Short Communication

Assessment of Inflammatory Indices in Women with Polycystic Ovarian Syndrome

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Abstract

Background: Polycystic ovarian syndrome (PCOS) is a typical example of a complex multifactorial disorder. Its genesis involves multiple systemic and local factors that have a multidirectional relationship. **Objectives:** We aimed to assess the level of inflammatory indices in women with polycystic ovarian syndrome. **Materials and Methods:** A case–control study was conducted at a Teaching Hospital in Hilla city from the first of April 2023 to the end of March 2024. A study included a sample of 200 women, aged between 19 and 39 years. The participants were evenly divided into two groups; PCOS group (n = 100) women included those who visited the infertility consultation clinic, while the control group included relatives of those patients and other patients whose cause of infertility was due to their husbands. Age, height, and weight were measured to calculate the BMI. The waist: hip ratio was measured for each participant. The matching for both groups regarding age, BMI, and waist: hip ratios was done. Blood samples were taken from all patients for FBS, insulin, platelets, neutrophils, lymphocytes, IL-6, TNF-α, and serum hsCRP. **Results:** The level of hsCRP in the PCOS group was (2.788 ± 1.092 mg/L) with a significant difference ($P < 0.001$). The leukocyte level in the PCOS group was (7562.4 ± 1431.3 mm^3) with a significant difference ($P < 0.001$), while the level of neutrophil/lymphocyte ratio in the PCOS group was (1.93 ± 0.8) with no significant differences. The levels of IL-6 and TNF-α in PCOS were (4.5 ± 0.52 pg/mL) and (4.07 ± 0.26 pg/mL), respectively, with significant differences ($P < 0.001$). **Conclusion:** There is a significant increase in inflammatory indices (hsCRP, leukocytes, IL-6, and TNF-α) in PCOS women than in healthy women.

Keywords: Inflammatory indices, neutrophil/lymphocyte ratio, PCOS, TNF-α

Introduction

Polycystic ovarian syndrome (PCOS) is the most common endocrine complex disorder in females of reproductive age. It is of multifactorial etiology characterized by the existence of chronic anovulation, hyperandrogenism, and polycystic-like ovaries on ultrasound.[1]

In May 2003, in Rotterdam, a meeting of experts took place that established by consensus the diagnostic criteria in force today: the presence of clinical and/or biochemical signs of hyperandrogenism, oligo and/or anovulation, and polycystic-like ovaries on ultrasound (a minimum one of these two criteria is required: the presence of ≥12 follicles with a diameter between 2 and 9 mm and an ovarian volume > 10 cm^3). It was agreed that to establish the identification of PCOS, at least two of the three criteria must be met.[2]

The prevalence of PCOS is difficult to establish as it depends on the diagnostics criteria that are applied. Based on the Rotterdam criteria, the prevalence in Europe and the USA is higher, reaching between 6% and 8%.[3]

The understanding of the mechanisms that lead to the development of PCOS remains fragmentary and not fully elucidated. Attempts have been made to attribute the main role to the following: hypothalamic–pituitary dysfunction, defects in steroidogenesis (ovarian or adrenal) and/or folliculogenesis, or IR. It is proposed that,

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like other elements of the syndrome, the pathophysiology is also heterogeneous, and there is no single mechanism but rather several pathways that lead to a common phenotype.[4]

Since PCOS is a multigenic and multifactorial disorder, various genetic variants can occur and be associated with different environmental factors that, regardless of the primary event, interact, overlap, and mutually aggravate each other, making it very difficult to determine what is the cause and what is the consequence. It is considered that IR could be the primary alteration only in specific cases because it is not a constant finding in women with PCOS. Insulin acts by direct stimulation of steroidogenesis and folliculogenesis or indirectly by enhancing the action of LH or promoting neuroendocrine dysfunction.[5]

At the ovarian level, it acts through its own receptors or those of IGF, which, due to their structural similarity, recognize both molecules interchangeably. Hyperinsulinism increases the synthesis of IGF-1, the effect of FSH on the synthesis of LH receptors in the granulosa and, in synergy with LH, promotes the activity of the cytochrome P450-17 alpha enzyme, the luteinization of the granulosa, and the proliferation of the theca and interstitium cells. It functions as a co-gonadotropin that modulates LH-induced steroidogenesis, causes hyperandrogenism, and promotes anovulation. It can also alter the expression of genes linked to the meiotic process of the oocyte and affect its quality.[6]

Excess insulin increases the pituitary release of basal and GnRH-stimulated LH, reduces the hepatic synthesis (SHBG) and IGF-BP (which leads to a rise in the free fraction of androgens and IGF with greater biological activity), increases the synthesis of adrenal androgens mediated by ACTH, and, due to its adipogenic action, promotes obesity and a pro-inflammatory state. The combined effect of hyperandrogenism and obesity worsens IR and creates a vicious cycle.[5,6] The current study aims to assess the level of inflammatory indices in women with PCOS.

Materials and Methods

Patients and study design

A case–control study was conducted at Imam Al Sadiq Teaching Hospital in Hilla City over the period from the first of April 2023 to the end of March 2024. A study had a sample of 200 women aged between 19 and 39 years. The participants were evenly divided into PCOS women case group who visited the infertility consultation clinic and the control group (who did not suffer from any symptoms), who included relatives of those patients and other patients whose cause of infertility was their husband (male factor infertility). Age, height, and weight were measured to determine the BMI, and waist: hip ratio was measured for each of the participants. The matching for both groups regarding age, BMI, and waist: hip ratio was done.

The absolute numbers of platelets were determined in blood (normal =150–450 × 10^3/mL), neutrophils in blood (normal = 2.00–6.910^3/ mL), and lymphocytes in blood (normal = 0.60 – 3.40 10^3/mL). The neutrophil–lymphocyte index is considered the relationship between absolute neutrophils and lymphocytes (abnormal > 2.15).

Laboratory investigation

From the elbow vein, we collected 5 cc of blood before breakfast, and the samples were evaluated for the following variables: FBS, insulin, hsCRP, complete blood count, including WBC, RBC, Hb, HCT, and platelets, using an automated device called an autoanalyzer. NLR was defined as the natural logarithm of the neutrophil count divided by the natural logarithm of the lymphocyte count in the peripheral blood, IL-6, and TNF-α. The measurement of hsCRP was conducted using immunoturbidimetry, and insulin level was measured using electrochemiluminescence (ECLIA) on a Cobas device. The insulin resistance is diagnosed if the level of HOMA-IR > 2.5.

Statistical analysis

Statistical analysis was carried out using Statistical Package for the Social Sciences (SPSS) version 23.0 (SPSS, IBM Company, Chicago, IL 60606, USA). In all cases, a significance level of $P < 0.05$ was adopted.

Ethical approval

This study was approved by the Ethics Committee of Hammurabi College of Medicine/University of Babylon on 1/3/2023 (approval number 334). All patients provided informed consent before being enrolled in the study. The study was performed in accordance with the guidelines of the Declaration of Helsinki.

Results

Table 1 showed the baseline criteria of the studied group regarding demographic criteria of the studied groups in which the age of the studied groups ranged between 19 and 39 years. As we matched both groups, there were no significant differences found among age, BMI, and waist-to-hip ratio between the groups ($P > 0.05$).

As shown in Table 2, significant differences were found between the studied groups in metabolic parameters ($P < 0.05$).

Table 3 illustrated the differences among the data of many inflammatory indices between the groups. The level of hsCRP in the PCOS group was (2.788 ± 1.092) (mg/L), while it was (1.279 ± 1.171) (mg/L) in the control group, with a significant difference ($P < 0.001$). The leukocyte

Table 1: Demographic criteria of the studied groups

Variables mean ± SD	PCOS (n = 100)	Control (n = 100)	P value
Age (years)	28.4 ± 7.2	27.5 ± 7.4	0.38 Ns
BMI (kg/m^2)	25.87 ± 4.3	25.46 ± 4.1	0.49 Ns
Waist: hip ratio %	0.832 ± 0.04	0.821 ± 0.07	0.3 Ns

Ns: not significant

Table 2: Metabolic assay of PCOS group and control group

Variables (mean ± SD)	PCOS (n = 100)	Control (n = 100)	P value
FBS (mg/dL)	90.3 ± 13.9	85.4 ± 12.6	0.02 [S]
Insulin (pm/mL)	16.1 ± 3.1	8.8 ± 3.9	<0.001 [S]
HOMA-IR	3.7 ± 0.2	1.9 ± 0.11	<0.001 [S]

S: significant

Table 3: Difference between different inflammatory indices data between the studied groups

Variables (mean ± SD)	PCOS (n = 100)	Control (n = 100)	P value
hsCRP (mg/L)	2.788 ± 1.092	1.279 ± 1.171	<0.001[S]
Leucocytes (/mm^3)	7562.4 ± 1431.3	6351.8 ± 1170.2	<0.001[S]
Neutrophil/ lymphocyte ratio	1.93 ± 0.8	1.7 ± 1.3	0.1 Ns
IL-6 (pg/mL)	4.5 ± 0.52	1.81 ± 0.27	<0.001[S]
TNF-α (pg/mL)	4.07 ± 0.26	3.2 ± 0.2	<0.001[S]

S: significant; Ns: not significant.

level in the PCOS group was (7562.4 ± 1431.3) (/mm^3), while it was (6351.8 ± 1170.2)(/mm^3) in the control group, with a significant difference (P < 0.001). The neutrophil/ lymphocyte ratio in the PCOS group was (1.93 ± 0.8), while it was (1.7 ± 1.3) in the control group, with no significant difference (P = 0.1). The level of IL-6 was (4.5 ± 0.52) and (1.81 ± 0.27) (pg/mL) in the PCOS and control group, respectively, with a significant difference (P < 0.001). The level of TNF-α in the PCOS group was (4.07 ± 0.26) (pg/mL), while it was (3.2 ± 0.2) (pg/mL) in the control group, with a significant difference (P < 0.001).

Discussion

This study aimed to assess and contrast the inflammatory marker levels in the serum of patients diagnosed suffering from disease (PCOS) and those without (i.e., with a healthy women). Our findings indicate a statistically significant elevation of inflammatory marker levels in patients with PCOS. Based on this evidence, it may be inferred that PCOS patients exhibit an inflammatory process.

In the current study, as shown in the results, no differences were found between both groups in the study regarding demographic criteria. This is similar to that found in a case–control observational study by Jamil *et al*.[7]

In Table 2, the present study revealed that a significant difference found between the studied groups among metabolic criteria (FBS, insulin, and HOMA-IR) is in agreement with that found by Lewandowski *et al*.[8]

Özay stated that a constant low degree of inflammation is associated with insulin-resistance, obesity, endothelial dysfunction, atherosclerosis, and CHD.[9]

There are many significant differences between the PCOS group and the control group regarding hsCRP, TNF-α, and IL-6, which are the most important findings in the current study Table 3. This finding was in agreement with those of numerous studies worldwide.

Recent investigations have demonstrated that patients with PCOS experience a gradual progression of low-grade inflammation, which is accompanied by elevated levels of CRP (C-reactive protein).[10] Nevertheless, certain studies propose that the inflammatory process observed in individuals with PCOS is not specific and does not correlate with hyperandrogenism and neuroendocrine dysfunctions.[11,12]

Orio *et al*. revealed that elevated leukocyte number is considered a hazardous agent for atherosclerotic vascular illness, and this increase in markers in women with PCOS is greater than in controls, which may lead to an increase in the rate of this vascular illness.[13]

In patients with PCOS, obesity correlates with several signs of inflammation: concentrations of CRP, IL-6 and the number of leukocytes, but not with testosterone concentrations. There is agreement with those of other studies in terms of a greater quantity of leukocytes and lymphocytes in women with polycystic ovary syndrome.[14,15] Visceral fat is more related to the leukocyte count than to the neutrophil–lymphocyte ratio and the elevated leukocyte count.[16,17]

Vgontzas *et al*. revealed that serum IL-6 levels were increased in the PCOS group than in the control group self-reliantly of obesity or sleep apnea.[18]

In the current study, there was no significant difference regarding neutrophil/ lymphocyte ratio, which is in agreement with the findings of ALhabardi *et al*., who stated that there are no significant differences regarding hematological parameters in lean patients in comparison to lean healthy women.[19] However, this result was incompatible with that reported by several authors who revealed that the neutrophil–lymphocyte ratio was significantly elevated in the patients' group compared to the normal group.[20-23]

Conclusion

There is a significant increment in hsCRP, leukocytes, IL-6, and TNF-α in the women with PCOS group than in the healthy group.

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Conflicts of interest
There are no conflicts of interest.

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