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Assessment of Serum Caspase-1, IL-10, and IL-18 Levels in Baghdad's Medical City in Women with Polycystic Ovary

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Abstract **Background:** Polycystic ovary syndrome (PCOS) is the most frequent endocrine disorder in women. Caspase-1 is implicated in several important inflammatory diseases and controls adipocyte differentiation and insulin sensitivity. Interleukin-10 (IL-10) is an anti-inflammatory cytokine and plays an important role in chronic inflammatory conditions. This study was planned to investigate the association between insulin resistance in (PCOS) and serum levels of caspase-1, IL-10, and IL-18. **Methods:** Fifty women with PCOS and forty healthy controls were evaluated in this controlled clinical study. Caspase-1 and IL-18, IL-10 levels, serum lipid sub-fractions, fasting glucose, fasting insulin, and other hormone levels were measured. Homeostasis model assessment (HOMA-IR) was used to estimate insulin resistance. **Results:** Regarding levels of obesity, the BMI of patients and controls was significantly different ($P > 0.01$). The tests of insulin, fasting glucose, HOMA, testosterone, progesterone, prolactin, LH, estradiol, SHBG, cholesterol, triglycerides, LDL, HDL, and VLDL all showed statistically significant changes. Research participants' serum FSH levels were greater than controls, but this difference was statistically insignificant. There was a highly significant difference in IL 10 and IL 18 levels. Additionally, PCOS patients had considerably greater Caspase-1 levels than controls. A significant positive link between age and caspase-1 ($r = -0.296^{**}, p = 0.036$), a significant positive relationship between BMI and IL-18 ($r = 0.338^{**}, p = 0.017$), and a significant positive relationship between IL-10 and VLDL levels ($r = 0.529^{**}, p = 0.00007$). **Conclusion:** There was an association between caspas-1, IL-10, IL-18 and polycystic ovary syndrome-related insulin resistance. Many recent proteins and interleukins are now considered potential new markers of insulin resistance in diagnostic and therapeutic polycystic ovary syndrome.

Key Words IL-10, IL-18, Caspase-1, Polycystic ovary syndrome (PCOS)

1. Introduction

The condition known as polycystic ovarian syndrome (PCOS) frequently affects how a woman's ovaries work. About 10% of women who are reproductive age have PCOS, according to Hasan et al. [1] study. It is a hormonal disease when ovaries develop collections of fluids as well as failing to produce eggs on a regular basis [2]. Despite that the precise etiology of PCOS is unclear. Numerous risk factors for PCOS have been discovered and are being researched, but none have been definitively linked to the disease [3]. Factors such as hereditary, environmental, and insulin level were all associated with PCOS [4]. Furthermore, it was suggested that Caspase-1 and Interleukin-10 (IL-10) may be involved in the events that set off the pathogenesis of PCOS. Nevertheless, the exact function in PCOS etiology remains unknown [3].

Pathogens and endogenous generated mediators both activate the inflammatory caspase Caspase-1. In immune cells, it converts the inactive versions of the transformed the inactive forms of the inflammatory cytokines IL-1 and IL-18 [5]. Sun and Scott evaluated Caspase-1's functions and shown that it is expressed in a wide range of cell types, including nonimmune cells. It controls lysosomal activity, cell death, and protein secretion within the cell. They conclude that understanding its activities will be critical for developing treatments that inhibit caspase1 activation [6]. Present study assessed the level of In a clinical investigation at the medical city of Baghdad, caspase-1, IL-18, and IL-10 were examined in women with PCOS to learn more about PCOS-dependent signaling revealing an elevated level of Caspase-1 in PCOS patients.

2. Materials and Methods

Materials

This study was conducted from October 2022 to April 2023 at the PCOS-endocrine section of Baghdad's medical center, which attracted fifty PCOS patients in a row. Rotterdam criteria were applied to these patients in order to identify PCOS. In this study, participants who had oligo/amenorrhea (menstrual intervals 35 days) along with hirsutism, a Ferriman-Gallwey score of 8, and high levels of androgen blood levels of testosterone were classified as having PCOS. We eliminated pregnancy, congenital adrenal hyperplasia, uncontrolled thyroid disease, irregular menstrual cycles, and other causes of these conditions. A set of 40 typically androgenic, frequently ovulating women were chosen as the control group. These prerequisites were verified by assessing progesterone levels throughout three successive cycles.

Each participant's venous blood was taken during the follicular phase of a naturally occurring or progesterone-induced menstrual cycle after a 12-hour overnight fast. The levels of hormones, lipids, insulin, and glucose were then measured. Following a thorough health history, each participant got a personalized clinical evaluation and underwent anthropometric measurements (weight, height). A biochemical auto analyzer (COBAS C11) was used to measure the levels of serum glucose, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides, and the profile of changes in alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Using a microparticle enzyme immunoassay, serum insulin levels, caspase-1, IL-10, and IL-18 were also measured. We estimated the homeostasis model assessment by using the formula (fasting serum glucose (ml mole per liter)/22.5) by the fasting serum insulin (micro units/ml). (HOMA) method for insulin resistance. The manufacturer's instructions, found in TOSO, were followed to investigate testosterone, progesterone, prolactin, FSH, LH, estradiol, and SHBG.

Statistical Analysis

System-SAS (2012), a statistical analysis application, was used to examine the effect of distinguishing characteristics on the study parameters. The LSD test, or least significant difference, was used to compare the means substantially using an ANOVA analysis of variance. The chi-square test was utilized to compare the percentage (0.05 and 0.01 likelihood) substantially. Calculation of the correlation coefficient between the study's different variables.

3. Results and Discussion (Or Separate Results, Discussion)

Features of the population in this case-control research: 50 PCOS patients were compared to 40 age-matched, seemingly healthy controls. Table 1 displays the fundamental aspects of the subject. The mean age did not differ significantly. Regarding levels of obesity, BMI of patients and controls was significantly different $(P > 0.01)$ [7]. The tests of insulin, fasting glucose, HOMA, testosterone, progesterone, prolactin, LH, estradiol, SHBG, cholesterol, triglycerides, LDL, HDL, and VLDL all showed statistically significant changes. Research participants' serum FSH levels were greater than controls, but this difference was statistically insignificant. Table 1 displays the cytokine concentrations. Between PCOS patients and controls, there was a highly significant difference in the levels of IL 10 and IL 18. Additionally, PCOS patients had considerably greater Caspase-1 levels than controls. A significant positive link between age and caspase-1 $(r = -0.296^{**}, p = 0.036)$, a significant positive relationship between BMI and IL-18 $(r = 0.338^{**}, p = 0.017)$, and a significant positive relationship between IL-10 and VLDL levels $(r = 0.529^{**}, p = 0.00007)$ were all found, see Table 2.

According to Bjeki-Macut et al. [4], there may be a familial link between insulin resistance (IR) and PCOS. It is believed that insulin levels in the blood are important factors in the genesis and clinical signs of PCOS. It was determined that signal transduction abnormalities inside the cytoplasm cause decreased glucose clearance into peripheral tissues. Ovarian, pituitary, and adrenal gland signal transduction abnormalities were present in PCOS patients [8]. According to recent research, IR and hyperinsulinemia may directly affect the ovaries and contribute to PCOS through several routes [4]. The evidence is strong that IR plays a crucial part in the genesis of PCOS. However, skepticism over its importance and prevalence has grown [9]. In chronic inflammation conditions, IL-10 functions as a regulatory cytokine [10]. It inhibits the production of IL-1a, IL-1b, IL-6, IL-8, IL-12, and tumor necrosis factor-alpha (TNF-a) in macrophages and interferon-gamma (IFNg) in T cells. The levels of IL-10 in the research participants increased statistically significantly. Interestingly, this rise in blood IL-10 levels could be a defense mechanism against the ongoing inflammatory process. These findings suggest that an abnormal balance between anti-inflammatory and proinflammatory cytokines may influence inflammatory responses in the etiology of PCOS. The connection between IL-10 and insulin resistance and increased androgen in PCOS-affected women may not be as significant as previously thought [11].

The most common types of dyslipidemia have raised LDL, total cholesterol, and triglyceride levels, together with decreased HDL. According to Zhang, Chunren, et al. [12], insulin resistance and dyslipidemia are connected. The current investigation found no evidence of a robust correlation between lipid fractions and serum Caspase-1 levels. Despite this significantly elevated total cholesterol, This study discovered increased LDL and triglyceride values in PCOS-afflicted women. HDL levels were lower in the study group; this difference was statistically significant. Caspase-1 is involved in several inflammatory severe disorders and regulates insulin sensitivity [13]. Although elevated circulating Caspase-1 was not linked with insulin resistance in women with PCOS, According to the study, Caspase-1 may contribute to the onset of PCOS-related persistent low-grade inflammation [3]. According to the current study, patients'

Factors	Mean ±SD		P value
		Patients with PCOS	
Age (year)	25.55± 3.7	25.58 ± 2.97	0.483
BMI (kg/m2)	28.41 ± 1.46	37.19 ± 6.74	0.00001**
Insulin(μ IU/ml)	8.78±2.41	12.65±1.28	0.00001**
F.B.G (mg/dl)	87.2±8.01	98.32±10.82	0.00001**
HOMA	1.55±0.88	2.10±0.53	0.00021**
Testosterone (nmol/l)	0.80±0.45	1.35±0.74	0.00041**
Progesterone (ng/ml)	23.93±4.82	0.58±0.18	0.00001**
Prolactin (ng/ml)	33.58±3.46	17.25±1.85	0.00001**
FSH (m IU/ml)	5.82±1.18	5.65±1.04	0.242
LH (m IU/ml)	6.87±1.69	10.19±2.71	0.00001**
Estradiol (pg/ml)	45.58±3.21	42.98±3.45	0.00001**
SHBG(nmol/l)	34.58±3.21	20.93±2.03	0.00001**
Cholesterol(mg/dl)	165.9±25.0	233.8±26.29	0.00001**
Triglyceride (mg/dl)	107.67±36.57	145.64±22.25	0.00001**
LDL(mg/dl)	98.45±22.14	134.26±17.49	0.00001**
HDL(mg/dl)	44.3±6.84	35.96±5.78	0.00001**
VLDL(mg/dl)	25.27±6.09	57.84±19.44	0.00001**
IL-10(ng/ml)	33.85±2.28	65.932±10.51	0.00001**
IL-18(ng/ml)	280.87±8.76	579.24±107.7	0.00001**
Caspase-1(pg/ml)	1.62±0.9	7.37±1.82	0.00001**

Table 1: Demographic, clinical and biochemical chartists, $^{**}(P < 0.01)$.

Parameters	IL-10		IL-18		Caspase-1	
	r	P	r	P	r	P
Age	-0.316	0.025	0.050	0.730	-0.296**	0.036
BMI	0.180	0.210	0.338**	0.017	0.049	0.730
Insulin	0.149	0.299	0.69	0.631	0.123	0.294
F.S.G	0.049	0.735	-0.211	0.141	0.001	0.990
HOMA	0.032	0.395	-0.045	0.754	0.021	0.884
Testosterone	0.165	0.252	0.196	0.170	0.049	0.733
Progesterone	0.033	0.375	-0.026	0.54	-0.0162	0.910
Prolactin	0.054	0.709	-0.064	0.656	-0.095	0.508
FSH	0.059	0.683	-0.029	0.839	0.184	0.199
LH	0.045	0.751	0.040	0.778	-0.274	0.054
Estradiol	0.008	0.952	-0.109	0.447	0.158	0.271
SHBG	0.048	0.736	-0.118	0.413	0.066	0.646
Cholesterol	-0.168	0.242	0.0004	0.997	0.073	0.612
Triglyceride	0.362	0.802	0.060	0.679	-0.205	0.152
LDL	0.036	0.803	0.189	0.186	0.067	0.641
HDL	-0.186	0.194	0.056	0.695	-0.270	0.057
VLDL	0.529**	0.00007	0.056	0.695	-0.018	0.900
IL-10	——	——	0.160	0.265	0.0575	0.691
IL-18	-0.0191	0.895	——	——	0.221	0.122
Caspase-1	0.057	0.691	-0.255	0.072	——	——

Table 2: Correlation between IL-10, IL-18, Caspase-1 and biochemical parameters in patients with PCOS (n = 50), $*(P : 0.01 - 0.05)$,$^{**}(P < 0.01), NS(P > 0.05)$

Caspase-1 levels were more significant in the PCOS group than in the healthy controls. Caspase-1 degrades cytokines IL-1β and IL-18 in immune cells to their active forms [5]. The cytokine IL-18 has been seen to be increased in PCOS [3]. We measured the concentrations of IL-10 and IL-18 here. Patients with PCOS showed a higher amount, although the outcome was inconsequential.

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Ethical Statement

This study was approved by Local ethical committee of each, Department of Basic Sciences, College of Nursing, University of Baghdad, and Department of Chemistry, College of Sciences, University of Baghdad approval number 12A/2023 .

Conflict of Interest

The authors declare no conflict of interests. All authors read and approved final version of the paper.

Authors Contribution

All authors contributed equally in this paper.

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