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Assessment of the Insulin Resistance, Inflammatory Markers and Gene Polymorphism in Polycystic Ovarian Syndrome Patients

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Abstract

Polycystic ovary syndrome (PCOS) is accepted as a risk factor for diabetes mellitus, and it is closely related to symptoms such as insulin resistance (IR) and obesity. The study aimed to compare the levels of pro-inflammatory markers Tumor necrosis factor alpha (TNF-α), Interleukin-6 (IL-6), and Interleukin-10 (IL-10), as well as C-reactive protein (CRP), in Polycystic ovary syndrome (PCOS) patients and controls. The association between these genotypes and Body Mass Index (BMI), insulin resistance measurements, and lipid profiles was investigated. In addition, gene polymorphisms will be determined in both groups. The study included 60 subjects divided into two groups. For the patients with PCOS and healthy control groups, the biochemical parameters were measured by the auto analyser, and hormonal, pro-inflammatory parameters were measured using the ELISA method. Serum levels of two groups, TNF-α, IL-6, and CRP, increase significantly. TNF-α, IL-6, and CRP have respective AUC values of 0.763, 0.999, and 1. The AUC value is statistically significant at a 95% confidence level when the p-value for each of the three parameters is less than 0.001. The optimal cut-off values for TNF-α (4.11 pg/ml), IL-6 (2.35 pg/ml), and CRP (1.96mg/l) are determined with a sensitivity of 0.997 and a specificity of 1.00. The total number of biomarkers and these cytokines are significantly correlated. The study concluded that women with PCOS exhibit significantly elevated levels of TNF-α and IL-6 in comparison to the control group. The IL-6 (-174G/C) polymorphism is associated with PCOS and particular metabolic disorders of the syndrome.

1. Introduction:

Polycystic ovary syndrome (PCOS) is an endocrine-metabo -lic disorder characterized essentially by hyperandrogenism, ovarian dysfunction and polycystic morphology of the ovaries, which has insulin resistance as its pathophysiological substrate [1], which perpetuates the clinical picture and exposes this population that suffers from it to a high.

Risk of suffering from type 2 diabetes mellitus (DM2), increasing their morbidity and mortality at an early stage of life. In these patients, waist circumference and waist/hip ratio (WHR) correlate positively with blood pressure values. PCOS progresses with chronic low-grade inflammation [2], [3]. It has been shown that proinflammatory cytokines such as IL-6 and IL-18, which increase CRP levels [4] in the serum and increase CRP synthesis in the liver, increase IL-6. In women with PCOS, the conversion of large lipoprotein particles to smaller particles is increased due to increased hepatic lipase activity. These are also more atherogenic. This explains the decrease in HDL and the increase in LDL [5].

TNF-α is a cytokine secreted primarily by adipocytes in subcutaneous fat tissue and visceral fat. Its actions include its role in the generation of insulin resistance. The actions of TNF-α occur through autocrine or paracrine mechanisms since, in various studies, a correlation between its plasma

concentrations and obesity has not been uniformly observed [6].

IL-6 is another cytokine synthesised by adipose tissue, its secretion by visceral fat being three times greater than that by subcutaneous fat, and TNF-α stimulates it. Early studies on inflammatory factors indicated that chemoattractant proteins induced recruitment and increase of macrophages in adipose tissue, which secreted TNF α and were associated with ectopic lipid accumulation and IR [7]. However, there is evidence that activated macrophages in adipose tissue can regulate their functions, such as the rate of lipolysis [8]. They can regulate lipid release and prevent excess lipid release, thereby avoiding ectopic fat accumulation and increased IR. Tumor necrosis factor alpha (TNFα), called cachectin, is a cytokine weighing 17-70kDa. TNFα, which has a homotrimeric structure, is produced by many cells, such as fibroblasts, endothelial cells, adipocytes, and B cells, especially macrophages and monocytes. TNFα mainly affects lipid metabolism, coagulation, insulin resistance and endothelium. It plays a role in activating the cytokine cascade in inflammatory events with IL-1 and IL-6. IL-10 is a homodimer cytokine belonging to the four alpha helix cytokine family [9]. Its three-dimensional structure is still unknown. The IL-10 gene, responsible for the synthesis of IL-10, whose molecular weight can vary between 17-40 kDa, is located on chromosome 1 [9].

In the literature review, although there are few studies on TNFα and IL-6 gene polymorphisms in women with PCOS, these results are pretty complex. We found no studies on IL-10 gene polymorphisms in women with PCOS. In light of this information, the first aim of our research is to examine the relationship between TNFα, IL-6 and IL-10 gene polymorphisms and PCOS. Our second aim is to investigate whether there is a connection between genotypes and some clinical and laboratory disease symptoms.

2. Material and Methods:

Data was collected from May 2023 to July 2024, and the study sample was women diagnosed with PCOS according to the Rotterdam criteria in an age range of 18 to 40 years.

The population consisted of 60 patients who attended the gynaecology clinic department in the medical city in Baghdad, and 30 control group population from the local population consulted for signs and symptoms related to PCOS. The sample consisted of 60 patients who met at least two of the three criteria of the Rotterdam Consensus of 2003 for diagnosing PCOS [10]. Inclusion criteria were women aged between 18-40 years, with a medical diagnosis of PCOS according to Rotterdam criteria, who were receiving medical treatment for PCOS, without modifications to their treatment or lifestyle, including diet and physical activity in the last three months.

Those who disagree and have other serious health issues, age under 18 years and over 40 years, desire for pregnancy or presence of pregnancy during the sample collection process, excluded from the current study, presence of systemic diseases such as diabetes mellitus (DM), arterial hypertension (AH), autoimmune diseases, cancer and hematological diseases, treatment in the last three months before this study with medications that modify the pituitary-ovarian axis, were excluded from the current research study [11].

The selected patients underwent a complete medical history, and the physical examination included anthropometric measurements. The nutritional status of the patients was evaluated by anthropometry, measuring weight with a bioimpedance scale and height with a wall-mounted stadiometer to calculate the body mass index and classify the patients according to the WHO scale as average weight, overweight or obese [12]. The nutritional status results were evaluated using the WHO criteria. Similarly, a transvaginal or pelvic ultrasound was performed, after explaining the procedure to the patient, between the 3rd and 5th day of spontaneous menstruation or induced by the administration of progesterone 10 mg orally daily for 14 days for amenorrheic patients to evaluate ovarian morphology as part of the Rotterdam criteria described above [10]; said study was performed by a General Electric brand ultrasound equipment, model Volsum E8®. A hepatobiliary ultrasound was also performed after fasting for six hours to determine ultrasound signs of fatty liver according to the Rumack criteria. Weight in kg and height in centimetres (cm), using a Lyon® brand height and weight scale.

Blood collection was performed at any time on PCOS women with chronic anovulation. In the serum/plasma samples taken, routine biochemical parameters fasting blood glucose, triglyceride, cholesterol, HDL, and LDL concentrations were measured with the 1800DPP Roche autoanalyzer (Baghdad hospital teaching laboratory); routine hormonal parameters, total testosterone, DHEA-S and insulin were measured with the modular EEE Electrod Elecsys Roche autoanalyzer (Baghdad hospital teaching laboratory). LH/FSH, fasting glucose/fasting insulin ratios, HOMA (Homeostatic Model Assessment) and body mass indexes were calculated. Hormones were measured using RIA techniques with commercial kits (catalog number EIA-6141, 5186 kit, DRG, Germany). Samples were processed in a refrigerated centrifuge and stored at -20°C until assay. Serum interleukin 6 (TNF-α) was measured using a photometric enzyme-linked ELISA method. In contrast, hs-CRP was measured using a two-step sandwich ELISA technique for human CRP and insulin.

DNA Isolation from peripheral blood leukocytes is done by using the procedure according to Angelini et al. (2002) [13] and Ciulla et al. (1988) [14], DNA Quantification by UV Absorption, according to García-Alegría et al. (2020) [15]. The nucleic acid concentration in the sample is calculated using a reading at a wavelength of 260 nm. An optical density of 1 indicates approximately 50 μg/ml of double-stranded DNA in the measured sample.

$$DNA(\mu g/ml) = OD\ at\ 260\ nm \times Dilution\ rate \times 50$$

2.1 DNA Replication by Polymerase Chain Reaction (PCR):

The PCR method allows the DNA sequence in a selected genome region to be amplified in vitro using a known nucleotide sequence [16]. Using this technique, the introductory amount of template DNA at the nanogram level in genomic DNA can be increased 10^5–10^6 times [16].

Primers and PCR conditions used in the amplification of TNFα (-308) and IL-6 (-174) gene regions:

a. TNFα(-308).
F: 5' – AGA TGG GTT CAA TGT CCA GAG GT – 3'
R: 5' – TCC CTC CTT ACT GCC GCT CG – 3'

These primers provide the formation of a PCR product of 107 bp.

b) IL-6 (-174)
F: 5' – TTA AAG TAC GGT AGT CAC GTG G – 3'
R: 5' – GCA GCT ACC GCC CGA GTT CAC C – 3'

These primers provide the formation of a PCR product of 304 bp.

3. Analytical Statistics:

Excel 2019 and IBM SPSS Statistics-28 (for Windows) were used for all statistical analyses (tables and figures). The Chi-square test was used to compare the significance between groups. Mann-Whitney U test was used to compare clinical and biochemical parameters, and the Spearman correlation test was used to evaluate whether there was a correlation between parameters.

4. Results:

Clinical and laboratory findings in controls and PCOS patients are given in Table 1. Age and FSH levels did not significantly differ between the two groups; however, Insulin, F.SG, HOMA, FSH, LH Testosterone, Prolactin, lipid profile, TNF-α, IL-6, and CRP levels were significantly higher in the PCOS group compared to the control group. The genotype distributions of all three genes in the control and PCOS groups were consistent with the Hardy-Weinberg equation [17] Figure 1.

4.1 Distribution of TNFα (-308 G/A) Genotype and Allele:

It was determined that 81% of the women in the control group were GG, 15.8% were GA, and 3.2% were AA genotypes. The G and A alleles distribution in these individuals was calculated as 88.9% and 11.1%, respectively Figure 2 . It was determined that 80.4% of the PCOS patients were GG, 16.5% were GA, and 3.1% were AA genotypes. The G and A alleles distribution in these individuals was calculated as 88.7% and 11.3%, respectively Figuer 2. No statistically significant difference (R2=0.229; P<0.001) was detected when

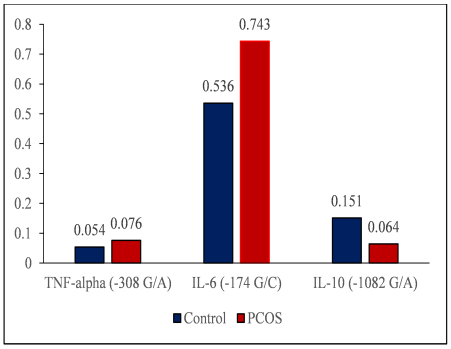

Figure 1. P-values of control and polycystic ovary syndrome (PCOS) groups.

the TNF (-308 G/A) genotype and allele distributions of the control and PCOS groups were compared. Figure 2. The genotype distributions of all three genes in the control and PCOS groups were consistent with the Hardy-Weinberg equation Figure 1.

4.2 Distribution of IL-6 (-174 G/C) Genotype and Allele:

The control group's GG, GC, and CC genotype carriage rates were 48.4%, 44.2%, and 7.4%, respectively. The G and C alleles distribution in the control group was 70.5% and 29.5%, respectively— Figure 2 The GG, GC, and CC genotype carriage rates in PCOS patients were 60.8%, 35.1%, and 4.1%, respectively. The distribution of G and C alleles in PCOS patients was 78.4% and 21.6%, respectively. The difference in the G and C alleles distribution between the groups was at the significance limit (2=3.09; p=0.078), even though there was no statistically significant difference between the distributions of the PCOS patient group and the control group. IL-6 (-174 G/C) genotype and allele frequencies in PCOS patients and the control group Figure 2.

4.3 Distribution of IL-10 (-1082 G/A) Genotype and Allele:

The control group's GG, GA, and AA genotype carriage rates were 16.8%, 56.8%, and 26.4%, respectively. The control group's G and A allele distributions were 45.7% and 54.7%, respectively. The PCOS patients' GG, GA, and AA genotype carriage rates were 15.5%, 58.8%, and 25.7%, respectively. The PCOS group's G and A allele distributions were 44.9% and 55.1%, respectively. No statistically significant difference was found when the distributions of the PCOS patient group were compared to those of the control group. Figure 2. The ROC curve analysis for TNF-, IL-6, IL-10, and CRP in the two groups is displayed in Table 2. The corresponding Area Under the curve (AUC) values of TNF (0.763pg/ml), IL-6 (0.999 pg/ml), and CRP (1.0 mg/l) were identified with p¡0.001. This AUC value is statistically significant at a 95% confidence level. TNF-α (pg/ml) has

Table 1. Clinical and laboratory findings of the control group and patients with polycystic ovary syndrome (PCOS) (mean ± SD).

Parameters	Control (n=30)	Patient (PCOS)	Test statistics	$\rho - value$
AGE	28.96 ± 6.39	28.6 ± 4.83	0.304	0.762 NS
BMI(Kg m^{-2})	24.79±3.64	34.85±4.46	10.68	<0.001 HS
Insulin(mlU ml^{-1})	12.16±2.81	32.47±8.77	11.11	<0.001 HS
F.S.G(mg dl^{-1})	86.47±9.03	98.33±10.6	5.248	<0.001 HS
HOMA	2.34±0.36	8.3±2.35	12.817	<0.001 HS
Testosterone(ng dl^{-1})	0.97±0.22	1.47±0.15	3.477	0.030 S
PRO(ng ml^{-1})	11.55±0.24	25.14±11.12	6.451	<0.001 HS
FSH(mlU ml^{-1})	4.39±1.36	3.62±1.83	2.027	0.055 NS
LH (mlU ml^{-1})	3.9±1.25	10.14±1.01	6.696	<0.001 HS
Cholesterol(mg dl^{-1})	168.07±24.56	241±26.36	12.65	<0.001 HS
Triglyceride(mg dl^{-1})	120.5±33.89	186.82±43.55	7.301	<0.001 HS
LDL(mg dl^{-1})	89.37±19.69	162.8±23.01	14.948	<0.001 HS
HDL(mg dl-1)	47.8±8.18	35.38±6.78	7.633	<0.001 HS
VLDL(mg dl^{-1})	22.43±6.46	55.63±8.74	9.405	<0.001 HS
TNF-α (pg ml^{-1})	4.72±1.33	6.12±1.35	4.628	<0.001 HS
IL-6(pg ml^{-1})	1.24±0.43	5.37±1.62	13.683	<0.001 HS
IL-10(pg ml^{-1})	1.08±0.02	6.21±0.01	14.02	<0.001 HS
CRP(mg l^{-1})	1.23±0.23	3.69±0.91	14.475	<0.001 HS
TSH (Mu mL^{-1})	2.638±0.09	2.932±0.03	3.632	<0.001 HS
FT3 (pmol L^{-1})	3.92±0.63	5.021±0.61	6.026	<0.001 HS
FT4 (pmol L^{-1})	13.27±1.02	15.03±1.23	16.34	<0.001 HS
Testosterone (ng mL^{-1})	0.61±0.20	0.81±0.17 *	0.932	<0.001 HS
Prolactin (ng mL-1)	14.01±3.1	14.55±1.35	15.21	<0.001 HS

NS: Non-significant difference between groups (ρ- value> 0.05)
S: significant difference between groups (ρ-value $\leq$ 0.05)
HS: High significant difference between groups (ρ-value $\leq$ 0.01)

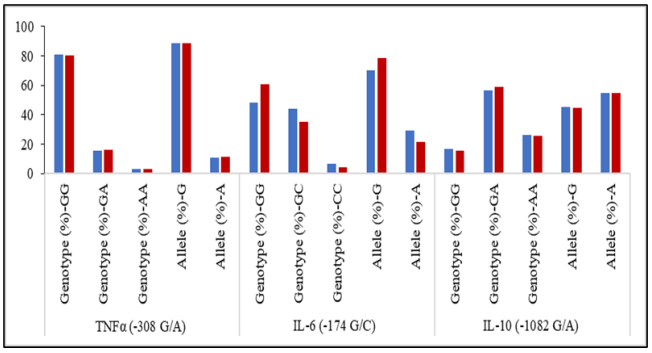

Figure 2. Genotype and allele frequencies in the control group and PCOS patients group.

an optimal cut-off value of 4.11 with a sensitivity of 0.94 and specificity of 0.84; IL-6 and IL-10 have optimal cut-off values of 2.35 with a sensitivity of 0.997 and specificity of 1; and CRP (mg/l) has optimal cut-off values of 1.96 with a sensitivity of 1 and specificity of 1 Figure 4, 5. Figure 3 provides a visual representation of these results, demonstrating the effectiveness and resilience of the parameters across the groups.

4.4 Clinical and Laboratory Findings according to TNFα (-308), IL-10 (-1082) and IL-6 (-174) Genotypes in the Control Group:

The clinical and laboratory parameters we found in the controls with the TNFα (GG) and (GA+AA) genotypes did not differ statistically significantly (R2=0.264; p<0.001). The clinical and laboratory parameters in the controls with the IL-

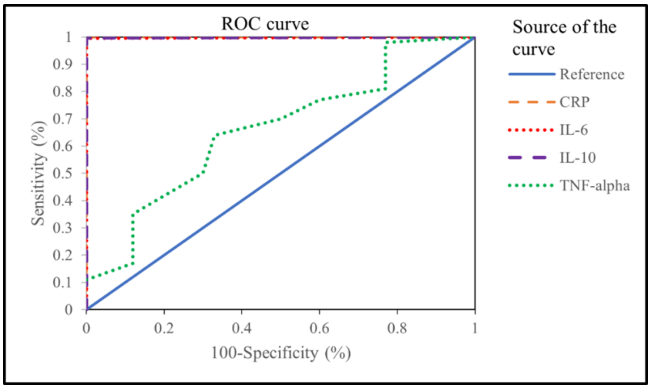

Figure 3. ROC curve results for TNF-α, IL-6, IL-10 and CRP.

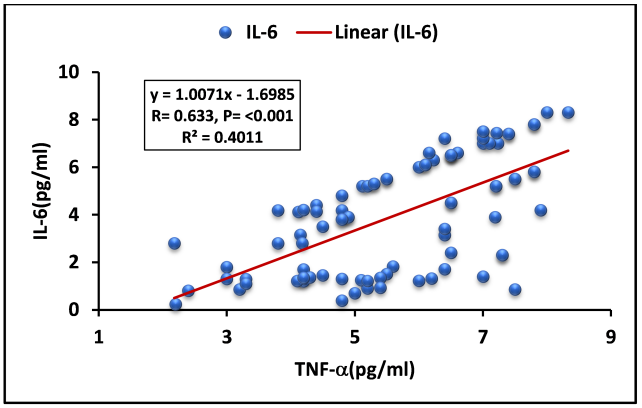

Figure 4. The Pearson correlation between TNF-α and IL-6.

10 (GG) and (GA+AA) genotypes did not differ significantly (R2=0.304; p<0.001). A comparison of the clinical and laboratory parameters found in the controls with the IL-6 (GG) and (GC+CC) genotypes revealed that the (GC+CC) genotype had significantly lower values for glucose, HOMA, and LDL cholesterol. In contrast, the glucose/insulin ratio and HDL cholesterol were significantly higher (R2=0.672; p>0.05). Statistical evaluations between genotypes were made with the Mann-Whitney U test.

4.5 Clinical and Laboratory Findings According to Genotype TNF (-308), IL-10 (-1082) and IL-6 (-174)in the PCOS Group:

The clinical and laboratory parameters we found in PCOS women with the TNF (GG) and (GA+AA) genotypes did not differ statistically significantly (R2=239; p<0.001). The clinical and laboratory parameters we found in PCOS women with the IL-10 (GG) and (GA+AA) genotypes did not differ significantly (R2=0.361; p<0.001). When comparing the clinical and laboratory parameters found in PCOS women with the IL-6 (GG) and (GC+CC) genotypes, it found that the (GC+CC) genotype had significantly lower values for glucose (R2= 0.328; p>0.01), HOMA, cholesterol, triglycerides,

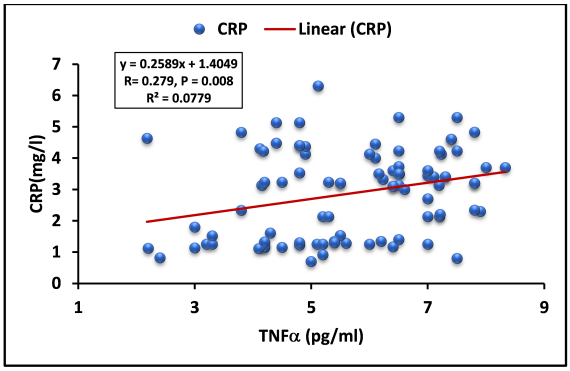

Figure 5. The Pearson correlation between TNF-α and CRP.

and LDL-cholesterol on the other hand, the glucose/insulin ratio and HDL-cholesterol values were substantially higher (R2=0.592; p>0.05). Statistical evaluations between genotypes were made with the Mann-Whitney U test. According to IL-6 (GG) and (GC+CC) Genotype Distributions, when the parameters of the Control and PCOS groups with the (GG) genotype were compared, insulin, HOMA and triglyceride values were found to be significantly higher (R2=0.637; p>0.05), while GIR and HDL cholesterol values were found to be considerably lower in the PCOS group (R2=0.251; p>0.001). When the parameters of the Control and PCOS groups with the (GC+CC) genotype were compared, HOMA was higher, and LDL-cholesterol was lower in the PCOS group (R2=0.228; p>0.001).

5. Discussion:

An investigation indicated that phenotype 1 (anovulation, hyperandrogenism, and polycystic ovaries) was the most common form of PCOS. This finding aligns with a prior study that reported phenotype 1 in 46% of PCOS patients. Additionally, it was discovered that the higher the level of HOMA-IR, the more severe the PCOS phenotype. The equal distribution of all four phenotypes found in this study, however, may be because Asians are less likely than other racial groups to have hyperandrogenism [18], [19].

Similar to a study in China [20], [21], [22], phenotype one was associated with higher levels of LH and the lowest ratio of LH to FSH. Relatively low levels of FSH may cause the release of LH in those who have PCOS [21]. Moreover, a study conducted in an Iranian community indicated high LH levels in phenotypic patients related to high levels of both testosterone and androgen [23]. The average age of PCOS patients in this study is 28.6 years; this is thought to be caused by a decrease in antral follicle count as patients age [23], [24]. However, the current investigation found no statistically significant differences in age groups among individuals with various PCOS characteristics [25].

Insulin resistance is one of the hypothesised underlying pathophysiologies of PCOS. It is estimated that between 50

Table 2. Clinical and laboratory findings of the control group and patients with polycystic ovary syndrome (PCOS) (mean ± SD).

Variables	Sensitivity	Specificity	AUC	Std. Error	P value	Cut off value	Accuracy	
							L.B.	U.B.
TNF-α(pg/ml)	0.94	0.84	0.763	0.051	<0.001	4.11	0.662	0.863
IL-6 (pg/ml)	0.997	1	0.999	0.002	<0.001	2.35	0.996	1.000
IL-10 (pg/ml)	0.996	1	0.998	0.001	<0.001	1.67	0.999	1.000
CRP (mg/l)	1	1	1.000	<0.001	<0.001	1.96	1.000	1.000

AUC: Area under the curve
L.B.: lower bound, UB.: upper bound

and 80% of PCOS patients also have insulin resistance. The most effective way to assess the prevalence of insulin resistance in PCOS still needs to be solved. Numerous articles suggested using HOMA-IR as a benchmark measurement to diagnose insulin resistance [26], [27].

Among PCOS patients, HOMA-IR levels were observed to be at their maximum point. Individuals who fit phenotype. All phenotypes have significantly different fasting insulin levels, but we did not find any differences in fasting plasma glucose levels, which aligns with another study [28]. Therefore, even when their plasma glucose levels are normal, PCOS patients may have aberrant insulin levels. When diagnosing diabetes in the general population, current guidelines focus on plasma glucose levels [29]. However, normal glucose levels alone should not be the sole factor used by doctors treating PCOS patients. Furthermore, these results may corroborate the beneficial effects of metformin therapy in reducing androgen levels in PCOS patients [30].

Studying inflammatory markers like TNF-, CRP, and IL-6 provides light on the complex interaction between immune response and reproductive health. These cytokines are vital parts of the immune system and are essential in controlling inflammation, which is becoming increasingly understood to affect many different elements of reproductive physiology [31]. This study aims to clarify our findings in light of previous research, emphasizing the potential impact of immune system variables on treatment outcomes and reproductive outcomes for women undergoing ICSI. Notably, in this investigation, it was identified that women with PCOS had higher serum levels of TNF-. These results are consistent with several studies reported in the systematic review of Gao et al (2016) [32] that showed PCOS individuals had noticeably increased TNF levels.

PCOS is associated with chronic inflammation, a known risk factor for cardiovascular illnesses. In contrast, the study's findings revealed that The PCOS group's elevated IL-6 levels suggest a possible disturbance in the anti-inflammatory pathways. This may have an impact on the chronic inflammatory state associated with PCOS. Research supports this theory, suggesting that other variables may be more crucial in determining the outcome of reproduction. These variables may include metabolic disorders that modify the hormonal and follicular milieu, genetic variants that impact cytokine expression and response, and environmental and lifestyle factors that impact overall reproductive health [31], [32], [33].

PCOS is accepted as a risk factor for Diabetes Mellitus and coronary artery disease. This is because PCOS is closely related to symptoms such as insulin resistance, obesity, dyslipidemia and hypertension [34]. There is a close relationship between the risk mentioned above factors and TNF-α, IL-6 and IL-10 plasma levels and polymorphic variants of the genes encoding these cytokines. TNF-α, IL-6 and IL-10 are essential in the etiopathogenesis of many diseases, such as atherosclerosis, coronary artery disease, osteoporosis, preeclampsia and diabetes mellitus [35], [36]. In the study conducted by K. Walch et al., it was shown that the single nucleotide change in the IL-6 (-174 G/C) gene was not a risk factor for the development of PCOS and that the C allele was associated with high BMI, testosterone and impaired OGTT. The C allele was also shown to be closely related to obesity [29]. On the other hand, in the study of Fernandez et al. in the Spanish population [26], it was shown that the G allele increased insulin resistance and glucose values and caused dyslipidemia. As can be seen from our findings, glucose, HOMA, and lipid values were significantly higher, and GIR and HDL values were significantly lower in individuals with the GG genotype compared to the (GC+CC) genotype in both the PCOS and control groups. In addition, when the parameters of control and PCOS women with the GG genotype were compared, insulin, HOMA and triglyceride values were significantly higher. GIR and HDL values were lower in the PCOS group.

It has been suggested that plasma levels of cytokines such as TNF-α, IL-6 and IL-10 are closely related to single nucleotide polymorphisms in the promoter regions of the genes responsible for their production. In the literature review, although a few studies have been conducted on TNF-α (-308 G/A) and IL-6 (-174 G/C) gene polymorphisms in women with PCOS; these results are quite complex (32, 80, 116). The

general opinion is that single nucleotide changes in TNF-α (-308 G/A) and IL-6 (-174 G/C) genes are not risk factors for developing PCOS. Our findings show that the TNF-α(-308 G/A) genotype and allele distributions of the control and PCOS groups are similar. However, when the IL-6 (-174 G/C) gene polymorphism was examined, no statistically significant difference was found when the distributions of the PCOS patient group were compared with the control group. Still, the difference in the G and C alleles distribution between the groups was at the significance limit (p= 0.078). The A allele distribution of the TNF-α (-308) gene in our control group (11.1%) is very close to the A allele distributions of the control group in the EARS II study (12% in Central Europe and 13% in Southern Europe) (85). In addition, the G and C allele distributions of the IL-6 (-174) gene in our control group (70.5% and 29.5%) are very close to the G and C allele distributions of the Italian healthy population (71.1% and 28.9%) [36].

The risky IL-6 (-174) G allele has been reported to cause increased plasma IL-6 levels. Partly, homology exists between the IL-6 gene and the gene encoding the Smad 4 protein binding element [37], [38]. TGFβ and activin, in turn, inhibit the expression of various pro-inflammatory molecules. This pathway is activated in the presence of the protective C allele, whereas it is suppressed in the presence of the risky G allele. Thus, the process of atherosclerotic change in PCOS is initiated, and perhaps the clinical manifestations of this syndrome will become more evident. [39].

6. Conclusion:

The study's findings indicate that women with PCOS had higher TNF-α, IL-6, and CRP serum levels than controls. Additionally, elevated serum immune marker levels may be associated with BMI and serum lipid levels, thus serving as a predictor of cardiometabolic risks. PCOS is considered a risk factor for diabetes mellitus. This is because PCOS is closely associated with symptoms such as insulin resistance, obesity, dyslipidemia, and hypertension. There is a close relationship between the risk mentioned above factors, TNF-α, IL-6, and IL-10 plasma levels, and polymorphic variants of the genes encoding these cytokines. TNF-α, IL-6, and IL-10 are essential in the etiopathogenesis of many diseases.

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Data Availability Statement: All of the data supporting the findings of the presented study are available from corresponding author on request.

Declarations:

Conflict of interest: The authors declare that they have no conflict of interest.

Ethical approval: Since there were no human or animal participants in this study, ethical approval was not required in compliance with national and institutional rules and regulations.

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تقييم مقاومة الأنسولين والعلامات الالتهابية وتعدد الأشكال الجينية لدى مرضى متلازمة تكيس المبايض

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الخلاصة

تعد متلازمة تكيس المبايض (*PCOS*) عامل خطر لمرض السكري، وترتبط ارتباطًا وثيقًا بأعراض مثل مقاومة الأنسولين (*IR*) والسمنة. هدفت الدراسة إلى مقارنة مستويات العلامات المؤيدة للالتهابات عامل نخر الورم ألفا ($TNF-\alpha$)، والإنترلوكين ـ 6 ($IL-6$)، والإنترلوكين ـ 10 ($IL-10$)، وكذلك البروتين التفاعلي سي (*CRP*) ، في مرضى متلازمة تكيس المبايض (*PCOS*) والمجموعة الضابطة. تم التحقيق في العلاقة بين الأنماط الجينية ومؤشر كتلة الجسم (*BMI*)، وقياسات مقاومة الأنسولين، وملف الدهون. وبالإضافة إلى ذلكتم تحديد تعدد الأشكال الجينية في كلا المجموعتين. شملت الدراسة 60 عينة تم تقسيمهم إلى مجموعتين. مجموعة المريضات اللاتي يعانين من متلازمة تكييس المبايض والمجموعة الضابطة، تم قياس المعلمات البيوكيميائية بواسطة جهاز التحليل الذاتي ، وتم قياس المعلمات الهرمونية والالتهابية باستخدام طريقة *ELISA* . لوحظ وجود فرق معنوي في قيم ، $TNF-\alpha$ ، $IL-6$ ، و *CRP* للمجموعتين. عامل نخر الورم الفا وانترلوكين ـ 6 ووبروتين التفاعلي سي اظهروا قيم *AUC* تبلغ 0.763 و 0.999 و 1 . تعتبر قيمة *AUC* ذات دلالة إحصائية عند مستوى ثقة 95% عندما تكون القيمة p لكل من المعلمات الثلاثة أقل من 0.001 . يتم تحديد قيم القطع المثالية لـ $TNF-\alpha$ (4.11) بيكوغرام / مل، $IL-6$ (2.34) بيكوغرام / مل)، و *CRP* (1.96) ملغم / لتر بحساسية 0.997 ونوعية 1.00 . يرتبط العدد الإجمالي للمؤشرات الحيوية وهذه السيتوكينات بشكل كبير. وخلصت الدراسة إلى أن النساء المصابات بمتلازمة تكيس المبايض يظهرن مستويات مرتفعة بشكل ملحوظ من $TNF-\alpha$ و $IL-6$ مقارنة بالمجموعة الضابطة. يرتبط تعدد أشكال ($IL-6$ ـ $174G/C$) بمتلازمة تكيس المبايض واضطرابات استقلابية معينة في المتلازمة.

الكلمات الدالة : السيتوكينات. تعدد الأشكال الجيني. إنترلوكين ـ 6 ، متلازمة تكيس المبايض، عامل نخر الورم ألفا.

التمويل: لايوجد.

بيان توفر البيانات: جميع البيانات الداعمة لنتائج الدراسة المقدمة يمكن طلبها من المؤلف المسؤول.

اقرارات:

تضارب المصالح: يقر المؤلفون أنه ليس لديهم تضارب في المصالح.

الموافقة الأخلاقية: نظرا لعدم وجود مشاركين من البشر أو الحيوانات في هذه الدراسة، لم تكن الموافقة الأخلاقية مطلوبة امتثالاً للقواعد واللوائح الوطنيةوالمؤسسية.