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EVALUATION OF SERUM LEVEL OF C-REACTIVE PROTEIN IN WOMEN WITH POLYCYSTIC OVARY SYNDROME AS INFLAMMATORY MARKER

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ABSTRACT

Background: Women with polycystic ovarian disease are labile for medical problem in regard to cardiovascular system and more liable to have diabetes mellitus. C-reactive protein (CRP) can be strong marker of future CVD. Objective: To determine whether there is an increased level of serum CRP and white cell count and their related factors in women with ovarian polycystic ovaries. Patients and Methods: case- control research which was conducted in Basrah Maternity Hospital. 116 women (26.5 ± 8 years) with PCOS were recruited from Basrah infertility center. The control group (31.5 ± 8 years) involved 94 fertile women who attend Gynecological and Obstetrical. Serum level were collected from patients and control groups. Hormonal estimation of both gonadotropin, estrogen, prolactin, thyroid stimulating hormone, free thyroxine, and serum blood sugar were measured. A lipid profile, complete blood picture and C-reactive protein (CRP) were estimated. Transvaginal ultrasound was done to all the participants. Results: The high level of CRP among women with PCOS was 36.8% in comparison to the control group. The body mass index, thyroid stimulating hormone, prolactin, serum blood sugar, lipid profile levels were not significantly different between the 2 groups while LH and estradiol were significantly different (P <0.001). White blood count was significantly more in the patient group compared with the control group. There is statistical significance between the patient and the normal group with high body mass index (> 30 Kg/ M 2) and the same observation in both group with other BMI (<25, 25-29 Kg/ M 2). Conclusion: It observed from the study that women with polycystic disease had high level of white cell count and CRP concentrations, which may suggested that women with polycystic ovarian is associated with low-grade inflammation.

KEYWORDS: Body mass index, Cardiovascular disease, C-Reactive protein, Lipid profile, Polycystic ovarian syndrome.

INTRODUCTION

The polycystic ovary syndrome (PCOS) is the common metabolic disorder in females, it account about 5–10% of women in the reproductive age.[1] This condition can be diagnosed by women with hirsutism, with menstrual irrgularity, increase weight, ultrasound crietra of ovarian polycystic disease.[2] At 1990 National Institutes of Health conference considered ovarian polycystic oraries, depend on menstrual irregularity which include oligo- or anovulation, and clinical evidence of hirsutism and biochemical hyperandrogenisum.[3]

Women with Polycystic ovary syndrome had some of components of the metabolic cardiovascular syndrome (syndrome X), which is charactrised by over weight, increase insulin resistance and atherosclerosis.[4]

It was observed in the distribution of atherosclerosis in the carotid arteries by carotid ultrasound in patients and controls (7.2 *vs.* 0.7%).[5] Therefore PCOS young women at high risk for the possible development of early-onset cardiovascular disease (CVD), which can be diagnosed many years before the clinical onset of the symptoms of cardiac disease.[6]

It was proved that women with PCOS the cardiovascular (CV) symptomezs are affected by environmental factors and life style beside genetic factors. There is relationship between genetic factor with insulin resistance and diabetes, and increase weight elevation of serum lipid and vascular stroke, in women with PCOS.[7]

It was observed that C-reactive protein (CRP) levels, and some markers like cytokines (such as interleukin-6 and interleukin-18), beside elevation of leucocyte count lead

to some sort of inflammation in women with PCOS.[8–10] Some studies proved that CRP is useful indicator of inflammation and useful indicator for cardiac stroke.[5,8,9] There was relationship between the level of growth factor beta (TGF-β), inhibins, anti-Müllerian hormone in women with polycystic disease which may have a role in the pathophysiology.[5,8-12] Increase in the internal fat may lead to increase insulin resistance and serum level of blood sugar. Visceral fat cells secrete inflammatory markers and pro-inflammatory markers which include oxidative stress factors, elevation of white blood cells, and other markers of endothelial inflammation, tumour necrosis factor alpha, interleukin-6 and interleukin-18, and complement C3.[5,8-12]

Polycystic ovary syndrome women exposed to metabolic syndrome which include overweight, glucose disturbance, high level of insulin, and elevation of blood pressure, sleep apnea, stroke, non-alcoholic fatty liver disease, uterine and breast cancer, and breast.[8,13,14]

The purpose of the present study is to found association between the elevation level of serum CRP and white cell count in women with PCOS.

PATIENTS AND METHODS

Case- control study, which was done at Basrah Maternity Hospital between the period 1/9/2020 till 1/9/2021. The work has been approved by the Ethical Committee of Basrah Medical College. Informed consent was obtained from all participants. One hundred sixteen women with PCOS were recruited from Basra Infertility Center and private clinics and 94 fertile women as control group include healthy women who are relative to the patients and attending gynecological and obstetrical outpatient clinic for periodical clinical examination.

PCOS was diagnosed depend on Rotterdam features: 1) menstrual disturbance, 2) clinical and serum elevation of androgen and 3) in ultrasound finding of polycystic ovary (1). The control women were experienced regular menstrual cycles (21-35 days), fertile and no clinical evidence of hyperandrogenism with normal ovaries by ultrasound examination.

The calculation of body mass index was depend on measuring the height and weight by using this formula: weight (kg)/height (m2). The patients presented with hirsutism were assessed according to Ferriman-Gallwey score (>7).[7]

The cases which were not included in the study were: pregnant women, lactating women, endocrine disorders conditions associated with elevation level of androgen like (Cushing syndrome, congenital adrenal hyperplasia, and androgen secreting tumors), diabetes mellitus, thyroid dysfunction, fever (defined as body temperature higher than 38°C) or Covid-19 infection. Avoid using of ral contraceptives or metformin for at least 3 months before the study.

Each patient underwent clinical assessment in regarded BMI and sign of hyperandrogenisum, and blood test, and U/S examination. Serum sample were obtained from all women in morning at 8 and 10 AM after an overnight fast. Basal serum levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), prolactin (PRL), thyrotropin (TSH), free thyroxine (T3), and blood sugar were estimated. A lipid profile (total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglyceride (TG), and full blood count, including differential white cell count and C-reactive protein (CRP) were assessed for each subject. Regular CRP analysis was done by System Reagent CRP (latex, Olympus, Melville, NY). The normal level is less than 5 Mg/L.

Transvaginal ultrasound was done to assess the criteria of polycystic ovaries, by measuring ovarian volume and the diagnosis of polycystic ovaries depend on the presence of 10 or more follicles 5-8 mm in diameter or/and increased ovarian volume > $10mm^3$.

Statistical Analysis. The statistical analysis was done by using IBM SPSS Software, version 20.

RESULTS

This table showed that the mean age of the patient group was 26.5 ± 8 years, and the mean age of the control group was 31.5 ± 8 years (Table 1).

Table 1. Comparison of mean (±SD) age between PCOS and control groups.

	PCOS (n : 116)	Control (n: 94)	*P*
Age (yr)	26.5 ± 8 (116)	31.5 ± 8 (94)	0.01
<19	21	20	0.466
19–25	31	21	0.801
26–30	41	34	0.50
>30	21	17	0.65

There is highly significant value of CRP level more than (>5 mg/liter) in the polycystic group which was 36.8% in comparison to the control groups which was 9.6% (*P* < 0.001) (Figure 1).

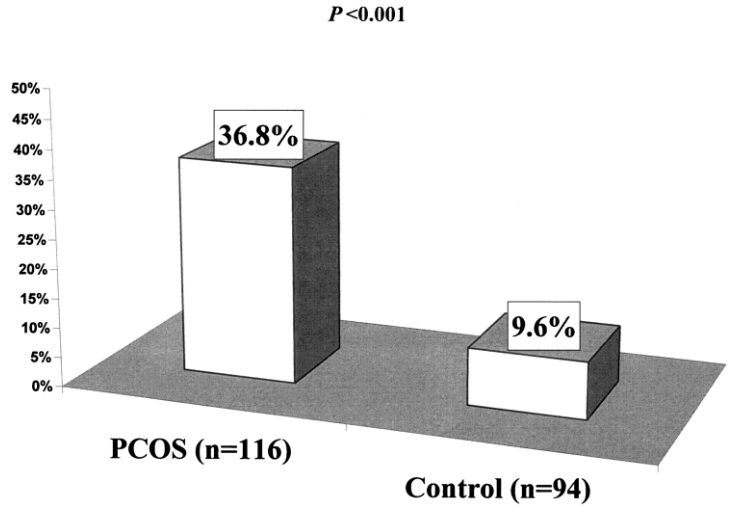

Figure 1: The level of CRP level which is more than (>5 mg/liter) in PCOS in comprising to control group.

The mean ± SD, of serum level of CRP was 5.46 ± 7.0 mg/liter in the PCOS group *vs.* 2.04 ± 1.9 mg/liter in the controls which is highly significant ($P < 0.001$). All the other variables which were estimated were not significantly different between the two groups except the white blood count (WBC) an serum levels of LH, estradiol were significantly higher in the PCOS group compared with the control group. (table 2).

Table 2. Comparison of different parameters between PCOS and control groups.

	PCOS	Control	*P*
CRP (mg/liter)	5.46 ± 7.0	2.04 ± 1.9	< 0.001
women with CRP level < 5 (%)	63.2 %	90.4 %	<0.001
women with CRP level > 5 (%)	36.8%	9.6 %	<0.001
Total cholesterol (mg/dl)	191.73 ± 47.11	182.25 ± 26.85	0.333
HDL (mg/dl)	54.56 ± 13.99	61.94 ± 13.03	0.127
LDL (mg/dl)	120.24 ± 39.46	102.88 ± 18.14	0.123
FSH(mIU/ml)	3.90 ± 1.30	3.04 ± 0.66	0.026
Estradiol(pg/ml)	41, 75 ± 23, 61	53, 14 ± 37, 11	0.032
Glucose (mg/dl)	89.37 ± 14.93	88.0 ± 26.96	0.77
Free testosterone(ng/ml)	1.54± 0.55	0.77± 0.66	0.005
TSH (mU/liter)	1.67 ± 0.79	1.77 ± 1.42	0.694
LH (mIU/ml)	7, 19 ± 3, 93	5, 02 ± 2, 09	< 0,001
Prolactin	30, 05 ± 13, 49	29, 13 ± 11, 26	0,938
WBC count	6, 30 ± 1, 71	5, 66 ± 1, 12	0,019

Table (3) was showed the level of CRP l in normal BMI, overweight, and obese women between the PCOS and control groups which was statistical significance between the groups with high BMI (> 30 Kg/ M ^{2}) and the same observation in both group with other BMI (<25, 25-29 Kg/ M ^{2}) (Table 3).

Table 3: The relation between the CRP levels and the body weight in both groups.

BMI (kg/m^2)	PCOS	Control	*P*
<25	3.843 ± 5.3	1.73 ± 1.62	<0.001
25–29	3.554 ± 2.49	2.08 ± 2.33	0.07
>30	10.571 ± 9.49	3.24 ± 1.98	<0.001

Logistic regression was done to evaluate the significant variable on the CRP and WBC results. The variables explaining the analysis were E2, LH, TSH, glucose, FSH, and BMI). CRP values are positively associated with BMI (beta = 0,374, $p < 0,001$) (Table 4). WBC and positively associated with E2 ($p = 0,024$) and body weight. CRP values are positively associated with BMI ($p < 0,001$) (Table 4).

Table 4. Multiple regression analysis between CRP, WBC, BMI and hormonal and biochemical parameters.

Parameter	*r* =spearman correlation coefficient	P values
FSH (mIU/ml)	-0,110	0,209
LH (mIU/ml)	-0,029	0,745
PRL(pg/ml)	-0,143	0,109
E2 (ng/ml)	-0,049	0,421
TSH (mIU/l)	0,111	0,207
fT4 (pmol/l)	-0,153	0,081
BMI (kg/m^2)	0,339	0,00

DISCUSSION

Recent studies proved great association between women with PCOS women and risk for cardiovascular stroke.[6,9,11,15]

It was observed from the present study no statistically significant differences in age in contrast to BMI which was significantly difference in both 2 groups. In addition, inflammatory process, in form of elevated WBC and CRP occurs more in women with PCOS. Which is in agreement with other studies.[16,17]

In the present study incomparising between both groups in regard to lipid and glucose level which is not significant this observation is in contrast to many studies who observed that PCOS patients have an high level of lipid and an impaired of glucose metabolism, and development of type 2 diabetes, and elevation of blood suger.[6,13,18,19] Women with PCOS have high chance of cardiac stroke.[9,20]

In relation to different level of CRP in the PCOS group, it was observed from the present study that PCOS group had higher level than normal group and the incidence of PCOS is increasing with elevated level of C reactive protein. What had been observed in the present study was the same with other studies which concluded that women with PCOS who are at high risk of cardiac stroke with the elevation of CRP level.[15,21]

It was observed in this research that 65% of women with PCOS are complaining from menstrual disturbance in form of oligomenorrea. a study has linked 80% of menstrual irregularity cases, can be attributed to PCOS, and increased risk of death due to cardiac stroke.[21]

In the present study, The serum level CRP in the patient group with normal body mass(<25) and over weight PCO women(BMI, >30) were significantly higher in the PCOS compared with the control subgroups of similar BMI ($P < 0.001$),previous studies have found significantly higher CRP levels in PCOS patients versus controls.[5,9] They suggest the useful of using C reactive protein as predictor marker to identify the young PCOS women who is liable for cardiac stroke in advancing age.

The level of free testosterone was assessed in both patient and control groups which was not significant which is in agreement with Previous studies which was found no relation between the level of CRP and testosterone levels.[22] and lipid or lipoprotein concentrations in PCOS patients.[22,23]

Previous studies concluded that there is no correlation between androgen level and cardiac stroke in women.[17,24]

The measures that decrease the level of CRP levels by diet control, avoid smoking, advice exercise, control blood pressure, admistration of low dose aspirin or use of metformin).[10,22,25]

In conclusion it was observed that women with PCOS women is associated with increased WBC, body mass index and CRP levels, which may the evidence that PCOS is associated with low-grade inflammation.

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