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Total cholesterol/high-density lipoprotein and inflammatory parameters in patients with polycystic ovary syndrome

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SUMMARY

OBJECTIVE: In this study, the hormone profile, lipid profile, and inflammatory parameters of patients with polycystic ovary syndrome were compared with those of non-polycystic ovary syndrome patients to determine predictive markers in young polycystic ovary syndrome patients who have not yet had children.

METHODS: Patients' age, height, weight, body mass index, waist circumference, degree of hirsutism, and ultrasound findings were recorded. Hormone profile, lipid levels, ratio of complete blood count parameters, monocyte/high-density lipoprotein ratio, and total cholesterol/high-density lipoprotein ratio were compared between groups.

RESULTS: No statistically significant differences were found between groups in terms of age, weight, waist circumference, body mass index, and dysmenorrhea ($p>0.05$). A significant relationship was found between the height and the degree of hirsutism in the groups ($p<0.05$). It was found that prolactin, total testosterone, and dehydroepiandrosterone sulfate levels were statistically significantly higher in the polycystic ovary syndrome group compared to the control group. The polycystic ovary syndrome group had hemoglobin, leukocytes, lymphocytes, neutrophils, platelets, and statistically higher ratios of total cholesterol/high-density lipoprotein, Low-density lipoprotein/high-density lipoprotein, and triglycerides/high-density lipoprotein. No statistically significant relationships were found between homeostatic model assessment insulin resistance, neutrophil-to-lymphocyte ratio, and monocyte-to-high-density lipoprotein ratio between the groups ($p<0.05$). There was no significant difference in systemic immune inflammation index values between the groups.

CONCLUSION: Polycystic ovary syndrome patients are at risk for short- and long-term complications, and the use of the total cholesterol/high-density lipoprotein, Low-density lipoprotein/high-density lipoprotein, and triglycerides/high-density lipoprotein ratios in clinical practice during the follow-up of these patients may allow easy follow-up for patients. The health status of polycystic ovary syndrome patients can be objectively determined by tracking these outcomes at regular intervals.

KEYWORDS: Polycystic ovary syndrome. Inflammation. Lipoprotein. Cholesterol. Monocyte. Neutrophils.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a common endocrinologic pathology in women of reproductive age with symptoms including menstrual cycle irregularity, hirsutism, hyperandrogenism, and infertility. It is closely related to many clinical conditions such as insulin resistance (IR), hyperinsulinemia, glucose intolerance, dyslipidemia, hypertension, obesity, hyperandrogenism, endothelial dysfunction, and chronic low-grade inflammation[1]. White blood cell subtype ratios are important in identifying low-grade inflammation, and neutrophil-to-lymphocyte ratios (NLR), platelet-to-lymphocyte ratios (PLR), and lymphocyte-to-monocyte ratios (LMR) are used to evaluate the prognosis in some diseases[1,2]. Chronic low-grade inflammation is also known to have a stimulatory effect on the development of endothelial disease and atherosclerosis[2]. High-density lipoproteins (HDL) play a role in reducing atherosclerosis and cardiovascular complications. Markers such as total cholesterol (TC)/HDL, low-density lipoprotein (LDL)/HDL, and triglycerides (TG)/HDL can provide information about long-term PCOS complications.

The study compared hormone profiles, lipid profiles, and inflammatory parameters of PCOS patients with those of non-PCOS patients and examined predictive markers in young PCOS patients who have not yet had children.

METHODS

A total of 46 women with the diagnosis of PCOS and 41 healthy women who applied to the Tokat Gaziosmanpaşa University Research and Application Hospital Gynecology and Obstetrics

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Clinic were included in the study. Informed consent was obtained from all participants. Approval was obtained from the Faculty Ethics Committee before the start of the study (dated: October 15, 2020, project number: 20-KAEK-263).

The Rotterdam criteria (clinical or biochemical hyperandrogenism, anovulation or oligomenorrhea, and sonographically polycystic appearance of the ovaries) were used to diagnose PCOS[3], and if at least two of the three major criteria were present, the diagnosis was made. The presence of hirsutism, which is one of the findings of hyperandrogenism, was also evaluated using the Ferriman-Gallwey scoring system[4] and score above 8 was considered hyperandrogenism. The patients' age, height, weight, body mass index (BMI), waist circumference (WC), degree of hirsutism, and ultrasonographic findings were recorded. The examinations, pelvic ultrasound, and peripheral venous blood sampling of the participants were performed between days 2 and 4 of the menstrual cycle. All women underwent transabdominal pelvic ultrasonography with a 1.4–5 MHz (GE Logiq P5, GE Healthcare, USA) 4C Convex probe by the same gynecologist. A regularly maintained device (Mindray BC-6800, China) was used for complete blood count. A regularly maintained Roche Cobas e601 (Roche Diagnostics GmbH, Germany) device was used for other tests. The parameters of complete blood count, follicle-stimulating hormone (FSH), luteinizing hormone (LH), serum estradiol (E2), thyroid stimulating hormone (TSH), free thyroxine (T4), prolactin, total testosterone, DHEA-SO_4, glucose, insulin, TC, TG, LDL, cholesterol, and HDL cholesterol levels were measured. A HOMA-IR (fasting blood glucose mg/dL × fasting insulin mIU/L/405) value of ≥2.5 was considered the presence of IR. TC/HDL, TG/HDL, LDL/HDL, NLR, monocyte/high-density lipoprotein (MHR), monocyte/PLT, PLT/lymphocyte ratio (PLR), LMR, and systemic immune-inflammation index (SII/SIRS) parameters (NLR×PLT; NLR/PLR) were also calculated.

Patients with chronic diseases (e.g., congenital adrenal hyperplasia, Cushing's syndrome, and androgen-secreting tumors), taking medications (diabetic, antihypertensive, antilipidemic, oral contraceptives), who gave birth, and who had a history of surgery were excluded from the study.

Power analysis was performed using G-Power 3.1.9.7. It was found that at least 64 subjects were required, with an effect size of 0.80, a margin of error of 0.05, and a power of 0.80 (80%). The SPSS (Statistical Package for Social Sciences) program for Windows 22.0 (IBM SPSS, USA) was used for statistical analysis. The statistical methods used were the t-test for the variables with a normal distribution, the significance test for the difference between two means, and the Mann-Whitney U test for the variables that did not have a normal distribution. The chi-square test was used for the comparison of categorical variables. A Pearson's correlation analysis was performed to determine the relationship between variables. The statistical significance level was accepted as $p<0.05$.

RESULTS

The demographic characteristics of the cases are shown in Table 1. A statistically significant difference was found between the values of height, weight, BMI, WC, and hirsutism scores of the groups ($p<0.05$) (Table 1).

The results of hormone profiles and biochemical parameters of PCOS patients and control group are shown in Table 2. Although fasting glucose level was similar between the groups ($p=0.946$), insulin and IR levels calculated using HOMA-IR were significantly higher ($p=0.001$) in the PCOS patients (Table 2). IR defined as HOMA-IR ≥2.1 was present in 41 (63.1%) patients with PCOS. The Pearson's correlation analysis of the PCOS group revealed a negative correlation between

Table 1. Comparison of baseline characteristics between the study and control group.

Hormonal parameters	PCOS (n=41)(mean±SD)	Control (n=46)(mean±SD)	p
Age (years)	22.5±1.58	22.6±1.63	0.930[a]
Height (m)	1.62±0.55	1.65±0.56	**0.048**[b]
Weight (kg)	63.1±7.29	58.83±9.87	**0.001**[a]
BMI (kg/m^2)	23.8±2.69	21.5±3.46	**0.001**[b]
WC (cm)	81.5±8.59	76.4±8.34	**0.005**[a]
Hirsutism score			
Mild (%)	17 (28.3)	43 (71.7)	**0.001**[c]
Moderate (%)	24 (88.9)	3 (11.1)	

PCOS: polycystic ovary syndrome; BMI: body mass index; WC: waist circumference. Bold indicates statistical significance: $p<0.05$. [a]Mann-Whitney U test for continuous variables. [b]Pairwise t-test for continuous variables. [c]χ^2 for categorical variables. Data were given as mean±standard deviation or number (%).

T4 and weight, BMI, and WC (r=-0.421, p=0.004; r=-0.374, p=0.010; r=-0.389, p=0.008, respectively). When comparing the SIRS parameters (NLR×PLT; NLR/PLR) between the control and PCOS groups, no statistically significant differences were found (p=0.185; p=0.580).

HDL cholesterol levels were found to be statistically significantly lower in the PCOS group (p=0.001). The PCOS group had hemoglobin, leukocytes, lymphocytes, neutrophils, platelets, and statistically higher ratios of TC/HDL, LDL/HDL, and TG/HDL (Table 2). The Pearson's correlation analysis showed a positive correlation between the TC/HDL ratio and the parameters TG/HDL, LDL/HDL, insulin, HOMA-IR, LDL, and triglycerides in the patients of the PCOS group (Table 3). When monocyte/HDL ratios were evaluated, a positive correlation between monocyte, TC/HDL, TG/HDL, LDL/HDL, and TG levels was found in the Pearson's correlation (Table 3).

Table 2. Comparison of hormonal and biochemical parameters between the study and control group.

Hormonal parameters	PCOS (n=41)(mean±SD)	Control (n=46)(mean±SD)	p-value
FSH (mIU/mL)	5.46±0.96	5.87±1.00	0.055[b]
LH (mIU/mL)	9.88±6.47	5.49±2.02	**0.001[b]**
E2 (pg/mL)	47.13±30.54	40.05±12.59	0.153[b]
Total testosterone (ng/dL)	0.43±0.19	0.31±0.21	**0.007*[b]**
Prolactin (ng/mL)	21.43±9.30	18.97±8.82	0.210[b]
DHEA-SO_4 (µg/dL)	316.81±118.98	262.37±62.77	0.011[b]
Insulin (µIU/mL)	20.29±3.84	11.93±10.79	**0.001*[b]**
HOMA-IR	4.51±0.96	2.70±2.66	**0.001*[b]**
HOMA-IR >2.1 (%)	41 (63.1)	24 (36.9)	**0.001*[c]**
TSH (µIU/L)	1.60±0.68	1.80±0.96	0.272[b]
T4 (µg/dL)	1.27±0.19	1.28±0.16	0.817[b]
Biochemical parameters			
Glucose (mg/dL)	89.87±7.26	89.77±6.18	0.946[b]
Triglyceride (mg/dL)	81.24±29.84	74.60±30.45	0.307[b]
Total cholesterol (mg/dL)	157.05±20.92	158.67±29.02	0.764[b]
HDL cholesterol (mg/dL)	49.66±9.25	61.33±13.82	**0.001*[b]**
LDL cholesterol (mg/dL)	91.15±19.25	91.83±23.62	0.884[b]
WBC (10^3/mL)	7.67±1.70	7.77±1.88	0.806[b]
Neutrophils (10^3/mL)	4.78±1.48	4.59±1.27	0.521[b]
Lymphocytes (10^3/mL)	2.33±1.58	2.17±0.51	0.522[b]
PLT (10^3/mL)	313.27±76.56	289.01±70.02	0.126[b]
Hemoglobin (g/dL)	13.42±1.02	13.12±1.15	0.218[b]
Monocyte (10^3/mL)	598.54±178.54	683.04±213.12	0.049[b]
MPV	9.12±1.27	9.39±1.14	0.292[b]
Neutrophil/lymphocyte ratio	2.34±1.01	2.18±0.67	0.367[b]
PLT/lymphocyte ratio	151.45±47.79	138.49±42.78	0.185[b]
MHR	12.68±4.96	11.56±3.99	0.249[b]
Total cholesterol /HDL	3.25±0.68	2.66±0.56	**0.001*[b]**
Monocyte/PLT	0.0020±0.000	0.0025±0.001	0.052[b]
Lymphocytes/monocyte	4.38±4.07	3.42±1.23	0.171[a]
LDL/HDL ratio	1.90±0.56	1.57±0.50	**0.004*[b]**
TG/HDL ratio	1.74±0.90	1.31±0.68	**0.011*[a]**

PCOS: polycystic ovary syndrome; FSH: follicle-stimulating hormone; LH: luteinizing hormone; E2: estradiol; DHEA-SO_4: dehydroepiandrosterone sulfate; HOMA-IR: homeostatic model assessment insulin resistance; TSH: thyroid-stimulating hormone; T4: thyroxine; 25OHD: 25-hydroxy vitamin D; HDL: high-density lipoprotein; LDL: low-density lipoprotein; TG: triglyceride; WBC: white blood cells; PLT: platelet; MPV: mean platelet volume; MHR: monocyte/high-density lipoprotein ratio. [a]Mann-Whitney U test for continuous variables. [b]Pairwise t-test for continuous variables. [c]χ^2 test for categorical variables, Data were given as mean±standard deviation or number (%). Bold indicates statistical significance: p<0.05.

DISCUSSION

PCOS is a common disease at reproductive age and it negatively affects women's health with its long-term effects. It can cause diseases such as coronary heart disease, impaired glucose tolerance, type 2 diabetes, endometrial cancer, and breast cancer[5]. PCOS is also associated with increased oxidative stress and low-grade chronic inflammation (CI)[6]. CI affects the clinical findings and complications of PCOS[7]. It is already known that IR is associated with low-grade CI. Hyperandrogenism and IR are common findings in women with PCOS[8]. In this study, the values for weight, BMI, WC, IR, and hirsutism scores were higher in the PCOS group than those in the control group, which is consistent with the literature data.

HDL cholesterol has anti-inflammatory, antioxidant, and antithrombotic effects[9]. Monocyte/HDL is a marker that has previously been associated with cardiovascular events[10]. In a study on 61 PCOS patients conducted by Usta et al, monocyte/HDL was found to be a useful marker for diagnosing PCOS and predicting cardiovascular complications[11]. Another study reported that the monocyte/HDL ratio was significantly higher in PCOS patients compared with the control group[12]. In contrast to reports in the literature, no significant differences in monocyte/HDL were found between the PCOS and control groups in this study. The measurement of ApoA/ApoB, which is one of the best known atherogenic and thus cardiovascular disease risk indicators, is the most studied[13]. The ratio of TC/HDL or LDL/HDL is the surrogate for ApoB/ApoA[14]. In a study of 99 PCOS patients conducted by Cakir and Simsek, the ratio of TC/HDL was significantly higher[9]. In this study, the ratios of TC/HDL and LDL/HDL were significantly higher in the PCOS group than those in the control group. It has been shown that the TG/HDL ratio can be used to define insulin-resistant individuals[15]. In this study, the TG/HDL ratio was found to be significantly higher in the PCOS group than that in the control group. This result was similar to the literature.

NLR is a peripheral blood marker associated with inflammation and has been used in many studies as a potential biomarker to reflect the inflammatory status of the body and evaluate disease prognosis[16]. Yılmaz et al. found that NLR was higher in the PCOS group than that in the control group[17]. Another study reported that NLR was significantly higher[9]. In this study, no significant differences were found for NLR between the PCOS and control groups. The greater the platelet volume, the easier the release of inflammatory factors. Based on this information, some studies have found that PLR and MPV can be used as markers to detect inflammation[18]. In a study of 48 PCOS patients, Kebapcilar et al. reported that WBC and MPV values were higher in the PCOS group than those in the group without PCOS[19]. In another study, MPV was found to be higher in the PCOS group than that in the control group[17]. In this study, no significant differences were found between the PCOS and control groups in terms of MPV values. SII/SIRS is defined as NLR×platelets and is another effective indicator of inflammatory status that has been widely used to predict disease prognosis in recent studies[20]. In a case-control study with 527 participants, it was found that patients with PCOS had higher NLR, PLR, and SII ratios than those in the control group, which indicated that PCOS patients were in an inflammatory state[18]. In this study, there was no difference in SII values between groups, which was due to the small number of patients in the study. The fact that the monocyte/HDL, NLR, MPV, and SII/SIRS values in our study were similar in the PCOS and control groups, in contrast to the literature, is probably because the patient population was young and had not given birth to children, and the number of patients was small. The limitations of this study were the relatively small number

Table 3. The Pearson correlation results between the hormone values, hemogram, and blood lipid ratios of the polycystic ovary syndrome group.

	TG/HDL		LDL/HDL		MPV		NLR/PLR	
	r	p	r	p	r	p	R	p
BMI	-0.034	0.833	-0.127	0.429	-0.243	0.126	0.171	0.286
Insulin	0.303	0.054	0.302	0.055	-0.249	0.117	-0.121	0.449
HOMA-IR	0.433	**0.005**	0.326	**0.037**	-0.254	0.109	-0.092	0.565
DEAS-SO_4	-0.084	0.603	-0.089	0.579	-0.173	0.280	-0.014	0.929
FSH	0.058	0.720	-0.103	0.524	-0.297	0.059	0.100	0.534
LH	-0.147	0.358	-0.237	0.136	0.261	0.099	-0.051	0.752
Testosterone	-0.197	0.218	-0.212	0.184	-0.207	0.194	-0.086	0.594

BMI: body mass index; HOMA-IR: homeostatic model assessment insulin resistance; HDL: high-density lipoprotein; LDL: low-density lipoprotein; TG: triglyceride; FSH: follicle-stimulating hormone; LH: luteinizing hormone; DHEA-SO4: dehydroepiandrosterone sulfate; MPV: mean platelet volume; PLR: platelet lymphocyte ratio; NLR: neutrophil/lymphocyte ratio. Bold indicates statistical significance: p<0.05.

of patients and the retrospective design. The strength of the study was that the hematologic parameters and lipid parameters were presented together in the same study.

CONCLUSIONS

PCOS patients are at risk of short- and long-term complications, and the practical use of the TC/HDL, LDL/HDL, and TG/HDL ratios in the follow-up of these patients may allow for easy patient follow-up. The health status of PCOS patients can be objectively determined by monitoring these results at regular intervals. Prospective studies with a large number of participants need to be conducted to obtain clearer results.

AUTHORS' CONTRIBUTIONS

SG: Conceptualization, Data curation, Formal analysis, Investigation, Resources, Writing – original draft, Writing – review & editing. **ISC:** Conceptualization, Formal analysis, Writing – original draft, Writing – review & editing.

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