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EVALUATION OF SERUM IL1B AND RESISTIN LEVELS IN WOMEN WITH PCOS

Marwa Karim Taha[1*] , Zaid Mohammed Mubarak[2] ,Saria Naji Muhsin[3]
1.Al-Qalam university College, Kirkuk , Iraq
2,3 Biology Department , Science College , University of Tikrit, salahdin , Iraq
The research from the thesis of the first researcher *

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Abstract:

The goal of this research is to evaluate the levels of IL-1β 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 IL1β, resistin and the evaluation the levels of Testosterone, Follicle-stimulating hormone (FSH), Estradiol (E2) and luteinizing hormone (LH) by using the enzyme-linked immunosorbent assay (ELISA) The results revealed that in PCOS women, blood levels of IL1β 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 menstrual irregularities, hirsutism , 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 et al. 2016)

Inflammatory cytokines play a significant role in PCOS development. There was compelling evidence that low-grade inflammation and cytokines play a major role in PCOS (Riley et al. 2016). PCOS is consider a pro-inflammatory 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 a cytokine produced in most times from macrophagesas a proinflammatory cytokine , and physiologically active IL-1β 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-1β 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-1β 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 ° 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 ± 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 ≤ 0.05
FSH**(mIU/ml)**	10.146 ± 2.614	8.113±2.611	3.886 ±1.218	P ≤ 0.05
T **(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-1β and resistin

Table-2 relaved there were a high significant increases in the serum of IL-1β 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-1β in patients with PCOS (31.22 ± 5.36 pg\ml and 25.39 ±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-1β 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*., 2020)

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 ± 0.731 ng\ml and 1.540 ±0.829 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 .

REFERENCES

1. Ashraf S, Nabi M, Rasool SA, Rashid F, Amin S. **2019**.Hyperandrogenism in polycystic ovarian syndrome and role of CYP gene variants: a review. *Egypt J Med Hum Genet*.;**20**(1):25.
2. Barcellos, C. R. G., Rocha, M. P., Hayashida, S. A. Y., Dantas, W. S., Yance, V. D. R. V. and Marcondes, J. A. M. **2015.** Obesity, but not polycystic ovary syndrome, affects circulating markers of low-grade inflammation in young women without major cardiovascular risk factors. *Hormones*, **14**(2): 251-7.
3. Chen B .**2015**.Is interleukin-1β a culprit in macrophage-adipocyte crosstalk in obesity?, *Adipocyte*, **4**:2, 149-152, DOI: 10.4161/21623945.2014.979661
4. Chen E. **2013**.Obesity, adipokines and metabolicsyndrome in polycystic ovary syndrome. *Front Horm Res*; **40**:40–50.
5. Chen X, Jia X, Qiao J, Guan Y, Kang J. **2013**.Adipokines in reproductive function: a link between obesity and polycystic ovary syndrome.*J Mol Endocrinol;* **50**(2):R21–37.
6. Escobar-Morreale HF, Villuendas G, Botella-Carretero JI, Alvarez-Blasco F, Sanchon R, Luque-Ramirez M, et al. **2006**.Adiponectin and resistin in PCOS: a clinical, biochemical and molecular genetic study. *Hum Reprod.* ; **21** (9) : 2257 -65
7. Heinrich P. C, Castell J. V. and Andus T. **1990.** Interleukin-6 and the acute phase response. *Biochem J,* **265**:621-636.
8. Hiam D, Moreno-Asso A, Teede HJ, Laven JS, Stepto NK, Moran LJ, et al. **2019**. The Genetics of Polycystic Ovary Syndrome: An Overview of Candidate Gene Systematic Reviews and Genome-Wide Association Studies. *J Clin Med* **8**(10):1606. doi: 10.3390/jcm8101606
9. Jager J, Gremeaux T, Gonzalez T, et al. **2010**.Tpl2 kinase is upregulated in adipose tissue in obesity and may mediate interleukin-1beta and tumor necrosis factor-{alpha} effects on extracellular signal-regulated kinase activation and lipolysis. *Diabetes*.;**59**(1):61–70.

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10. Kershaw EE, Flier JS .**2004**. Adipose tissue as an endocrine organ. *Journal of Clinical Endocrinology & Metabolism* **89**: 2548–2556.
11. Kim KH, Lee K, Moon YS & Sul HS**.2001** A cysteine-rich adipose tissue-specific secretory factor inhibits adipocyte differentiation. *Journal of Biological Chemistry* **276**: 11252–11256.
12. Knebel, B., Janssen, O.E., Hahn, S., Jacob, S., Gleich, J., Kotzka, J., & Muller–Wieland, D. **2008**. Increased low grade inflammatory serum markers in patients with Polycystic ovary syndrome (PCOS) and their relationship to PPARgamma gene variants. *Experimental and clinical endocrinology & diabetes : official journal, German Society of Endocrinology [and] German Diabetes Association,* **116** 8, 481-6 .
13. Legro, R. S., Castracane, V. D. and Kauffman, R. P. **2004.** Detecting insulin resistance in polycystic ovary syndrome: purposes and pitfalls. *Obstetrical & gynecological survey*, **59**(2): 141-154.
14. Lehr S. et al. **2012.** Adipokines: a treasure trove for the discovery of biomarkers for metabolic disorders . *Proteomics Clin Appl*. Jan;**6**(1-2):91-101. doi: 10.1002/prca.201100052.
15. Lin K, Sun X, Wang X, Wang H and Chen X .**2020**.Circulating adipokines in non-obese PCOS patients: a systematic review and meta-analysis *medRxiv* .10.11.20210716.
16. Merkin, S. S., Phy, J. L., Sites, C. K. and Yang, D. **2016.** Environmental determinants of polycystic ovary syndrome. *Fertility and sterility*: **106**(1), 16-24.
17. Moustafa, S. R., & Al-Hakeim, H. K. **2020**. The impact of serum visfatin, and resistin levels on insulin resistance in patients with polycystic ovary syndrome. *Zanco Journal of Medical Sciences (Zanco J Med Sci)*, **24**(1), 80–88.
18. Munir I, Yen H-W, Baruth T, Tarkowski R, Azziz R, Magoffin DA, et al. **2005**.Resistin stimulation of 17α-hydroxylase activity in ovarian theca cells in vitro: relevance to polycystic ovary syndrome. *The Journal of Clinical Endocrinology & Metabolism.*;**90**(8):4852–7.
19. Panidis D, Koliakos G, Kourtis A, Farmakiotis D, Mouslech T, Rousso D. **2004**.Serum resistin levels in women with polycystic ovary syndrome. *Fertility and sterility.*;**8**1(2):361–6. pmid:14967374
20. Piltonen, T. T. **2016.** Polycystic ovary syndrome: endometrial markers. *Best Practice and Research Clinical Obstetrics and Gynaecology*, **37**: 66-79.
21. Popovic M. , Sartorius G. , Christ-Crain M. **2019**.Chronic low-grade inflammation in polycystic ovary syndrome: is there a (patho)-physiological role for interleukin-1?,*Semin Immunopathol*, **5** , pp. 1-13
22. Raeisi T, Rezaie H, Darand M, Taheri A, Garousi N, Razi B, et al. **2021** .Circulating resistin and follistatin levels in obese and non-obese women with polycystic ovary syndrome: A systematic review and meta-analysis. *PLoS ONE* **16**(3): e0246200.
23. Riley, J. K. and Jungheim, E. S**. 2016.** Is there a role for diet in ameliorating the reproductive sequelae associated with chronic low-grade inflammation in polycystic ovary syndrome and obesity? *Fertility and sterility*, **106**(3) 520-527.
24. Sharma, M., Boytard, L., Hadi, T. *et al.* **2020**.Enhanced glycolysis and HIF-1α activation in adipose tissue macrophages sustains local and systemic interleukin-1β production in obesity. *Sci Rep* **10,** 5555 (). https://doi.org/10.1038/s41598-020-62272-9
25. Sims JE, Smith DE. **2010**.The IL-1 family: regulators of immunity. *Nat Rev Immunol*; **10**:89-102.
26. Steppan CM, Bailey ST, Bhat S, Brown EJ, Banerjee RR, Wright CM, Patel HR, Ahima RS & Lazar MA.**2001** .The hormone resistin links obesity to diabetes. *Nature* **409** :307–312.
27. Vejrazkova D, Lischkova O, Vankova M,Stanicka S, Vrbikova J, Lukasova P, et al. **2017**. Distinct response of fat and gastrointestinaltissue to glucose in gestational diabetes mellitusand polycystic ovary syndrome. *Physiol Res;* **66**(2):283–92.
28. Yilmaz M, Bukan N, Demırcı H, Öztürk Ç, Kan E, Ayvaz G, et al. **2009**.Serum resistin and adiponectin levels in women with polycystic ovary syndrome. *Gynecological Endocrinology.;***25**(4):246–52. pmid:19408174
29. Zafari Zangeneh, F., Naghizadeh, M. M., & Masoumi, M. **2017**. Polycystic ovary syndrome and circulating inflammatory markers. *International journal of reproductive biomedicine*, **15**(6), 375–382.
30. Zhang J, Zhou L, Tang L, Xu L. **2011**.The plasma level and gene expression of resistin in

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
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ISSN: 2749-3644

polycystic ovary syndrome. *Gynecological Endocrinology.*;**27**(12):982–7. pmid:21557697