

Changes of serum Interleukin and Chemerin levels in patients with Polycystic Ovary syndrome

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ABSTRACT

To determine serum chemerin, as well as interleukin (IL)-6, IL-10, and IL-17 in polycystic ovary syndrome patients and investigate the possible relationship between them. The study was conducted from 15 March 2017 to 15 March 2018 in obstetrics and gynecology of Tikrit Teaching Hospital in Tikrit city.

Fifty-seven women with polycystic ovary syndrome and 57 healthy women of ages 23-35 years were recruited while obtaining their written consent, divided into two groups using Rotterdam Criteria, and included in this study. There was not any statistically significant difference in the levels of IL-17 between polycystic ovary syndrome women and the control group (45.57 ± 1.49 vs 42.79 ± 1.31 pg/ml). Serum levels of chemerin, IL-6, IL-10, and IL-17 were assessed by enzyme-linked immunosorbent assay (ELISA) methods. Data were analyzed using Statistical Package for the Social Sciences v.21.0. IL-6 and chemerin were significantly higher, and IL-10 was significantly lower in polycystic ovary syndrome patients compared with the healthy controls. No significant difference was observed in IL-17 between healthy controls and polycystic ovary syndrome patients. These findings suggest that chemerin, IL-6, and IL-10 could be a biomarker for the risk of polycystic ovary syndrome.

Keywords: Polycystic ovary syndrome, Interleukin-17, Chemerin, Patients, Interlukin

Introduction

Polycystic Ovary Syndrome is a complex, heterogeneous, multifaceted endocrine disorder that affects 4 to 18 percent of women of reproductive age with significant collateral negative effects on reproductive health metabolic, and psychological characteristics [1, 2]. Hyperandrogenism, ovulatory dysfunction, and polycystic ovary morphology are all symptoms of this condition [3-6].

Cytokines are small soluble polypeptides of immunological

origin manufactured by macrophages, lymphocytes, monocyte, dendritic cells, neutrophils, endothelial cells, and fibroblasts [7].

Polycystic ovary syndrome is an inflammatory condition. Several studies in the literature have found that Polycystic ovary syndrome patients have higher levels of circulating inflammatory molecules. It is unclear whether their increase is caused by Polycystic ovary syndrome or is a result of obesity and/or abdominal adiposity [8].

Interleukin-10 (IL10) is a pleiotropic cytokine created by T cells, B cells, monocytes, thymocytes, and macrophages typically delivered locally from insusceptible cells to help settle irritation, and is best described for its capacity to repress macrophage initiation [9, 10]. It can restore equilibrium by inhibiting the development of proinflammatory cytokines and stimulating the production of defensive antibodies [11].

Interleukin-17 (IL-17) is a recently depicted T cell-inferred incendiary cytokine, delivered principally by Th17 cells and by T cells and neutrophils. 4 IL-17 is additionally alluded to as IL-17A [12]. IL-17 also causes a wide range of cells to

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produce other proinflammatory cytokines and chemokines, which mediates immune responses. IL-17 is a potent inflammatory cytokine that causes tissue inflammation and inflammatory cell infiltration into target organs [13].

Aim of study

The study goal was the determination of the levels of TNF- α , IL 6, and IL 17 in Polycystic ovary syndrome women and compare them to those in a seemingly healthy control group.

Materials and Methods

Fifty-seven women with Polycystic ovary syndrome were involved in this case-control study. Patients were collected from the obstetrics and gynecology department of Tikrit Teaching Hospital in Tikrit city during the period from March 15, 2017, to March 15, 2018, whose ages ranged from 23 to 35 years.

After a 12-hour overnight fast, 5ml of venous blood was drawn from each of the subjects, transferred to a tube, and allowed to clot at 37 °C before being centrifuged for 10min at 4000rpm. The supernatant was separated and kept at -20°C until analyses. Statistical analysis was performed using Statistical Package for the Social Sciences v. 21. Data are presented as mean SD with P< 0.05 being considered statistically significant.

Results and Discussion

The interleukin-6 (IL-6) and chemerin levels were significantly higher in Polycystic ovary syndrome patients in comparison to the control group, (4.72 ± 0.5 vs 1.84 ± 0.3 pg/mL: <0.001) (301.62 ± 72.54 vs 242.09 ± 56.012 ng/mL: 0.001), respectively. Whereas, there is a significant reduction in the level of IL-10 between Polycystic ovary syndrome women and the control group (6.4 ± 2.3 vs 19.8 ± 3.3 pg/ml).

There was not any statistically significant difference in the levels of IL-17 between Polycystic ovary syndrome women and the control group (45.57 ± 1.49 vs 42.79 ± 1.31 pg/ml) (Table 1).

Table 1. The Mean Concentration of IFN- γ , TNF- α , and IL-8 (pg/ml) in Male Thalassemia Major Patients and Control Group

Items	Patients	Control	P-value
BMI (kg/m ²)	25.99 \pm 0.36	25.11 \pm 0.64	2
IL-6 (pg/mL)	4.72 \pm 0.5	1.84 \pm 0.3	<0.001
IL-17(pg/ml)	45.57 \pm 1.49	42.79 \pm 1.31	NS
IL-10 [pg/ml]	6.4 \pm 2.3	19.8 \pm 3.3	<0.05
Chemerin (ng/mL)	301.62 \pm 72.54	242.09 \pm 56.012	0.001*

Interleukin-6 (IL-6) is a notable multifunctional to inflammatory cytokine, which is for the most part synthesized by T cells and macrophages, renal cells, myocytes, adipocytes, and osteoblasts that is considered a significant part in the

reaction to ecological stress and has been ensnared in the pathogenesis of numerous ongoing infections, and stimulates the advancement of insulin opposition [14, 15]. Its synthesis is likewise influenced by different cytokines, i.e. TNF and IL-1. IL-6 has mostly proinflammatory properties [16] Furthermore, when compared to healthy people, serum IL-6 levels in Polycystic ovary syndrome patients were found to be significantly higher. Our findings are in agreement with the findings of previous reports [17-19].

Besides, IL-6 leads to increased levels of acute-phase protein in the inflammatory reactions and the liver, as well as hemocyte growth. By upregulating AR expression in the ovary, IL-6 may also increase androgen activity, resulting in Polycystic ovary syndrome. Furthermore, IL-6 may be the first to cause insulin resistance, followed by Polycystic ovary syndrome [20].

CD4 Th17 cells produce IL-17, a proinflammatory cytokine that stimulates the production of proinflammatory mediators [11]. IL-17 can enhance neurite outgrowth by acting on distal neurites and sympathetic somata, indicating a new role for IL-17 in the neuroanatomical plasticity, which occurs with inflammation [5, 21]. This abnormal cytokine pattern plays a significant role in the immunopathogenesis of Polycystic ovary syndrome [22]. The IL-17 levels were not significantly different between healthy women and those with polycystic ovaries in this study. This result was in line with what was predicted by Foroozand *et al.* (2017) [23]. However, Knebel *et al.* (2008) found a significant difference in the IL17 level between Polycystic ovary syndrome and healthy women [24].

Interleukin 10 is a major cytokine inhibitor that suppresses macrophage function and moderates the response to injury by lowering TNF and IL-6 levels. Low capacity in the production of IL-10 is linked to metabolic syndrome [25, 26]. The level of IL-10 in the blood was found to be significantly lower in patients with Polycystic ovary syndrome. These findings were in line with those of a study conducted by Artmani *et al.* (2015) [27].

Chemerin (16 kDa), also known as TIG2 or RARRES2, is a newly discovered adipocyte-secreted factor that has both pro- and anti-inflammatory properties [16, 26, 28, 29].

In our study, Polycystic ovary syndrome cases had significantly higher plasma levels of chemerin, which could be explained by lower secretion of estradiol, as well as suppressed FSH-induced secretion of estradiol and progesterone in granulosa cells and prenatal follicles due to inhibition of p450sc and aromatase expression in granulosa cells and prenatal follicles. In line with previous findings, it is possible that chemerin plays a role in the development of Polycystic ovary syndrome, and that manipulating the expression or signaling of the chemerin gene could lead to new therapeutic approaches for Polycystic ovary syndrome [30]. Tan *et al.* (2009) discovered a significant elevation in serum chemerin, as well as chemerin mRNA and protein expression in omental and subcutaneous adipose tissue in Polycystic ovary syndrome patients [31]. So, in Polycystic ovary syndrome, changes in chemerin serum level might be one of the diagnostic criteria.

Conclusion

These findings suggest that high IL-6 and low IL-10 levels are not intrinsic characteristics of Polycystic ovary syndrome, but they may be useful monitoring biomarkers for the Polycystic ovary syndrome treatment. Chemerin is an interesting adipokine, which may predict insulin resistance and adipose mass and may be important in Polycystic ovary syndrome women.

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