Observational Study

Medicine

OPEN

Assessment of neutrophil to lymphocyte ratio, C-reactive protein, mean platelet volume in obese, and nonobese patients with polycystic ovary syndrome

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Abstract

Polycystic ovary syndrome (PCOS) is associated with low-grade chronic inflammation.

This was a retrospective case–control study.

In the present study, the risk coefficients of neutrophil to lymphocyte ratio (NLR), high-sensitive C-reactive protein (hs-CRP), and mean platelet volume (MPV) in obese patients with PCOS were determined. This study was designed to investigate NLR, hs-CRP, and MPV levels in 68 obese patients with PCOS and 44 nonobese patients with PCOS, and our study group was matched with 47 obese and 43 nonobese controls, respectively.

PCOS group had higher MPV, NLR, insulin, glucose, and HOMA-IR rates than those of the controls. Subgroup analyses revealed that the obese PCOS group had higher NLR, hs-CRP, and MPV levels compared to those of controls. The obese PCOS group had higher NLR, hs-CRP, and MPV levels compared to those of the nonobese PCOS group. The odds ratios and 95% confidence intervals of those variables (NLR, hs-CRP, MPV) were found significant ($P < .05$). NLR, hs-CRP, and MPV variables were found statistically significant in the analysis of receiver operating characteristics.

Our study demonstrated that NLR, hs-CRP, and MPV levels are increased in patients with obese PCOS.

Abbreviations: FINS = fasting insulin, FPG = fasting plasma glucose, IR = insulin resistance, HOMA-IR = hemostasis of model assessment-insulin resistance, hs-CRP = high-sensitive C-reactive protein, MPV = mean platelet volume, NLR = neutrophil to lymphocyte ratio, PCOS = polycystic ovary syndrome.

Keywords: C-reactive protein, mean platelet volume, neutrophil to lymphocyte ratio, polycystic ovary syndrome

1. Introduction

Polycystic ovary syndrome (PCOS) is the most common gynecological endocrine disease in the reproductive age of women, with its incidence of 5% to 10%.[1] The characteristics of this syndrome are hirsutism, hyperandrogenism, menstrual disturbance, infertility, and infertility. Obesity, impaired glucose tolerance, insulin resistance, endothelial dysfunction, and increased inflammation are other well-known features. Chronic low-grade inflammatory state plays a key role in insulin resistance, type 2 diabetes mellitus, and atherosclerosis. Observation of the coexistence of PCOS with insulin resistance and atherosclerosis may be the result of the common pathway of inflammation in these clinical conditions.[2]

In previous studies, high-sensitive C-reactive protein (hs-CRP) was reported as a commonly used laboratory parameter in the detection of subclinical inflammation in patients with PCOS. Additionally, increased leukocyte counts were found to be an additional independent marker and prognostic factor in the development of inflammation.[3,4] In recent years, neutrophils to lymphocyte ratio (NLR) was widely studied in a variety of inflammatory diseases, such as PCOS, diabetes mellitus, ulcerative colitis, hypertension, and NLR is positively correlated with hs-CRP levels. NLR is an economic, effective, and convenient marker that can be an alternative to hs-CRP for inflammation.[5,6]

Several studies have confirmed that mean platelet volume (MPV) levels increase can also be a maker to assess inflammation.[7] Large platelets are metabolically more active and tend to stimulate the release of inflammatory cytokines. Further studies show that MPV values are higher in patients with PCOS than in controls.[8] In the present study, the risk coefficients of serum NLR, hs-CRP, and MPV in obese patients with PCOS were determined.

The authors have no funding and conflicts of interest to disclose.

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

The study protocol has been approved by the research institute's ethics committee (approval no. 2019-A-10-6).

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How to cite this article: Liu W, Li S, Lou X, Li D, Wang F, Zhang Z. Assessment of neutrophil to lymphocyte ratio, C-reactive protein, mean platelet volume in obese, and nonobese patients with polycystic ovary syndrome. Medicine 2022;101:29(e29678).

Received: 7 December 2021 / Received in final form: 21 April 2022 / Accepted: 11 May 2022

http://dx.doi.org/10.1097/MD.0000000000029678

2. Material and Method

2.1. Data source and collection

The protocol was approved by the Ethics Committee of Hangzhou Women's Hospital and informed consent was obtained from all of the participants. A total of 112 patients between 16 and 40 years of age (mean 26.06 ± 4.84 years) who presented to the clinic of Gynecological Endocrinology in Hangzhou Women's Hospital between December 2019 and December 2020 were diagnosed with PCOS based on their clinical and endocrinological data were included in this study. Additionally, age- and body mass index (BMI)-matched healthy subjects (n = 90) between 16 and 36 years of age (mean 26.54 ± 4.48 years) were divided into the study as the control group.

Obese PCOS patients with BMI of ≥25 kg/m^2 (n = 68) and no-obese PCOS patients with BMI of <25 kg/m^2 (n = 44) were enrolled into the study. Age- and BMI-matched 47 obese and 43 nonobese healthy subjects were divided into the study as the control group.

Diagnosis of PCOS was based on the Rotterdam criteria as having at least 2 of the following 3 criteria: first, oligomenorrhea (cycles lasting >35 days), or amenorrhea (<2 menstrual cycles in the past 6 months); second, clinical or biochemical hyperandrogenism; third, the polycystic appearance of the ovary on ultrasonography (senlarged ovaries with increased stromal volume and >10 follicles which measure 2 to 8 mm in diameter and localize along the periphery of the ovary in a way to form a pearl necklace' appearance) and the exclusion of other causes of hyperandrogenism, such as Cushing syndrome, congenital adrenal hyperplasia, or virilization. Exclusion criteria: alcohol consumption, tobacco use, taking drugs in the last 6 months (drugs that may interfere or affect insulin resistance and inflammation, such as estrogens, oral contraceptives, corticosteroids, immunosuppressants, antihyperlipidemic, antihypertensive, antihyperglycemic drugs, insulin-sensitizing drugs, and anti-inflammatory drugs), and other 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. Demographic information included age, menarche age, height, weight, BMI, and menstrual history. The study was explained to each subject, and written informed consent was read and signed by all the participants. The study protocol was approved by the ethics committee of Hangzhou Women's Hospital.

2.2. Blood samples determination

Fasting venous blood samples of the subjects were collected and centrifuged at 3500 rpm for 10 minutes at room temperature. The samples were stored at −80°C until being analyzed. Blood cell analysis was measured using an automatic blood analyzer (UniCelDxH 800, BECKMAN, USA). Serum levels of follicle-stimulating hormone, LH, estradiol progesterone, total testosterone, dehydroepiandrosterone sulfate, thyroid-stimulating hormone, fasting insulin (FINS), fasting plasma glucose (FPG), and hs-CRP were measured using commercially available kits on an autoanalyzer by enzyme chemiluminescent immunoassay (ADVIA1800, Siemens, Germany). Insulin resistance was calculated by the homeostasis model assessment-insulin resistance (HOMA-IR; FPG [mmol/L] × FINS [μIU/mL]/22.5).

2.3. Statistical analysis

Summary statistics are presented as the mean ± standard deviation for continuous variables. The Kolmogorov–Smirnov test was used to test the normal distribution of variables. The means of variables for the PCOS group and control group were tested using Student *t* test for independent groups. Binary logistic regression analysis was used to appraise the risk factors of obese patients with PCOS, including FPG, FINS, HOMA-IR, NLR, hs-CRP, and MPV levels. The variables were considered statistically significant for the model at a *P* value of <.05. All statistical analyses were carried out using the statistical packages for SPSS 19.0 version.

3. Results

Before subgroup analyses of obese and nonobese PCOS patients, our participants were compared with 2 groups as all PCOS patients (n = 112) and all controls (n = 90). Compared with controls, the PCOS group had significantly higher FPG, FINS, HOMA-IR, NLR, hs-CRP, and MPV levels. The anthropometric, hormonal, and metabolic characteristics of patients are summarized in Table 1.

In the comparison of obese PCOS patients and obese controls, the obese PCOS group had higher NLR, hs-CRP, and MPV levels. In the comparison of nonobese PCOS patients and nonobese controls, the nonobese PCOS group had higher FPG, FINS, HOMA-IR, NLR, hs-CRP, and MPV levels were found not significant. The results are shown in Tables 2 and 3.

When obese PCOS patients were compared to nonobese PCOS patients, the obese PCOS group had higher NLR, hs-CRP, and MPV levels, but no significant differences were identified in FPG, FINS, or HOMA-IR. The results are shown in Table 4.

Binary logistic regression analysis was used to appraise the risk factors of obese patients with PCOS, including FPG, FINS, HOMA-IR, NLR, hs-CRP, and MPV. NLR, hs-CRP, MPV are related to obesity with PCOS, The odds ratios and 95% confidence intervals of those variables (NLR, hs-CRP, MPV) were found to be significant and specific results were as follows: 0.616 (0.509–0.747), 0.004 (0.000–0.040), and 0.004 (0.000–0.036), respectively, the difference was statistically significant (*P* < .05). The results are shown in Table 5.

The variables found significant in the analysis of logistic regression were further analyzed using receiver operating characteristics (ROCs). The ROC curves are presented in Figure 1. NLR, hs-CRP, and MPV were found to be significant in the analysis of ROCs. The area under the curves (95% CI) value of NLR, hs-CRP, and MPV were found to be significant and

Table 1

Characteristics and the results of comparison between PCOS and control groups.

	PCOS (n = 112)	Controls (n = 90)	t	*P*value
Age (yr)	26.06 ± 4.84	26.54 ± 4.48	0.727	.468
BMI (kg/m^2)	26.48 ± 3.44	25.74 ± 3.45	1.502	.135
FPG (mmol/L)	4.96 ± 0.80	4.70 ± 0.67	2.379	**.018**
FINS (mmol/L)	13.76 ± 9.76	10.58 ± 6.50	2.648	**.009**
HOMA-IR	3.05 ± 2.37	2.25 ± 1.50	2.885	**.004**
NLR	1.94 ± 1.06	1.54 ± 0.92	2.855	**.005**
hs-CRP (mg/L)	4.63 ± 3.03	3.35 ± 2.28	3.341	**.001**
MPV (fL)	10.76 ± 0.68	10.28 ± 0.97	4.122	**<.001**
TT (ng/mL)	2.04 ± 1.02			
DHEA-S (nmol/L)	8.53 ± 4.12			
FSH (IU/L)	5.78 ± 1.81			
LH (mIU/mL)	11.30 ± 7.53			
E2 (pg/mL)	50.36 ± 26.33			
P (ng/mL)	0.65 ± 0.25			
TSH (mIU/mL)	1.81 ± 0.71			

BMI = body mass index, DHEA-S = dehydroepiandrosterone sulfate, E2 = estradiol, FINS = fasting insulin, FSH = follicle-stimulating hormone, FPG = fasting plasma glucose, HOMA-IR = hemostasis of model assessment-insulin resistance, hs-CRP = high-sensitive C-reactive protein, LH = luteinizing hormone, MPV = mean platelet volume, NLR = neutrophil to lymphocyte, P = progesterone, PCOS = polycystic ovary syndrome, TT = total testosterone, TSH = thyroid-stimulating hormone.

Table 2

Characteristics and the results of comparison between obese PCOS and obese control groups.

	Obese PCOS (n = 68)	Obese control (n =47)	t	*P* value
Age (yr)	25.73 ± 5.20	26.82 ± 4.65	1.157	.250
BMI (kg/m^2)	28.84 ± 2.08	28.58 ± 2.24	0.642	.522
FPG (mmol/L)	5.00 ± 0.83	4.85 ± 0.75	0.948	.345
FINS (mmol/L)	15.03 ± 10.53	12.64 ± 7.00	1.359	.177
HOMA-IR	3.34 ± 2.39	2.76 ± 1.68	1.433	.155
NLR	2.61 ± 0.75	2.13 ± 0.76	3.295	**.001**
hs-CRP (mg/L)	5.94 ± 2.79	4.19 ± 2.44	3.462	**.001**
MPV (fL)	11.13 ± 0.64	10.38 ± 1.34	3.942	**.001**

BMI = body mass index, FINS = fasting insulin, FPG = fasting plasma glucose, HOMA-IR =hemostasis of model assessment-insulin resistance, hs-CRP = high-sensitive C-reactive protein, MPV = mean platelet volume, NLR = neutrophil to lymphocyte, PCOS = polycystic ovary syndrome.

Table 3

Characteristics and the results of comparison between nonobese PCOS and nonobese control groups.

	Nonobese PCOS (n = 44)	Nonobese control (n = 43)	t	*P* value
Age (yr)	26.56 ± 4.23	26.23 ± 4.31	0.366	.715
BMI (kg/m^2)	22.82 ± 1.12	22.63 ± 1.23	0.735	.464
FPG (mmol/L)	4.89 ± 0.74	4.54 ± 0.52	2.513	**.014**
FINS (mmol/L)	11.79 ± 8.15	8.33 ± 5.09	2.366	**.020**
HOMA-IR	2.65 ± 2.29	1.67 ± 1.01	2.563	**.012**
NLR	0.90 ± 0.47	0.88 ± 0.55	0.229	.820
hs-CRP (mg/L)	2.60 ± 2.14	2.41 ± 1.67	0.468	.641
MPV (fL)	10.21 ± 0.15	10.17 ± 0.12	1.142	.257

BMI = body mass index, FINS = fasting insulin, FPG = fasting plasma glucose, HOMA-IR = hemostasis of model assessment-insulin resistance, hs-CRP = high-sensitive C-reactive protein, MPV = mean platelet volume, NLR = neutrophil to lymphocyte, PCOS = polycystic ovary syndrome.

Table 4

Characteristics and the results of comparison between obese PCOS and nonobese PCOS groups.

	Obese PCOS (n = 68)	Nonobese PCOS (n = 44)	t	*P* value
Age (yr)	25.73 ± 5.20	26.56 ± 4.23	0.888	.377
BMI (kg/m^2)	28.84 ± 2.08	22.82 ± 1.12	17.543	**<.001**
FPG (mmol/L)	5.00 ± 0.83	4.89 ± 0.74	0.698	**.014**
FINS (mmol/L)	15.03 ± 10.53	11.79 ± 8.15	1.727	.087
HOMA-IR	3.34 ± 2.39	2.65 ± 2.29	1.515	.133
NLR	2.61 ± 0.75	0.90 ± 0.47	13.273	**<.001**
hs-CRP (mg/L)	5.94 ± 2.79	2.60 ± 2.14	6.733	**<.001**
MPV (fL)	11.13 ± 0.64	10.21 ± 0.15	9.233	**<.001**

BMI = body mass index, FINS fasting insulin, FPG fasting plasma glucose, HOMA-IR hemostasis of model assessment-insulin resistance, hs-CRP high-sensitive C-reactive protein, MPV = mean platelet volume, NLR = neutrophil to lymphocyte, PCOS polycystic ovary syndrome.

specific results were as follows: (0.959–1.000), (0.736–0.903), and (0.848–0.965), respectively.

4. Discussion

Studies have shown that inflammatory markers such as serum hs-CRP level increase in PCOS patients. The underlying mechanism of increased hs-CRP is yet to be elucidated, and whether it is related to PCOS itself or accompanying obesity, and its potential mechanism remains to be further clarified.[4,8] We consider PCOS is a chronic inflammatory disease,[2] and obesity aggravates hs-CRP, our further subgroup analysis showed that the obese PCOS group had a significantly higher hs-CRP level than

Table 5

The results of logistic regression and ORs.

Variables	B	SE	Wald	OR (95% CI)	*P* value
FPG (mmol/L)	–0.182	0.262	0.483	0.834 (0.499–1.393)	.487
FINS (mmol/L)	–0.038	0.023	2.817	0.962 (0.920–1.006)	.093
hs-CRP (mg/L)	–0.484	0.098	24.461	0.616 (0.509–0.747)	**<.001**
HOMA-IR	–1.414	0.095	2.182	0.869 (0.721–1.047)	.140
NLR	–5.556	1.188	21.868	0.004 (0.000–0.040)	**<.001**
MPV (fL)	–5.645	1.183	22.763	0.004 (0.000–0.036)	**<.001**

CI = confidence interval, FINS = fasting insulin, FPG = fasting plasma glucose, HOMA-IR = hemostasis of model assessment-insulin resistance, hs-CRP = high-sensitive C-reactive protein, MPV = mean platelet volume, NLR = neutrophil to lymphocyte, OR = odds ratio.

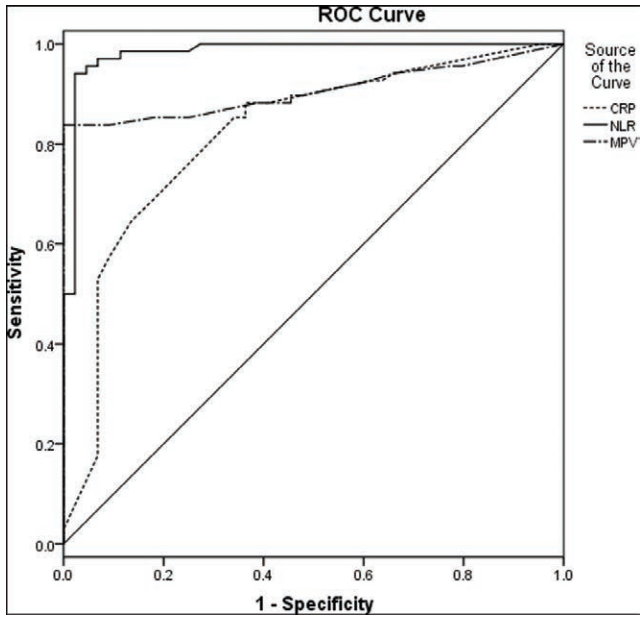

Figure 1. ROC curves, AUC values, SE, *P* value, and 95% CI of AUC of NLR, hs-CRP, and MPV. AUC = area under the curve, CI = confidence interval, CRP = C-reactive protein, hs-CRP = high-sensitive CRP, MPV = mean platelet volume, NLR = neutrophil to lymphocyte, OR = odds ratio, ROC = receiver operating characteristic, SE = standard error.

those of the control, which indicated that obesity is one of the important factors for the elevation of hs-CRP, and the results were consistent with Kahal et al.[3]

Several studies have found that PCOS patients' MPV levels were significantly higher than those of controls.[7] Another study found that patients with PCOS had higher MPV levels and after the treatment with ethinyl estradiol/cyproterone acetate or metformin, a significant decrease was observed in MPV level.[9] We speculated that the anti-inflammatory treatment in patients with PCOS regulates abnormal metabolism. Our study found that obese PCOS patients had higher MPV levels than those of obese controls. In the comparison of nonobese PCOS patients and nonobese controls, we failed to find similar results, which was consistent with Kebapcilar et al.[10] However, in another study performed by Yilmaz,[5] MPV level was found higher in nonobese patients with PCOS compared to nonobese controls. Therefore, the correlation between MPV, obesity, and PCOS remains to be further researched.

Elevated leukocyte count is an independent risk and prognostic factor in the development of inflammation and atherosclerosis, and several studies have shown that PCOS patients with elevated leukocyte count.[11,12] Recent studies confirmed that patients with PCOS had higher leukocyte count, NLR, and hs-CRP compared to controls, and their further study found that NLR was associated with HOMA-IR, hs-CRP.[13] In the

common inflammatory response system, leucocyte count, and NLR were expected to be increased along with CRP.[13] NLR, hs-CRP, and MPV variables were found statistically significant in the analysis of ROCs, the results show that NLR, hs-CRP, and MPV can be potent diagnostic makers to assess PCOS with metabolic abnormalities.

There were some limitations to this study. A cause–effect relation could not be established, since it was a retrospective analysis. It only reports there is an association between NLR, hs-CRP, and MPV in obese and nonobese patients with PCOS.

To sum up, our study found that obese PCOS patients had higher NLR, hs-CRP, and MPV levels. NLR, hs-CRP and MPV can be makers to assess PCOS with metabolic abnormalities.

Acknowledgments

The authors thank all participants who made this work possible and gratefully acknowledge the support of the clinicians and researchers who contributed to this study.

Author contributions

WL and FW contributed to the conception, design, SL and DL contributed to the data collection, statistical analysis, and drafting of the manuscript. WL and ZZ contributed to the preliminary review. All authors have seen and approved the final manuscript.

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