J Endocrinol Invest (2016) 39:45–53
DOI 10.1007/s40618-015-0335-2

ORIGINAL ARTICLE

The mean platelet volume and neutrophil to lymphocyte ratio in obese and lean patients with polycystic ovary syndrome

M. A. Yilmaz[1] · C. Duran[2] · M. Basaran[3]

Received: 2 April 2015 / Accepted: 9 June 2015 / Published online: 23 June 2015

Abstract
Purpose Mean platelet volume (MPV) and neutrophil to lymphocyte ratio (NLR) are the new markers of the detection of inflammation. Our aim is to investigate MPV and NLR in lean and obese patients with polycystic ovary syndrome (PCOS).
Methods This study was designed to investigate MPV, NLR, and high-sensitive C-reactive protein (hsCRP) levels in 25 obese patients with PCOS and 16 lean patients with PCOS, and our study group was matched with 16 obese and 14 non-obese controls, respectively.
Results PCOS group had higher MPV, NLR, neutrophil count, neutrophil to total leucocyte ratio, basophil count, waist circumference (WC), insulin, glucose, and HOMA-IR rates than those of controls. hsCRP levels were similar in both groups. Subgroup analyses revealed that obese PCOS group had higher insulin and HOMA-IR levels, compared to those of controls. In this subgroup, total leucocyte counts, MPV, and hsCRP levels were similar. On the other hand, lean PCOS group had higher WC, NLR, MPV, and basophil count than controls. In correlation analysis, hsCRP was positively correlated with body mass index (BMI), WC, total leucocyte count, neutrophil count, while negatively correlated with lymphocyte ratio. Although leucocyte count was positively correlated with BMI, MPV was negatively correlated with BMI, total leucocyte, platelet, and neutrophil counts. NLR was positively correlated with HOMA-IR, hsCRP, BMI, WC, and insulin.
Conclusion Our study demonstrated that MPV and NLR levels are increased despite similar hsCRP levels in patients with PCOS. However, we failed to demonstrate these differences in obese PCOS patients. Further studies with larger sample size are required to determine the significance of BMI in the inflammation of PCOS patients.

Keywords Polycystic ovary syndrome · Neutrophil to lymphocyte ratio · Mean platelet volume · High-sensitive CRP

Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in reproductive age of women with a worldwide prevalence of 5–10 % [1, 2]. The characteristics of this syndrome are hirsutism, hyperandrogenism, menstrual disturbance, and infertility. Obesity, impaired glucose tolerance, insulin resistance, endothelial dysfunction, and increased inflammation are other well-known features [3–7]. Low-grade inflammation plays a key role in the development and progression of insulin resistance, type 2 diabetes mellitus (DM), and atherosclerosis [8–10]. Observation of coexistence of PCOS with insulin resistance and atherosclerosis may be the result of common pathway of inflammation in these clinical conditions [11, 12].

In previous studies, hsCRP was reported as a commonly used laboratory parameter in the detection of subclinical inflammation in patients with PCOS [13, 14]. Additionally, increased leucocyte counts were found to be an additional

✉ C. Duran
drcduran@gmail.com

[1] Department of Internal Medicine, Konya Training and Research Hospital, Konya, Turkey

[2] Division of Endocrinology and Metabolism, Department of Internal Medicine, Clinic of Endocrinology and Metabolism, Konya Training and Research Hospital, 42100 Konya, Turkey

[3] Department of Obstetrics and Gynecology, Konya Training and Research Hospital, Konya, Turkey

independent marker and prognostic factor in the development of inflammation and atherosclerosis [4, 7, 15–17]. In recent years, neutrophil to lymphocyte ratio (NLR) has gained a popularity in the detection of inflammation in different inflammatory diseases such as PCOS, DM, ulcerative colitis, and hypertension, and it has been shown that NLR is correlated with hsCRP levels [4, 18, 19]. As a marker, NLR is a cost-effective and convenient marker that could be an alternative to hsCRP for inflammation.

Similarly, increased levels of mean platelet volume (MPV) can also be used as a marker to detect inflammation [20–25]. It is known that larger platelets are metabolically more active and prone to inflammatory cytokine release. It was shown that MPV values are higher in patients with PCOS than controls [26–28].

In this study, we aimed to compare hsCRP, MPV, and NLR levels in lean and obese PCOS patients using two different control groups matched with age and body mass index (BMI).

Patients and methods

This prospective study was conducted in Konya Training and Research Hospital, in the clinics of Internal Medicine (Division of Endocrinology) and Obstetrics and Gynecology between June and December 2014. Informed consents were obtained from all participants. Study protocol was approved by the ethics committee of Necmettin Erbakan University, Meram Faculty of Medicine.

Obese PCOS patients with BMI $\geq$25 kg/m^2 ($n = 25$) and lean PCOS patients with BMI <25 kg/m^2 ($n = 16$) were enrolled into the study. Age- and BMI-matched 16 obese and 14 non-obese healthy subjects were included into the study as control group. All patients were aged between 18 and 40 years.

Diagnosis of PCOS was based on the Rotterdam criteria as having at least two of the following three criteria: first, oligomenorrhea (cycles lasting longer than 35 days) or amenorrhea (<2 menstrual cycles in the past 6 months); second, clinical or biochemical hyperandrogenism; third, polycystic appearance of ovary on ultrasonography (USG) and the exclusion of other causes of hyperandrogenism, such as Cushing's syndrome, congenital adrenal hyperplasia, or virilization [29]. Subjects taking drugs in the last 6 months that may interfere or affect insulin resistance and inflammation, such as estrogens, oral contraceptives, corticosteroids, immunosuppressants, anti-hyperlipidemics, anti-hypertensive, anti-hyperglycemic drugs, insulin sensitizing drugs, and anti-inflammatory drugs in the last month or with any known active infection or inflammatory diseases such as Crohn, ulcerative colitis, rheumatoid arthritis, systemic lupus erythematosus or benign or malignant hematologic disorders, hypertension, or any surgical intervention within the past 6 months were excluded from the study.

Height (m) and weight (kg) were measured with underwear clothing. Waist circumference was measured as the minimum size between iliac crest and lateral costal margin. BMI was calculated as weight (kg) divided by height square (m^2).

All blood samples were drawn after an overnight fasting between the third and fifth days of menstruation, separated by centrifugation, and stored in deep freeze at −70 °C until being analyzed.

Complete blood count was measured by Sysmex XE-2100 (Sysmex Corp. Kobe, Japan) with fluorescence flow cytometry or electrical impedance method. NLR was calculated as the ratio of the neutrophil count to lymphocyte count. hsCRP levels were measured by BN™ II (Siemens Healthcare Diagnostics, Siemens AG, Germany) with nephelometric method. Glucose levels [normal range (NR), 70–105 mg/dl] were measured by Abbott C-16000 Autoanalyzer (Abbott Laboratories, Abbott Park, IL) with glucose oxidized method. Insulin levels were measured by Advia Centaur XP (Siemens Healthcare Diagnostics, Siemens AG, Germany) with chemiluminescence method. Insulin resistance was calculated by homeostasis model assessment-insulin resistance (HOMA-IR) [fasting plasma glucose (mmol/l) × fasting serum insulin (μIU/ml)/22.5]. Intra- and inter-assay coefficients of variations for insulin were 4.6 and 5.9, respectively.

Statistical analysis

The student's t test for independent samples was used to compare normally distributed measurements. The Kolmogorov–Smirnov test was used to test normal distribution of variables. The Pearson and Spearman's correlation analyses were performed to determine the correlation of parametric and non-parametric data, where appropriate. The Chi-square test was used to compare categorical data. Mean ± standard deviation and frequencies (%) were used to summarize parametric and categorical data, respectively. The statistical analyses of data were carried out using SPSS 21 statistical software for Windows version (IBM Corp., Armonk, NY). Statistical significance level was set to 0.05.

Results

The anthropometric, hormonal, and metabolic characteristics of patients are summarized in Table 1.

Before subgroup analyses of lean and obese PCOS patients, our participants were compared in two groups as all PCOS patients ($n = 41$) and all controls ($n = 30$). Compared with

Table 1 Some anthropometric, metabolic, and hormonal data of the study population

	PCOS	Controls	*p* value
Age (year)	23.83 ± 4.71	26.03 ± 5.02	0.070
Body mass index (kg/m^2)	29 ± 7.35	26.32 ± 7.13	0.116
Waist circumference (cm)	85.85 ± 17.19	78.43 ± 19.19	0.041
Ferriman–Gallwey score	16.56 ± 6.6	5.9 ± 1.06	0.0001
Insulin (μIU/ml)	14.1 ± 6.69	9.61 ± 4.14	0.004
Glucose (mg/dl)	88.34 ± 8.84	83.9 ± 8.38	0.036
HOMA-IR	3.11 ± 1.67	2.02 ± 0.95	0.004
hsCRP (mg/l)	2.778 ± 3.201	2.583 ± 3.091	0.545
Leucocytes (/mm^3)	7616.34 ± 1735.55	7093.33 ± 1558.88	0.195
Neutrophil (/mm^3)	4655.85 ± 1450.84	4015.67 ± 1245.23	0.039
Neutrophil (%)	60.17 ± 6.95	56.11 ± 7.42	0.021
Lymphocytes (/mm^3)	2303.41 ± 500.03	2406.33 ± 586.55	0.429
Lymphocytes (%)	31.04 ± 6.42	34.4 ± 6.69	0.036
Monocyte (/mm^3)	516.34 ± 145.36	530.33 ± 143.44	0.688
Basophil (/mm^3)	28.29 ± 12.83	21.67 ± 12.89	0.012
Eosinophil (/mm^3)	114.63 ± 91.84	115.01 ± 83.61	0.670
Neutrophil to lymphocyte ratio	2.08 ± 0.74	1.74 ± 0.63	0.029
Platelet (K/μl)	297.41 ± 54.78	275.37 ± 63.44	0.122
Mean platelet volume (fl)	10.69 ± 0.81	10.25 ± 0.83	0.026
Total testosteron (mmol/l)	43.18 ± 18.62		
Free testosteron (pg/ml)	2.15 ± 0.75		
DHEA-S (ng/ml)	294 ± 102.58		
FSH (mIU/ml)	5.41 ± 1.52		
LH (mIU/ml)	10.65 ± 6.50		
Estradiol (pg/ml)	48.78 ± 33.21		
Progesteron (ng/ml)	0.99 ± 1.24		
TSH (μIU/ml)	2.22 ± 1.20		
Prolaktin (ng/ml)	15.22 ± 8.25		
17-OH progesteron (ng/ml)	061 ± 0.42		

PCOS polycystic ovary syndrome, *HOMA-IR* hemostasis of model assessment-insulin resistance, *hsCRP* high-sensitive C-reactive protein, *DHEA-S* dehydroepiandrosterone sulfate, *FSH* follicle-stimulating hormone, *LH* luteinizing hormone, *TSH* thyroid-stimulating hormone

controls, PCOS group had significantly higher waist circumference (WC), HOMA-IR, insulin, glucose, MPV, neutrophil count, neutrophil to total leucocyte ratio, NLR, and basophil count. hsCRP levels were similar in both groups (Table 1).

In PCOS group ($n = 41$), correlation analyses revealed that hsCRP was positively correlated with BMI, WC, total leucocyte count, neutrophil count, and NLR, while MPV was negatively correlated with BMI, total leucocyte count, platelet count, and neutrophil count. NLR was positively correlated with HOMA-IR, hsCRP, BMI, WC, insulin, total leucocyte count, and neutrophil count while negatively correlated with lymphocyte count (Table 2).

Subgroup analyses

Correlation analysis of subgroups is shown in Table 3. In the comparison of obese PCOS patients ($n = 25$) and controls ($n = 16$), obese PCOS group had higher insulin and HOMA-IR levels. The counts of total leucocyte, its subgroups, MPV, and hsCRP were not significantly different among groups. In the comparison of lean PCOS patients ($n = 16$) and controls ($n = 14$), lean PCOS group had higher WC, NLR, MPV, and basophil count. hsCRP levels and counts of total leucocyte and its subgroups except for basophil were similar.

In the correlation analyses of obese PCOS group, hsCRP was positively correlated with BMI (Table 4). In lean PCOS group, hsCRP was positively correlated with BMI, WC, insulin, and HOMA-IR levels, as well as positive correlation of NLR with BMI, insulin, and HOMA-IR. In obese controls, hsCRP was positively correlated with glucose. In lean PCOS group, hsCRP was also positively correlated with BMI. In lean controls, hsCRP was negatively correlated with HOMA-IR and insulin levels.

Table 2 Correlation analyses in PCOS group and controls

	Controls ($n = 30$)											
	BMI	WC	Insulin	Glucose	HOMA-IR	hsCRP	WBC	Neutrophil	Lymphocyte	NLR	PLT	MPV
Polycystic ovary syndrome group ($n = 41$)												
BMI												
r	1.000	**.929**	.346	.253	**.399**	**.553**	**.426**	.275	.246	.052	.309	−.102
p	**<.001**	.061	.178	**.029**	**.002**	**.019**	.141	.190	.786	.096	.591	
WC												
r	**.919**	1.000	**.428**	.165	**.453**	**.506**	**.341**	.232	.251	.057	.353	−.099
p	**<.001**		**.018**	.383	**.012**	**.004**	**.065**	.217	.180	.764	.056	.601
Insulin												
r	**.641**	**.653**	1.000	**.409**	**.980**	.079	.260	.167	.119	.018	**.368**	−.153
p	**<.001**	**<.001**		**.025**	**<.001**	.676	.166	.378	.532	.923	**.045**	.420
Glucose												
r	**.366**	.238	.306	1.000	**.538**	.081	−.020	−.012	.099	−.117	.291	−.107
p	**.019**	.135	.052		**.002**	.671	.915	.950	.603	.537	.119	.575
HOMA-IR												
r	**.631**	**.620**	**.978**	**.464**	1.000	.095	.277	.175	.163	−.030	.452	−.156
p	**<.001**	**<.001**	**<.001**	**.002**		.616	.138	.356	.389	.877	.012	.410
hsCRP												
r	**.748**	**.704**	**.645**	.208	**.601**	1.000	**.466**	**.502**	.137	**.361**	.300	−.101
p	**<.001**	**<.001**	**<.001**	.192	**<.001**		**.009**	**.005**	.470	**.050**	.107	.595
WBC												
r	**.502**	**.444**	**.464**	.283	**.492**	**.369**	1.00	**.705**	**.683**	.130	.267	.181
p	**.001**	**.004**	**.002**	.073	**.001**	**.018**		**<.001**	**<.001**	.494	.153	.338
Neutrophil												
r	**.464**	**.398**	**.462**	.236	**.474**	**.374**	**.956**	1.000	.115	**.712**	.095	.108
p	**.002**	**.010**	**.002**	.138	**.002**	**.016**	**<.001**		.546	**<.001**	.617	.569
Lymphocyte												
r	.203	.158	.056	.213	.111	.059	**.494**	.273	1.000	**−.503**	**.365**	.230
p	.203	.324	.728	.181	.491	.715	**.001**	.084		**.005**	**.047**	.221
NLR												
r	**.351**	**.310**	**.409**	.048	**.379**	**.365**	**.579**	**.762**	**−.336**	1.000	−.153	−.025
p	**.024**	**.049**	**.008**	.765	**.015**	**.019**	**<.001**	**<.001**	**.032**		.420	.894
PLT												
r	.330*	.287	.103	.143	.097	.145	**.408**	**.324**	**.353**	.087	1.000	−.206
p	.035	.068	.522	.371	.547	.366	**.008**	**.039**	**.023**	.589		.276
MPV												
r	**−.336**	−.261	−.167	−.203	−.188	−.190	**−.430**	**−.366**	−.273	−.181	**−.566**	1.000
p	**.032**	.099	.297	.204	.239	.235	**.005**	**.018**	.084	.258	**<.001**	

BMI body mass index, *WC* waist circumference, *HOMA-IR* homeostasis of model assessment-insulin resistance, *hsCRP* high-sensitive C-reactive protein, *WBC* white blood cell, *NLR* neutrophil to lymphocyte ratio, *PLT* platelet, *MPV* mean platelet volume. Significant results are given in bold

According to the presence of obesity, our cases were divided into two main groups as the lean and the obese (BMI ≥25 kg/m^2), each including both patients with PCOS and healthy controls. Obese group had higher age, BMI, WC, glucose, insulin, HOMA-IR, hsCRP, leucocyte, neutrophil and platelets levels, and lower lymphocyte, compared to lean group. MPV and NLR levels were found to be similar (Table 5).

Discussion

In this study, we found higher neutropil and basophil counts, NLR, MPV levels in patients with PCOS, compared to controls. In addition, in the subgroup analysis, we found that obese PCOS patients had higher insulin and HOMA-IR levels while lean PCOS group had higher WC,

Table 3 Some anthropometric, metabolic, and hormonal data of the obese and lean PCOS groups

	Obese PCOS	Obese control	*p*	Lean PCOS	Lean control	*p*
Age (year)	25.12 ± 4.76	27.71 ± 5.44	0.141	21.81 ± 3.97	24.56 ± 4.26	0.067
Body mass index (kg/m^2)	33.62 ± 5.48	32.69 ± 5.39	0.613	21.79 ± 2.23	20.75 ± 1.45	0.128
Waist circumference (cm)	95.68 ± 14.54	94.71 ± 15.62	0.847	70.5 ± 6.12	64.19 ± 6.02	0.006
Insulin (μIU/ml)	16.01 ± 6.09	11.56 ± 4.47	0.041	11.12 ± 6.66	7.91 ± 3.04	0.305
Glucose (mg/dl)	90.44 ± 8.23	86 ± 8.62	0.120	85.06 ± 9.02	82.06 ± 7.99	0.327
HOMA-IR	3.63 ± 1.62	2.48 ± 1.02	0.033	2.3 ± 1.45	1.62 ± 0.7	0.287
hsCRP (mg/l)	4.06 ± 3.524	4.037 ± 3.188	0.965	0.774 ± 0.662	1.311 ± 2.442	0.926
Leucocyte (/mm^3)	8125.6 ± 1668.06	7943.57 ± 1580.48	0.741	6820.63 ± 1572.54	6349.38 ± 1126.17	0.338
Neutrophil (/mm^3)	5029.6 ± 1448.77	4626.43 ± 1477.42	0.346	4071.88 ± 1287.74	3481.25 ± 673.28	0.118
Neutrophil (%)	61.09 ± 7.03	57.59 ± 9.84	0.253	58.72 ± 6.79	54.81 ± 4.32	0.062
Lymphocyte (/mm^3)	2418.4 ± 531.95	2604.29 ± 618.79	0.330	2123.75 ± 396.9	2233.13 ± 514.52	0.696
Lymphocyte (%)	30.43 ± 6.58	33.41 ± 8.36	0.227	31.99 ± 6.24	35.26 ± 4.92	0.110
Monocyte (/mm^3)	523.2 ± 130.73	550.71 ± 159.4	0.564	505.63 ± 169.7	512.5 ± 130.51	0.899
Basophil (/mm^3)	28.8 ± 14.53	25.71 ± 12.22	0.718	27.5 ± 10	18.13 ± 12.76	0.004
Eosinophil (/mm^3)	129.2 ± 103.11	127.15 ± 106.57	0.988	91.88 ± 67.65	104.38 ± 58.42	0.580
Neutrophil to lymphocyte ratio	2.17 ± 0.83	1.91 ± 0.84	0.303	1.94 ± 0.57	1.59 ± 0.32	0.046
Platelet (K/μl)	311.52 ± 53.23	298.57 ± 64.17	0.503	275.38 ± 51.17	255.06 ± 57.18	0.298
Mean platelet volume (fl)	10.55 ± 0.82	10.24 ± 1.02	0.303	10.92 ± 0.77	10.27 ± 0.65	0.015

PCOS polycystic ovary syndrome, *HOMA-IR* hemostasis of model assessment-insulin resistance, *hsCRP* high-sensitive C-reactive protein

NLR, MPV, and basophil counts, compared to age- and BMI-matched controls.

In our study, similar hsCRP levels were found in both groups. Increased inflammatory markers such as hsCRP have been reported in patients with PCOS [14, 30]. The underlying mechanism of increased hsCRP is yet to be elucidated, and whether it is related to PCOS itself or the accompanying obesity still remains uncertain. According to the presence of obesity, we reclassified our participants into two as the lean and the obese (BMI ≥25 kg/m^2), and obese group showed higher hsCRP levels than lean group. It is well known that obesity is an important factor leading to an increase of hsCRP [31]. In a study with small sampling size by Kahal et al., as consistent with our findings, it was reported that hsCRP levels in obese patients with PCOS were similar to those of controls [13]. We consider PCOS as an inflammatory disease, and obesity a contributing factor to the elevation of hsCRP; therefore, we anticipated to observe higher level of hsCRP in PCOS patients. However, because of small sample size of groups in our study, we failed to demonstrate the increase of hsCRP in our patients with PCOS. Despite this limitation in our study, we were able to demonstrate increased levels of MPV and NLR. We consider that the condition reflects higher sensitivity of these markers in PCOS patients, and that further studies are required to support these hypotheses.

In literature, there are several studies investigating MPV levels in patients with PCOS. Gursoy et al. [26] and Kebapcilar et al. [28] reported that patients with PCOS had higher MPV levels, compared to controls. In another study performed by Kabil Kucur et al. [27], MPV levels were found higher in patients with PCOS, and after the treatment with ethinyl estradiol/cyproterone acetate or metformin, a significant decrease was observed in MPV levels. It could also be speculated that anti-inflammatory effects of these treatment modalities might contribute to the protective effect on cardiovascular diseases in patients with PCOS. Additionally, platelets with higher volumes are known to be associated with increased agility in thrombotic processes. In our study, as well as lean subgroup, PCOS patients had higher MPV levels than controls. However, we found no similar results in obese subgroup, compared to obese controls. Silfeler Beng et al. [32] and Dogan et al. [33] reported similar MPV levels in patients with lean PCOS and BMI- matched controls, and our findings are different from theirs. They concluded that as to obesity, their results are more important contributors to MPV levels than the existence of PCOS per se. Interestingly, as opposed to the findings in previous studies by Coban et al. [34], we observed a significant negative correlation between BMI and MPV levels ($r = -0.336$, $p = 0.03$), which could not be reproduced in subgroup analysis. When we divided our cases into two main groups as the lean and the obese (BMI ≥25 kg/m^2), MPV levels were found to be similar. Although some other contributing factors related to this finding might be present, the further discussion and comparison with the previous studies would be impossible due to the paucity of data on the subject. Therefore, we consider that this condition

Table 4 Correlation analyses in subgroup of patients

	Obese control ($n = 14$)							
	BMI	WC	İnsülin	Glucose	HOMA-IR	hsCRP	NLR	MPV
Obese PCOS group ($n = 25$)								
BMI								
r	1.000	**.819**	.024	.257	.081	−.103	−.411	−.374
p		**<.001**	.935	.375	.782	.725	.144	.187
WC								
r	**.860**	1.000	.225	−.057	.244	.192	.447	−.173
p	**<.001**		.440	.846	.400	.512	.109	.554
Insülin								
r	**.697**	**.719**	1.000	.196	**.965**	.147	−.134	−.148
p	**<.001**	**<.001**		.503	**<.001**	.615	.648	.615
Glucose								
r	.196	.207	.388	1.000	.327	**.640**	−.455	.007
p	.347	.320	.055		.253	**.014**	.102	.982
HOMA-IR								
r	**.647**	**.685**	**.974**	**.535**	1.000	.033	−.222	−.106
p	**<.001**	**<.001**	**<.001**	**.006**		911	.446	.719
hsCRP								
r	**.565**	**.442**	**.512**	.167	**.484**	1.000	.389	.123
p	**.003**	**.027**	**.0.09**	.426	**.014**		.169	.674
NLR								
r	**.508**	.314	**.444**	.062	**.395**	.393	1.000	−.064
p	**.010**	.127	**.024**	.768	**.050**	.052		.828
MPV								
r	−.313	−.159	−.227	−.265	−.262	−.248	.020	1.000
p	.127	.448	.274	.201	.205	.232	.924	
	Lean control ($n = 16$)							
	BMI	WC	İnsülin	Glucose	HOMA-IR	hsCRP	NLR	MPV
Lean PCOS group ($n = 16$)								
BMI								
r	1.000	**.748**	−.185	.013	−.200	.331	−.026	.013
p		**.001**	.492	.961	.458	.210	.922	.961
WC								
r	**.559**	1.000	.052	−.087	.004	−.058	.071	−.158
p	**.024**		.849	.749	.987	.831	.793	.560
Insülin								
r	.225	.124	1.000	.392	**.985**	**−.530**	.056	−.099
p	.402	.648		.133	**<.001**	**.035**	.837	.715
Glucose								
r	.213	−.475	.029	1.000	.477	−.026	.227	−.223
p	.428	.063	.914		.062	.924	.398	.406
HOMA-IR								
r	.240	.021	**.929**	.312	1.000	**−.502**	.121	−.129
p	.371	.939	**<.001**	.239		**.048**	.656	.635
hsCRP								
r	**.629**	.337	.394	.072	.333	1.000	.018	−.110
p	**.009**	.202	.131	.790	.208		.948	.684

Table 4 continued

	Lean control ($n = 16$)							
	BMI	WC	İnsülin	Glucose	HOMA-IR	hsCRP	NLR	MPV
NLR								
r	.430	.347	.268	−.090	.241	.160	1.000	.003
p	.097	.188	316	.741	.368	.553		.991
MPV								
r	−.221	−.186	.096	.030	.066	.174	−.420	1.000
p	.412	.489	.724	.911	.807	.519	.105	

PCOS polycystic ovary syndrome, *BMI* body mass index, *WC* waist circumference, *HOMA-IR* homeostasis of model assessment-insulin resistance, *hsCRP* high-sensitive C-reactive protein, *NLR* neutrophil to lymphocyte ratio, *PLT* platelet, *MPV* mean platelet volume. Significant results are given in bold

Table 5 Some anthropometric, metabolic, and hormonal data of study population [cases were divided into two main groups as the lean (BMI < 25 kg/m^2) and the obese (BMI ≥ 25 kg/m^2)]

	Lean ($n = 39$)	Obese ($n = 32$)	*p*
Age (years)	23.19 ± 4.28	26.05 ± 5.1	**0.012**
BMI (kg/m^2)	21.27 ± 1.92	33.28 ± 5.39	**<0.001**
WC (cm)	67.34 ± 6.78	95.33 ± 14.73	**<0.001**
Glucose (mg/dl)	83.56 ± 8.51	88.85 ± 8.53	**0.01**
Insulin (μIU/ml)	9.51 ± 5.34	14.40 ± 5.91	**<0.001**
HOMA-IR	1.96 ± 1.17	3.02 ± 1.52	**<0.001**
hsCRP (mg/l)	1.78 ± 1.04	4.05 ± 3.36	**<0.001**
WBC (/mm^3)	8585 ± 1366.5	8060.2 ± 1618.5	**<0.001**
Neutrophil (/mm^3)	3776.5 ± 1054.4	4884.8 ± 1452.8	**0.002**
Lymphocyte (/mm^3)	2178.4 ± 455.4	2485.1 ± 563.8	**0.021**
Neutropil to lymphocyte ratio	1.76 ± 0.48	2.07 ± 0.83	0.102
Platelets (K/μl)	265.2 ± 54.3	306.8 ± 56.9	**0.003**
MPV (fl)	10.05 ± 0.77	10.43 ± 0.89	0.442

BMI body mass index, *WC* waist circumference, *HOMA-IR* homeostasis of model assessment-insulin resistance, *hsCRP* high-sensitive C-reactive protein, *WBC* white blood cell, *MPV* mean platelet volume. Significant results are given in bold

should be further discussed, and more comprehensive studies to enlighten the correlation between MPV, obesity, and PCOS are needed.

Increased leucocyte count is an independent risk and prognostic factor in the development of inflammation and atherosclerosis [17], and there are several studies reporting increased leucocyte counts in patients with PCOS [4, 7, 15, 16, 35]. In our study, leucocyte counts were similar in patients with PCOS and controls; still, differential count of leucocytes revealed that patients with PCOS had higher neutrophil count and ratio, basophil count and lower lymphocyte count, compared to controls. Basophil count was higher only in lean PCOS patients than controls, and no significant difference regarding to other leucocytes was present. To our knowledge, no study investigating and accounting for the increase of basophil is present, and our study is the first to indicate this increase. However, we failed to elucidate such an increase, and so further studies should be performed. In a study similarly designed to ours by Keskin Kurt et al., it was reported that higher hsCRP, leucocyte count, and NLR were present in PCOS patients [4]. Additionally, they also reported a moderate, but significant correlation among NLR and HOMA-IR, BMI, and hsCRP, reflecting the higher statistical power of their study. Considering the common inflammatory process, leucocyte count and NLR were expected to be increased along with CRP. As opposed to the findings in the study by Keskin Kurt et al., we found higher NLR with similar hsCRP levels in PCOS group compared to matched controls. However, we failed to demonstrate the same findings as those in obese PCOS patients, probably due to small sample sizes of subgroups. Nonetheless, we consider that even in case of similar hsCRP levels, NLR might be a more sensitive parameter to demonstrate ongoing subclinical inflammation in PCOS patients. In a recent study published by Papalou et al., it has been reported that higher leucocyte counts were observed in patients with PCOS than controls, and while androgenism did not seem to affect leucocyte counts, obesity and insulin resistance were major contributing factors in the development of leukocytosis [35]. In our study, although a significant association was present between leucocyte and BMI in PCOS and control groups, the association was observed between HOMA-IR and leucocyte only in PCOS group (Table 2). In an analysis investigating the association between androgens and leucocyte counts, no correlation was found except for between NLR and free testosteron ($p = 0.451$, $r = 0.021$) (unexisting data).

On the other hand, the analysis of NLR and BMI, as expected, showed a significant correlation ($r = 0.351$, $p = 0.024$, Table 2). However, this finding was not persistent in obese PCOS group, as opposed to the one found in lean PCOS patients (Table 4). We consider that this condition was a reflection of decreased power of the study in subgroup analyses. Similarly, positive correlations were

observed among total leucocytes, neutrophil, and BMI. Additionally, when we divided our cases into two main groups as the lean and the obese (BMI $\geq$25 kg/m^2), NLR levels were found to be similar.

In conclusion, we found that the patients with PCOS had higher NLR and MPV levels even when similar hsCRP levels were present. This result may be attributed to the fact that NLR and MPV levels are good indicators in the detection of inflammation as independent of hsCRP levels in patients with PCOS. On the other hand, no similar results were shown when patients were reclassified as the lean and the obese, and this may be due to small sample size in our study. New studies with larger sample size are needed.

Acknowledgments Authors thank Numan Duran for language editing. This study was supported by Konya Training and Research Hospital's Research Fund.

Conflict of interest The authors declared no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Nandi A, Chen Z, Patel R, Poretsky L (2014) Polycystic ovary syndrome. Endocrinol Metab Clin North Am 43(1):123–147. doi:10.1016/j.ecl.2013.10.003
2. Fauser BC, Tarlatzis BC, Rebar RW, Legro RS, Balen AH, Lobo R, Carmina E, Chang J, Yildiz BO, Laven JS, Boivin J, Petraglia F, Wijeyeratne CN, Norman RJ, Dunaif A, Franks S, Wild RA, Dumesic D, Barnhart K (2012) Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group. Fertil Steril 97(1):28–38e25. doi:10.1016/j.fertnstert.2011.09.024
3. Chen L, Xu WM, Zhang D (2014) Association of abdominal obesity, insulin resistance, and oxidative stress in adipose tissue in women with polycystic ovary syndrome. Fertil Steril 102(4):1167–1174e1164. doi:10.1016/j.fertnstert.2014.06.027
4. Keskin Kurt R, Okyay AG, Hakverdi AU, Gungoren A, Dolapcioglu KS, Karateke A, Dogan MO (2014) The effect of obesity on inflammatory markers in patients with PCOS: a BMI-matched case-control study. Arch Gynecol Obstet 290(2):315–319. doi:10.1007/s00404-014-3199-3
5. Kelly CC, Lyall H, Petrie JR, Gould GW, Connell JM, Sattar N (2001) Low grade chronic inflammation in women with polycystic ovarian syndrome. J Clin Endocrinol Metab 86(6):2453–2455. doi:10.1210/jcem.86.6.7580
6. Tarkun I, Arslan BC, Canturk Z, Turemen E, Sahin T, Duman C (2004) Endothelial dysfunction in young women with polycystic ovary syndrome: relationship with insulin resistance and low-grade chronic inflammation. J Clin Endocrinol Metab 89(11):5592–5596. doi:10.1210/jc.2004-0751
7. Ruan X, Dai Y (2009) Study on chronic low-grade inflammation and influential factors of polycystic ovary syndrome. Med Princ Pract 18(2):118–122. doi:10.1159/000189809
8. Bloomgarden ZT (2003) Inflammation and insulin resistance. Diabetes Care 26(5):1619–1623
9. Dandona P, Aljada A, Chaudhuri A, Bandyopadhyay A (2003) The potential influence of inflammation and insulin resistance on the pathogenesis and treatment of atherosclerosis-related complications in type 2 diabetes. J Clin Endocrinol Metab 88(6):2422–2429. doi:10.1210/jc.2003-030178
10. Wilson PW, Kannel WB, Silbershatz H, D'Agostino RB (1999) Clustering of metabolic factors and coronary heart disease. Arch Intern Med 159(10):1104–1109
11. Ravn P (2015) New paradigms in PCOS: Impaired glucose tolerance and cardiovascular risk. Clinical approach. Minerva Ginecologica
12. Legro RS, Kunselman AR, Dodson WC, Dunaif A (1999) Prevalence and predictors of risk for type 2 diabetes mellitus and impaired glucose tolerance in polycystic ovary syndrome: a prospective, controlled study in 254 affected women. J Clin Endocrinol Metab 84(1):165–169. doi:10.1210/jcem.84.1.5393
13. Kahal H, Aburima A, Ungvari T, Rigby AS, Dawson AJ, Coady AM, Vince RV, Ajjan RA, Kilpatrick ES, Naseem KM, Atkin SL (2013) Polycystic ovary syndrome has no independent effect on vascular, inflammatory or thrombotic markers when matched for obesity. Clin Endocrinol 79(2):252–258. doi:10.1111/cen.12137
14. Kim JW, Han JE, Kim YS, Won HJ, Yoon TK, Lee WS (2012) High sensitivity C-reactive protein and its relationship with impaired glucose regulation in lean patients with polycystic ovary syndrome. Gynecol Endocrinol 28(4):259–263. doi:10.3109/09513590.2011.613967
15. Herlihy AC, Kelly RE, Hogan JL, O'Connor N, Farah N, Turner MJ (2011) Polycystic ovary syndrome and the peripheral blood white cell count. J Obstet Gynaecol 31(3):242–244. doi:10.3109/01443615.2011.553693
16. Phelan N, O'Connor A, Kyaw Tun T, Correia N, Boran G, Roche HM, Gibney J (2013) Leucocytosis in women with polycystic ovary syndrome (PCOS) is incompletely explained by obesity and insulin resistance. Clin Endocrinol 78(1):107–113. doi:10.1111/j.1365-2265.2012.04454.x
17. Margolis KL, Manson JE, Greenland P, Rodabough RJ, Bray PF, Safford M, Grimm RH Jr, Howard BV, Assaf AR, Prentice R, Women's Health Initiative Research G (2005) Leukocyte count as a predictor of cardiovascular events and mortality in postmenopausal women: the Women's Health Initiative Observational Study. Arch Intern Med 165(5):500–508. doi:10.1001/archinte.165.5.500
18. Celikbilek M, Dogan S, Ozbakir O, Zararsiz G, Kucuk H, Gursoy S, Yurci A, Guven K, Yucesoy M (2013) Neutrophil-lymphocyte ratio as a predictor of disease severity in ulcerative colitis. J Clin Lab Anal 27(1):72–76. doi:10.1002/jcla.21564
19. Imtiaz F, Rashed MS, Al-Mubarak B, Allam R, El-Karaksy H, Al-Hassnan Z, Al-Owain M, Al-Zaidan H, Rahbeeni Z, Qari A, Meyer BF, Al-Sayed M (2011) Identification of mutations causing hereditary tyrosinemia type I in patients of Middle Eastern origin. Mol Genet Metab 104(4):688–690. doi:10.1016/j.ymgme.2011.06.019
20. Demir M, Cosar S, Melek M (2014) Evaluation of plasma eosinophil count and mean platelet volume in patients with coronary slow flow. Clinics 69(5):323–326
21. Sahin DY, Gur M, Elbasan Z, Yildirim A, Akilli RE, Koyunsever NY, Ozaltun B, Gozubuyuk G, Kivrak A, Cayli M (2014) Mean platelet volume associated with aortic distensibility, chronic inflammation, and diabetes in patients with stable coronary artery disease. Clin Appl Thromb Hemost 20(4):416–421. doi:10.1177/1076029612468941

22. Coban E, Yazicioglu G, Berkant Avci A, Akcit F (2005) The mean platelet volume in patients with essential and white coat hypertension. Platelets 16(7):435–438. doi:10.1080/09537100500163572
23. Gasparyan AY, Ayvazyan L, Mikhailidis DP, Kitas GD (2011) Mean platelet volume: a link between thrombosis and inflammation? Curr Pharm Des 17(1):47–58
24. Schafer A, Bauersachs J (2008) Endothelial dysfunction, impaired endogenous platelet inhibition and platelet activation in diabetes and atherosclerosis. Curr Vasc Pharmacol 6(1):52–60
25. Tavil Y, Sen N, Yazici H, Turfan M, Hizal F, Cengel A, Abaci A (2010) Coronary heart disease is associated with mean platelet volume in type 2 diabetic patients. Platelets 21(5):368–372. doi:10.3109/09537101003628421
26. Gursoy A, Ertugrul DT, Pamuk B, Sahin M, Asik M, Yilmaz H, Haydardedeoglu F, Tutuncu NB, Demirag NG (2006) Mean platelet volume in patients with polycystic ovary disease. Platelets 17(7):505–506. doi:10.1080/09537100600901590
27. Kabil Kucur S, Gozukara I, Aksoy A, Uludag EU, Keskin H, Kamalak Z, Carlioglu A (2014) How medical treatment affects mean platelet volume as a cardiovascular risk marker in polycystic ovary syndrome? Blood Coagul Fibrinolysis. doi:10.1097/MBC.0000000000000229
28. Kebapcilar L, Taner CE, Kebapcilar AG, Sari I (2009) High mean platelet volume, low-grade systemic coagulation and fibrinolytic activation are associated with androgen and insulin levels in polycystic ovary syndrome. Arch Gynecol Obstet 280(2):187–193. doi:10.1007/s00404-008-0884-0
29. Rotterdam EA-SPCWG (2004) Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril 81(1):19–25
30. Diamanti-Kandarakis E, Alexandraki K, Piperi C, Protogerou A, Katsikis I, Paterakis T, Lekakis J, Panidis D (2006) Inflammatory and endothelial markers in women with polycystic ovary syndrome. Eur J Clin Invest 36(10):691–697. doi:10.1111/j.1365-2362.2006.01712.x
31. Farhangi MA, Keshavarz SA, Eshraghian M, Ostadrahimi A, Saboor-Yaraghi AA (2013) White blood cell count in women: relation to inflammatory biomarkers, haematological profiles, visceral adiposity, and other cardiovascular risk factors. J Health Popul Nutr 31(1):58–64
32. Silfeler DB, Kurt RK, Yengil E, Un B, Arica S, Baloglu A (2014) Evaluation of Mean Platelet Volume values in lean women with polycystic ovary syndrome. Pak J Med Sci 30(3):589–592. doi:10.12669/pjms.303.4475
33. Dogan BA, Arduc A, Tuna MM, Karakilic E, Dagdelen I, Tutuncu Y, Berker D, Guler S (2014) Association of mean platelet volume with androgens and insulin resistance in nonobese patients with polycystic ovary syndrome. Int J Endocrinol Metab 12(4):e18642. doi:10.5812/ijem.18642
34. Coban E, Ozdogan M, Yazicioglu G, Akcit F (2005) The mean platelet volume in patients with obesity. Int J Clin Pract 59(8):981–982. doi:10.1111/j.1742-1241.2005.00500.x
35. Papalou O, Livadas S, Karachalios A, Tolia N, Kokkoris P, Tripolitakis K, Diamanti-Kandarakis E (2015) White blood cells levels and PCOS: direct and indirect relationship with obesity and insulin resistance, but not with hyperandrogenemia. Hormones 14(1):91–99. doi:10.14310/horm.2002.1563