

Estimating of the Levels of Some Biochemical Variables, Adipokines and Cytokines in Women with Polycystic Ovarian Syndrome

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Abstract

Aim: This study aims to determine the relationship between age and body mass index (BMI) in women with polycystic ovarian syndrome (PCOS) and to estimate the concentration of sex hormones (Testosterone, Follicle-Stimulating Hormone (FSH), and Luteinizing Hormone (LH)), as well as the concentration of adipokines (Adropin, Irisin, Visfatin, and Chemerin). Additionally, the study examines the association between PCOS and immune responses through the measurement of interleukins (IL-6 and IL-17). **Methods:** This study included 120 women, comprising 80 PCOS patients who visited Azadi Teaching Hospital from April to August 2024 and 40 healthy women as a control group. Hormonal and adipokine concentrations were measured and analyzed to identify significant differences between PCOS patients and healthy individuals. **Results:** The highest prevalence of PCOS was observed in the 26-35 years age group (57.5%), while the lowest prevalence was in the 15-25 years age group (13.75%). The average age of PCOS patients was 29.15±5.17 years. Regarding BMI, the highest prevalence was in the 30-35 kg/m² group (67.5%), whereas the lowest was in the 21-<25 kg/m² group (8.75%). Hormonal analysis revealed significantly lower FSH levels in PCOS patients, while Testosterone and LH levels were significantly higher compared to healthy individuals (P=0.001). Adipokine analysis indicated significantly lower levels of Adropin and significantly elevated levels of Irisin, Visfatin, and Chemerin in PCOS patients (P=0.001). Additionally, interleukin levels (IL-6 and IL-17) were significantly elevated in PCOS patients compared to healthy controls (P=0.001). **Conclusion:** The study highlights a strong association between PCOS and BMI, as well as alterations in sex hormone levels and adipokine concentrations. PCOS was also linked to increased immune responses, as evidenced by elevated interleukin levels. These findings suggest that metabolic and inflammatory factors play a crucial role in the pathophysiology of PCOS. Further research is recommended to explore the mechanisms underlying these associations.

Keywords: PCOS, Adipokines, Adropin, IL-17, Testosterone, Visfatin, Irisin, Interleukins.

INTRODUCTION

Millions of women worldwide who are of reproductive age suffer from PCOS, a diverse endocrine condition.^[1,2] This syndrome has been associated with ovaries that are oversized and dysfunctional, high testosterone levels, insulin resistance, and other disorders.^[3] As per estimates, more than 10% of women have PCOS before menopause and struggle with related complications.^[4,5] PCOS is estimated to affect 4–10% of women globally who are of reproductive age.^[6] According to the World

Health Organization, 8–13% of women of reproductive age have PCOS, and over half of these instances go untreated.^[7] The high prevalence of PCOS and its relation to abnormal menstruation cycle and ovulation, hair loss, and metabolic issues highlight the high-cost burden of

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the disease.^[8] Most PCOS cases occur in the age group of 20–30 years, even though it may happen at any age, beginning with menarche.^[9] 1.55 million women of reproductive age worldwide suffer from PCOS, which causes 0.43 million years of disability-adjusted life. In females of reproductive age, the age-standardized incidence of PCOS increased by 1.45% from 2007 to 82.44 per 100,000 in 2017.^[10] It has been hypothesized that early adipose tissue malfunction, likely brought on by in-utero androgen hyperexposition and resulting in large abdominal fat depots, insulin resistance, and aberrant androgen metabolism in PCOS may have a significant effect.^[11] White adipose tissue is well known for its metabolic activity since it can synthesize and produce several endocrine chemicals known as adipokines.^[12] In PCOS patients, adipokines affect endocrine and metabolic signaling. Various adipokines have been shown to locally modify ovarian steroidogenesis or influence the functioning of the hypothalamic-pituitary-gonadal axis. Females with PCOS have been shown to exhibit dysregulation of adipocyte-secreted adipokines, such as decreased adiponectin levels and more significant leptin levels.^[13] Interleukins, on the other hand, perform a variety of activities and patterns, such as supporting pro- and anti-inflammatory pathways and immunomodulatory actions. Biomolecules of interleukin-1 α bind to cell receptors, which may induce immunological responses. Nonetheless, the effectiveness and specificity of these processes are determined by the corresponding receptors, ligands, and signaling pathways.^[14,15] Since inflammatory signals encourage the ovaries to generate more androgen, which results in hyperandrogenism, PCOS and inflammation are connected.^[15] Chronic inflammation in obese people has been linked to metabolic syndrome.^[16] The pathophysiology of PCOS is deeply intertwined with endocrine and metabolic dysfunctions, primarily involving hyperandrogenism, insulin resistance, and chronic low-grade inflammation. Normal follicular development is disrupted in women with PCOS due to elevated androgen levels, leading to anovulation and menstrual irregularities. Insulin resistance, a hallmark feature of the syndrome, exacerbates hyperandrogenism by promoting excessive androgen production in ovarian theca cells while simultaneously suppressing sex hormone-binding globulin (SHBG), which increases free testosterone levels in circulation. In addition, compensatory hyperinsulinemia is accompanied by metabolic derangements such as dyslipidemia and increased visceral adiposity that further complicate PCOS management.^[17] Inflammation also plays a role in the pathogenesis of PCOS, with increased levels of inflammatory markers detected in individuals with the disorder. Pro-inflammatory cytokines including IL-6, TNF- α , and CRP are often elevated in PCOS patients, which encourages insulin resistance and excess testosterone. This inflammatory environment is complemented by increased oxidative stress and adipose tissue dysfunction that favor further endocrine disruptions.

Chronic low-grade inflammation in PCOS women increases the risk for cardiovascular complications in addition to deteriorating metabolic outcomes.^[18] Since it is linked to obesity, dyslipidemia, and insulin resistance, PCOS significantly increases the risk for cardiovascular disease (CVD). Hypertension, endothelial dysfunction, and arterial stiffness that increase the risk for atherosclerosis and other cardiovascular conditions are more common in women with PCOS, studies show. In addition, dysregulated lipid metabolism with increased levels of triglycerides and low levels of high-density lipoprotein (HDL) cholesterol exacerbates CVD risks in PCOS individuals. Given these metabolic and cardiovascular comorbidities, detection and management at an early stage with interventions against lipid and glucose homeostasis are key to curtailing long-term risk factors in women who have PCOS.^[19] PCOS is a major cause of infertility due to its effect on ovulatory function. Anovulation due to hormonal dysregulation and follicular arrest prevents the consistent release of eggs, rendering conception challenging for most women who have PCOS. Moreover, changes in the hypothalamic-pituitary-gonadal axis also led to irregular menstrual cycles, further adding to reproductive complications. Apart from infertility, Additionally, PCOS increases the risk of pregnancy issues such as preterm birth, pre-eclampsia, and gestational diabetes. Assisted reproductive technologies (ART) like ovulation induction and in vitro fertilization (IVF) are usually needed by women with PCOS who are challenged by infertility, underscoring the need for specific therapeutic measures.^[20] PCOS is a major cause of infertility due to its effect on ovulatory function. Anovulation due to hormonal dysregulation and follicular arrest prevents the consistent release of eggs, rendering conception challenging for most women with PCOS. Moreover, changes in the hypothalamic-pituitary-gonadal axis also led to irregular menstrual cycles, further adding to reproductive complications. Apart from infertility, PCOS also confers an increased risk for pregnancy complications such as gestational diabetes, pre-eclampsia, and pre-term delivery. ART like ovulation induction and IVF are usually needed by women with PCOS who are challenged by infertility, underscoring the need for specific therapeutic measures.^[21] Therefore, the current investigation was objected to study of the levels of some biochemical variables, adipokines and cytokines in women with polycystic ovarian syndrome.

LITERATURE REVIEW

Adipokines are essential for controlling metabolism, and one of the key contributing factors to PCOS pathophysiology is their dysregulation. Compared adipokine concentrations in PCOS patients and healthy women, such as leptin, adiponectin, and resistin. According to their findings, PCOS women have considerably higher levels of leptin and resistance, whereas adiponectin concentrations were significantly lower. Such adipokine level changes indicate a disruption

in energy homeostasis and metabolic signaling, resulting in the development of hyperandrogenism and insulin resistance in PCOS. Similarly, Saleh^[1] investigated the association between adipokines and oxidative stress markers in PCOS patients. Their study highlighted lower levels of adiponectin and an increased oxidative stress index (GSSG), which were positively correlated with leptin levels. These findings suggest that oxidative stress may exacerbate metabolic dysfunction in PCOS through adipokine-mediated pathways. Chronic low-grade inflammation is recognized as a central component of PCOS pathogenesis. Bushell and Crespi^[2] conducted a case-control study in Basra, Iraq, assessing cytokine levels in PCOS patients. According to their research, PCOS women's serum had noticeably greater amounts of IL-6, IL-18, and TNF- α than the control group. The results suggest that inflammation in PCOS is independent of obesity or hyperandrogenism, showcasing the job of cytokines in reproductive and metabolic dysfunctions connected with the problem. Becker and Bilezikian^[3] further explored inflammatory markers by analyzing serum CRP and fibrinogen levels in PCOS patients. Their research supported the idea that systemic inflammation contributes to the metabolic disturbance of PCOS by confirming that both fibrinogen and CRP were significantly higher in the PCOS group than in the control group. The metabolic implications of PCOS extend beyond insulin resistance to include an increased risk of cardiovascular disease (CVD). Al-Hadidy and Al-Kotobe^[4] examined the link between adipocyte dysfunction and metabolic syndrome in PCOS patients, demonstrating that adipokine changes in levels have a role to play in obesity-related cardiovascular risk. The study emphasized that increased leptin Thus the pathophysiology of insulin resistance and dyslipidemia is significantly influenced by decreased adiponectin levels, both of which are important risk markers of CVD in PCOS patients. Christ and Cedars^[5], they examined more closely the role of leptin and its correlation with metabolic parameters in PCOS. The results demonstrated that we had a major correlation between higher levels of leptin and markers of obesity, showcasing the job of leptin in the derangement of metabolic processes and increased risk of cardiovascular problems in people with PCOS. One of the most recognized areas of PCOS is the link between adipokines and insulin resistance.^[6] The correlation between adipokines and insulin-like growth factor binding protein 3 (IGFBP-3) was examined in patients with polycystic ovary syndrome (PCOS). Their results concluded that high levels of adiponectin were related to improved insulin sensitivity, and there was no significant correlation between levels of TNF- α and IGFBP-3. These results demonstrate that adiponectin has a beneficial effect on metabolic control, and the decrease in levels of this hormone in PCOS patients can be one factor implicated in the development of insulin resistance. Current studies confirm this, highlighting the key part of adiponectin deficiency in the pathogenesis of

metabolic disturbances in PCOS.

Research Questions

- Is there a correlation between age and increased BMI in women with POCS?
- Are there significant changes in sex hormone levels in women with POCS compared to healthy controls?
- Are there significant changes in adipokines levels in women with POCS compared to healthy controls?
- Are there significant changes in interleukins levels in women with POCS compared to healthy controls?

MATERIAL AND METHODS

Subjects

This study included 120 women, of which 80 were patients (POCS) who visited Azadi Teaching Hospital from April to August 2024, and 60 were a normal. Both groups have been categorized into three age brackets: 15-25 years, aged 26 to 35, and 36-45 years. Before collecting blood for testing in the lab, all of the women completed a questionnaire.

Blood Collection

Blood samples were collected from the examined groups, The serum was isolated via centrifugation at 3000 revolutions per minute for 15 minutes and thereafter frozen until analysis.

Biochemical Measurements

Serum was used to measure the vital parameters: The sexual hormones (testosterone, FSH, and LH) were determined using the Roche Kit (Germany) on the Cobas C 111 system. The levels of Adipon, Irisin, Visfatin, and Chemerin were evaluated using the SUN-LONG Kit (China) with ELISA. IL-6 and IL-17 levels were measured using the SUN-LONG Kit (China) applied to ELISA.

Inclusion and Exclusion Criteria

The individuals met eligibility criteria if they were aged 15 years and older, and didn't use any drug irrespective of sociodemographic aspects. The individuals with female reported as chronic disease were excluded from the study.

Statistical Analysis

The data was analyzed using Version 21.0 for the Statistical Package in Social Science. The mean of continuous variables and the frequency distribution of categorical parameters were determined. Using the ANOVA statistical test, the mean parameters have been contrasted between research groups. P-values below 0.05 were considered statistically significant.^[1]

RESULTS AND DISCUSSION

The highest percentage of POCS was identified in the 26-35 age range, reaching 57.5%. While, the low rate of POCS was identified in the 15-25 year group, which reached 13.75%. Table 1 shows that women with POCS had an average age of 29.15 \pm 5.17 years. The highest percentage of POCS was identified in the 30-35 kg/m² category, which reached 67.5 percent. The lowest percentage of POCS was identified in the 21-25 kg/m² group, reaching 8.75%, as shown in Table 1.

Table 1: The Correlation between Age and BMI in POCS Female.

BMI (kg/m ²)	Age (year)			Total
	15-25	26-35	36-45	
21-<25	4(36.4%)	2(4.4%)	1(4.4%)	7(8.75%)
25-29	3(27.2%)	11(23.9%)	5(21.7%)	19(23.75%)
30-35	4(36.4%)	33(71.7%)	17(73.9%)	54(67.5%)
Total	11(13.75%)	46(57.5%)	23(28.75%)	80(100.0%)

Sexual Hormones

Table 2 compares testosterone, FSH, and LH levels in POCS and healthy females. POCS females had significantly higher testosterone concentrations (1.93±0.15) than healthy females (0.84±0.09) (Figure 1). FSH levels

decreased significantly (P<0.05) among individuals (4.61±0.82) in contrast to healthy females (7.12±0.42) (Figure 2). POCS females had significantly higher LH concentrations (12.35±1.61) compared to healthy females (6.27±0.53) (P<0.05) (Figure 3).

Table 2: The Concentrations of some Sexual Hormones.

Groups Parameter	Control (60)	Patients (80)	P-Value
Testosterone (nmol/L)	0.84±0.09	1.93±0.15*	0.001
FSH (mIU/mL)	7.12±0.42	4.61±0.82*	0.001
LH (mIU/mL)	6.27±0.53	12.35±1.61*	0.001

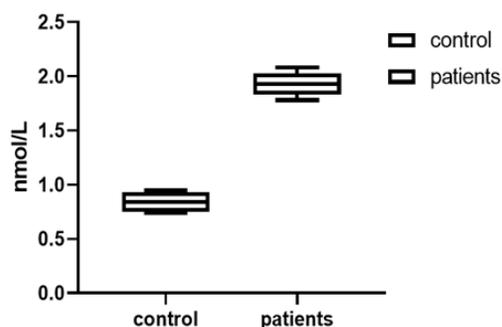


Figure 1: Testosterone (nmol/L) Concentration in Groups.

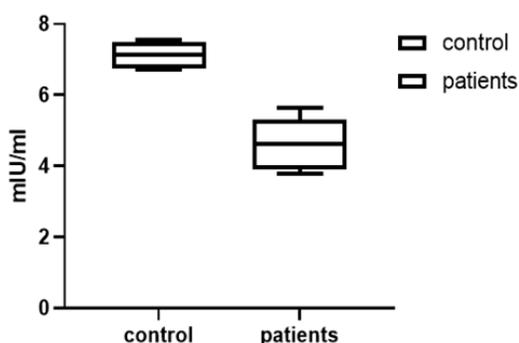


Figure 2: FSH (mIU/ml) Concentration in Groups.

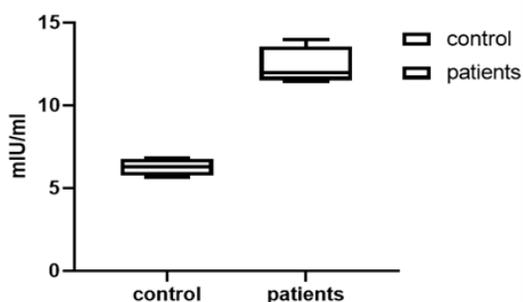


Figure 3: LH (mIU/ml) Concentration in Groups.

Testosterone levels are significantly elevated in cohorts of women with PCOS. This outcome aligns with other research,^[2] which discovered that women with PCOS have larger ovaries and higher levels of LH and testosterone in their serum. Additionally, PCOS women have higher serum levels of free Testosterone, which is usually no more than twice the upper normal range. Increasing testosterone levels relates to normal LH, and ovarian overproduction of androgens,^[3] and at baseline, women with PCOS had a greater LH pulse response to GnRH, which led to theca cell hyperplasia and increased androgen production.^[4] Furthermore, according to Jacob and Marcelle,^[5] the mean testosterone concentration was greater in patients with POCS, but no threshold value was established between the two groups based solely on testosterone level. This is consistent with a study,^[6] which linked an increase in this hormone to limited fertility and reproduction in women. Despite their decreased predictive power, FSH and LH levels are widely utilized to estimate ovarian reserve during the early follicular phase. A recent study found that IVF-embryo transfer cycles with a day 3 FSH/LH ratio of ≥ 2 are more likely to be canceled.^[7]

Adipokines

Table 3 shows the levels of some adipokines in PCOS females and healthy females, Adropin levels demonstrated a significant (P<0.05) reduction in PCOS individuals (61.39±7.05) than healthy individuals (104.67±3.12) (Figure 4). Irisin levels demonstrated a significant (P<0.05) elevated in patients (38.04±4.62) compared to healthy individuals (13.84±0.87) (Figure 5). Visfatin levels demonstrated a significant (P<0.05) elevated in individuals (30.52±1.19) than healthy individuals (18.42±1.35) (Figure 6). Chemerin levels demonstrated a significant (P<0.05) elevated in patients (27.84±1.73) than healthy individuals (13.55±0.63) (Figure 7).

Table 3: The Concentrations of some Adipokines in PCOS Females and Healthy Females.

Groups Parameter	Control (40)	Patients (75)	P-Value
Adropin (pg/mL)	104.67±3.12	61.39±7.05*	0.001
Irisin (ng/mL)	13.84±0.87	38.04±4.62*	0.001
Visfatin (ng/mL)	18.42±1.35	30.52±1.19*	0.001
Chemerin (ng/mL)	13.55±0.63	27.84±1.73*	0.001

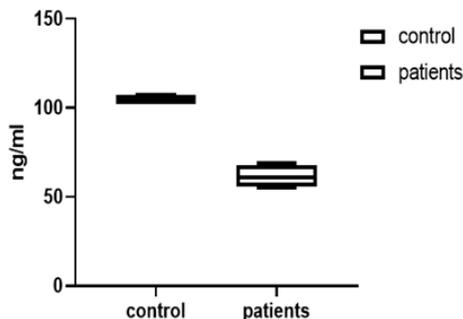


Figure 4: Adropin Concentration in Groups.

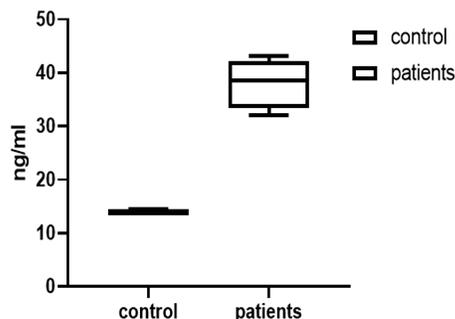


Figure 5: Irisin Concentration in Groups.

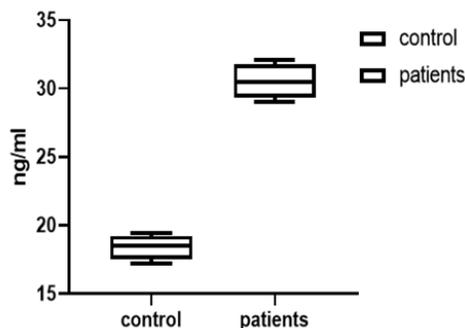


Figure 6: Visfatin Concentration in Groups.

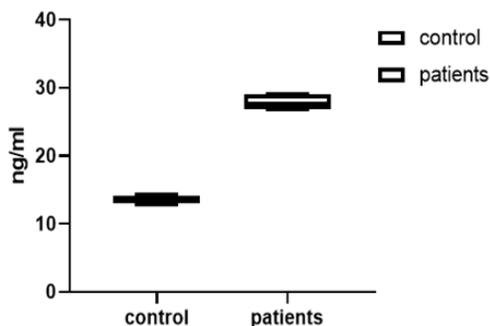


Figure 7: Chemerin Concentration in Groups.

A drop in levels decreased significantly ($P \leq 0.05$) in PCOS patients. This is in line with other studies that have shown that the pathology of PCOS and the ensuing hormone disruption are the causes of the low level of adoption. Research indicates that diminished adropin levels correlate with elevated hyperandrogenism in the bloodstream of individuals with PCOS via hormone-binding globulin and that a reduction in adropin relates to the onset of insulin resistance, a significant contributor to the disease.^[8] Islam and colleagues^[9] A decrease in adropin levels was more pronounced in obese women as well as those with PCOS, with the reduction in adropin correlating to an elevated BMI score, demonstrating that a decrease in adropin may play a role in the metabolic disorders seen in PCOS. Serum irisin in individuals with PCOS has previously been investigated, and the results differed greatly between researchers. Serum irisin levels were shown to be higher in some investigations,^[10] similar to the current study, while others reported lower irisin levels^[11] or similar levels between patients and controls.^[12,13] Performed a meta-analysis of eight studies and identified comparable elevations in serum irisin levels relative to controls. However, when BMI was matched, the significance between cases and controls was eliminated, which contradicted the current findings. This investigation showed that the levels of irisin among PCOS individuals were elevated in overweight/obese persons compared to those of normal weight. These findings were consistent with five previous investigations that found greater irisin levels in the obese group.^[13,14] According to the current study, the PCOS group's serum visfatin levels were noticeably greater than those of the control group. According to Dikmen *et al.*^[15] visfatin levels were equivalent in normal-weight PCOS and control groups. However, obese and overweight PCOS patients had greater visfatin levels than control women of equal BMI,^[16] and subjects with PCOS had greater visfatin levels than healthy subjects. Visfatin and the free androgen index were found to be positively correlated in PCOS patients. Subjects with PCOS had a much higher level of chemerin hormone in their Sera blood than healthy women. The findings were consistent with previous research,^[17,18] Compared to their normal-weight counterparts, it was shown that overweight PCOS participants had significantly higher levels of chemokines. Nevertheless, the results are inconsistent with earlier research.^[19]

Interleukins

Table 4 shows the levels of some interleukins in PCOS females and healthy females, IL-6 levels demonstrated a significant ($P \leq 0.05$) reduction in patients (46.72 ± 5.18)

compared to healthy females (21.45 ± 6.51) (Figure 8). IL-17 level demonstrated a significant ($P \leq 0.05$) elevated

in patients (297.15 ± 15.74) compared to healthy females (208.19 ± 11.93) (Figure 9).

Table 4: The Concentrations of some Interleukins in PCOS Females and Healthy Females.

Groups Parameter	Control (40)	Patients (75)	P-Value
IL-6 pg/ml	21.45 ± 6.51	$46.72 \pm 5.18^*$	0.001
IL-17 level (ng/ml)	208.19 ± 11.93	$297.15 \pm 15.74^*$	0.001

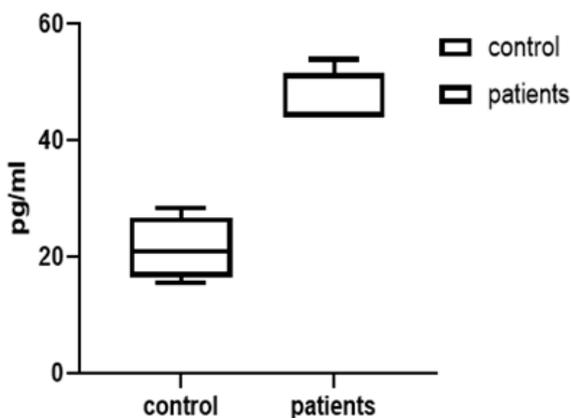


Figure 8. IL-6 Levels in Groups

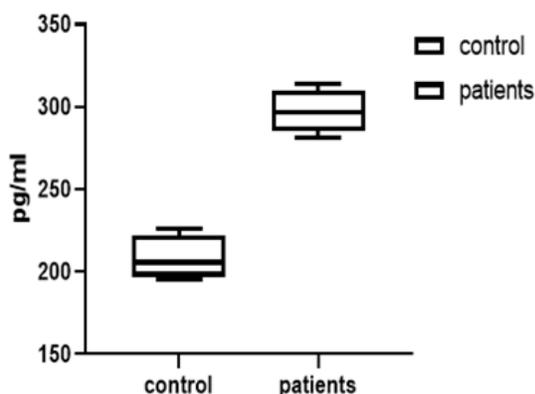


Figure 9. IL-17 Levels in Groups.

According to this study, PCOS patients had higher levels of IL-6 and IL-17 than healthy controls ($p < 0.001$). These results align with other prior investigations that identified markedly elevated IL-17 levels in patients with PCOS.^[20,21] Women with PCO showed lower levels of IL-17 than the control ($p < 0.001$), according to Zafari Zangeneh *et al.*^[22]. Elevated IL-17 levels in PCOS patients could indicate an inflammatory response in the ovaries. This cytokine is an important component of the body's immune response, and excessive IL-17 production can worsen inflammatory reactions and lead to tissue damage.^[23] Inflammatory responses in PCOS, Particularly elevated levels of IL-17 are associated with issues including insulin resistance and anomalies in metabolism.^[24]

CONCLUSIONS

Considering the findings of the present investigation, a

strong association was found between adipokines and PCOS, resulting in some adipokines' parameters rising and others decreasing in level. In addition, PCOS was associated with the occurrence of immune responses that led to an increase in the levels of the interleukins that were studied, with irregularity in the levels of sex hormones in females compared to healthy females. To reduce the impact of PCOS on women, it is possible to pay attention to following a diet to lose weight, especially with advancing age, as the study revealed a strong correlation between the factors of age and body mass index, which increases the impact of PCOS on various body parameters. Many studies can also be conducted to discover some genes that may be affected by PCOS in women.

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APPENDICES *Questionnaire*

Name:

Age:

Blood pressure:

Number of children:

Body mass index:

Headache:

Marital status:

Chronic diseases:

Residency: