, 15 seemingly healthy women without PCOS were chosen at random from laboratories . Controls had no signs of hyperandrogenism and a regular menstrual cycle with ages ranges (17- 45) , and were exposed to an ultrasonography examination with normal hormone levels. Controls were excluded if they had abnormal menstrual periods, malignant tumors, or autoimmune diseases.

Blood sampling

Each woman with PCOS and control had drawn 4ml of blood sample in tubes containing gel , which was then allowed to have clotted at 20 to 25 C $^{\rm o}$ for 10 min before being inter centrifuge at 5000 rpm for five minutes to get the serum. After centrifugation, the serum was divided into two Eppendorf tubes and kept refrigerated in order to avoid multiple freezing and thawing.

Laboratory methods

Serum level of IL- 1β , resistin were measured as well as the hormones of reproductive (FSH, LH, E2 and Testosterone) on menstrual cycle third day and was determined by using (ELISA).

Statistical analysis

The results was expressed as a mean \pm standard deviation, and the probability (two-tailed) was expressed using an independent t-test and an ANOVA table at the level ≤ 0.05 .

Hormonal assay

When comparing PCOS patients and control, the results revealed that PCOS women had significantly higher levels of FSH, LH and Testosterone, but significantly lower levels of E2, as shown in Table-one

Parameters	PCOS patients (n=50)		Control (n=15)	Probability
	Single (n=22)	Married (n=28)		
LH(mIU/ml)	12.794 ± 2.436	13.543 ±2.647	3.111±0.836	$P \le 0.05$
FSH(mIU/ml)	10.146 ± 2.614	8.113±2.611	3.886 ±1.218	$P \le 0.05$
⊤ (ng /mL)	0.9637± 0.3221	1.0166± 0.3567	0.4086 ±0.0490	P ≤ 0.05
E2 (pg/mL)	119.21 ± 20.25	86.10±9.71	129.13 ±18.75	P ≤ 0.05

Table 1-Levels of (FSH,LH,T,E2) blood samples of PCOS women and healthy controls,

Serum level of IL-1 β and resistin

Table-2 relaved there were a high significant increases in the serum of IL-1 β and resistin (P<0.001) in PCOS women in compare to controls.

Parameters	PCOS patients (n=50)		Control (n=15)	Probability
	Single (n=22)	Married (n=28)		
Resistin (ng/ml)	1.171 ± 0.731	1.540 ±0.829	0.171±0.0605	P < 0.001
IL1β (pg/mL)	31.22 ± 5.36	25.39 ±6.30	14.27±3.389	P < 0.001

Results described as means ±SD in both tables

Table 2-Interleukin-1β and resistin levels of PCOS patients group compared to controls

DISCUSSION

The interleukin-one family is involved in the immune system as well as the inflammatory process. Endothelial cells, epithelial cells ,monocytes and macrophages, are the principal producers of IL-1. The reduction of development of dominant follicle and ovulation may be caused by IL-1-mediated estradiol

production inhibition that released by granulosa cells. IL-1 overactivity in PCOS has been the subject of recent research. (Popovic *et al.*,2019). The present study are revealed that there were a significant increase (P<0.001) in the level of serum IL-1 β in patients with PCOS (31.22 \pm 5.36 pg\ml and 25.39 \pm 6.30 pg\ml respectively) as compared with the



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control (14.27±3.389 pg\ml) and this results agreed with(Knebel et al., 2008; Zafari Zangeneh et al, 2017; Hiam et al., 2019 and Ashraf et al., 2019) Increased amounts of several circulating cytokines, such as IL1β, have been reported in studies of inflammation (Knebel et al. 2008). The mechanisms of persistent low-grade inflammation in PCOS is hypertrophy of adipocyte, which causes stromal vascular compression, resulting in adipose tissue hypoperfusion and, as a result, hypoxia .Also IL-1 β plays a role in the development of IR and DM 2. Low-grade inflammation has been linked to an increased risk of type 2 diabetes, and greater levels of IL-1 in the blood have been linked to an increased risk. (Sharma et al.,

Resistin is adipokine secreted by adipose tissues, and have a role in insulin resistance (IR) and obesity. Table-2 are revealed that there is a significant increase (P<0.001) in the serum of resistin in patients with PCOS($1.171 \pm 0.731 \text{ ng/ml}$ and $1.540 \pm 0.829 \text{ ng/ml}$ respectively) as compared with the control (0.171±0.0605 ng\ml) and this result was concordant with previous studies Chen E.,(2013); Vejrazkova et al,(2017); Moustafa et al.,(2020); Lin et al.,(2020) and Raeisi et al., (2021) that it was previously reported that a higher levels of serum resistin was linked to insulin resistance and obesity, which matched the findings of the current investigation. The reason for this large increase in resistin levels in the blood was that serum resistin levels were abnormally high in PCOS patients suggesting that resistin may play a role in PCOS (Chen et al., 2013; Chen E., 2013; Moustafa et al.,2020) as a result of the presence of insulin resistance. These findings back up the theory that there is a link between resistin and IR in peoples.(Panidis et al.,2004; Raeisi et al.,2021). Insulin resistance and obesity have been linked with resistin which has been identified as a possible relationship (Zhang et al., 2011). It has been discovered that serum resistin and T levels have a beneficial relationship (Munir et al.,2005; Raeisi et al.,2021). In PCOS patients, increased resistin levels may boost ovarian androgen expression (Yilmaz et al.,2009). These observations, along with our findings, suggest that adipokine (resistin) may have an active role in PCOS and its clinical symptoms. (Raeisi and colleagues, 2021).

CONCLUSION

The recent findings revealed that the PCOS group had considerably higher levels of IL-1 and resistin in patients with PCOS, on the other hand, significantly

high levels observed of FSH, LH, free testosterone and a significantly lower of E2 levels compared to control.

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