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Monocyte high density lipoprotein ratio and neutrophil lymphocyte ratio a novel marker in polycystic ovary syndrome

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ABSTRACT

Polycystic ovary syndrome (PCOS) is the most common endocrinological problem and is the cause of irregular menstruation in the women of reproductive age. The present study was undertaken to find out novel inflammatory markers in polycystic ovary syndrome (PCOS). Study population was divided into two groups controls (n=100) and cases (n=100) diagnosed with PCOS were recruited for the study. The anthropometric data such as Height, Weight, BMI and, hormonal profile LH, FSH, LH/FSH ratio, Thyroid profile, Testosterone, HOMA-IR, Lipid profile, Monocytes, Neutrophils were noted for all the participants. Taking BMI 25 kg/m^2 as the boundary, the control group was divided into Group A and Group B. Group A includes 53 subjects which is normal BMI group and Group B includes 47 subjects in the High-BMI group and among the cases Group C and Group D. Group C consists of 67 cases (normal BMI group) and 33 cases in the Group D (high BMI group). It is observed that monocyte HDL ratio (M/HDL ratio) and Neutrophil lymphocyte ratio (N/L ratio) in PCOS case group increased significantly (P<0.05) when compared to control group. Through the analysis of differences between the subgroups along with LH, LH/FSH, Total Testosterone, M/HDL ratio, and N/L ratio can be considered as specific indicators of PCOS disease. Through correlation analysis, M/HDL ratio and N/L ratio showed association with hormone levels of LH and Total Testosterone respectively. Through ROC curve, it is found that M/HDL ratio is >10.139 or N/L ratio is >1.7 had diagnostic value for PCOS, and the combined diagnostic value of the two was higher. From the observation of this study, it can be concluded that M/HDL ratio and N/L ratio are not chronic inflammatory indicators caused by obesity but caused by the PCOS disease itself. Therefore, M/HDL ratio and N/L ratio can be used as diagnostic markers for PCOS.

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1. Introduction

Polycystic ovary syndrome (PCOS) is a heterogeneous endocrinopathy with diverse clinical manifestations affecting women of reproductive age group.[1] It is the most common endocrinological problem and the most common cause of irregular menstruation in women of childbearing age.[1,2] The incidence of PCOS is 5%-20% of the total world population, and accounts for 75% of the anovulatory infertility cases. It is reported that, excessive androgen is the key hormone problem in anovulatory infertility cases with PCOS. In addition, obesity and insulin resistance (IR) can cause infertility in patients with PCOS,[1,3] but the specific mechanism of infertility is unclear as it is multifactorial. This creates research interest for clinicians to study about more new factors affecting women with PCOS to understand the pathophysiology.

Obesity, as a high-risk factor for PCOS infertility, can increase certain symptoms of PCOS, such as hyperandrogenism, hirsutism, infertility and pregnancy

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complications. In addition, obesity increases the risk of IR, hyperinsulinemia, and hyperlipidemia. Obesity and IR can lead to type 2 diabetes and cardiovascular disease, thereby exacerbating the reproductive and metabolic problems of PCOS.[4] It is reported that the pregnancy outcome of obese PCOS infertile patients will be improved after their weight is reduced to 5% of their initial weight.[5,6] It shows that obesity plays an important role in the pathological changes of PCOS.

Clinical studies show that PCOS patients are generally in a chronic low-grade inflammatory state, which can not only lead to ovarian dysfunction, but also promote the occurrence and development of PCOS, and is related to the metabolic abnormalities of PCOS patients.[7] Studies have shown that obesity can induce low-grade inflammation (LGI), and obesity itself is also a state of chronic LGI.[8]

More and more studies have shown that a variety of inflammatory factors, such as IL-18 and IL-1β, TNF-α, High sensitivity C-reactive protein (hs-CRP), CRP and MCP-1 all play a key role in the process of follicular formation, ovulation, luteal formation and withdrawal and follicular atresia in patients with PCOS.[9] It shows that chronic inflammatory response plays an important role in the process of follicular development disorder. So are these chronic inflammation caused by obesity or PCOS? Therefore, the study of inflammatory markers of PCOS is very important for the diagnosis of PCOS.

Studies have shown that serum hs-CRP is an indicator that reflects the subclinical inflammatory response in PCOS patients.[10] Monocyte/HDL-C ratio (MHR) and neutrophil/lymphocyte ratio (NLR) are used as biomarkers of systemic inflammation.[11] In recent years, it has been discovered that they are related to the occurrence and development of a variety of chronic inflammation-related diseases, such as cardiovascular disease, diabetes, hypertension, etc., and are related to hs-CRP levels.[12] MHR and NLR are economical and convenient to detect. It has been shown that MHR and NLR can be used as predictive markers for many diseases,[13] but there is little research on the direct relationship between MHR and NLR and PCOS and obesity. By detecting the inflammatory indexes such as MHR and NLR of PCOS, this study aims to explore the correlation between PCOS with MHR and NLR, so as to determine that it can be used as an inflammatory marker for the diagnosis of PCOS.

2. Materials and Methods

Present study was conducted at the Karpaga Vinayaga Institute of Medical Sciences and Research Centre, Madhuranthgam, Tamil Nadu during the period of February 2020 – February 2022 in the Department of Obstetrics and Gynecology after obtaining the institutional ethics committee approval.

Total 200 subjects were considered for the study which was divided into two groups controls (n=100) and cases (n=100). Infertile women other than PCOS were taken as control group and those who diagnosed with PCOS based on Rotterdam criteria[14] were considered as cases group. The anthropometric data such as Height, Weight, BMI and, hormonal profile LH, FSH, LH/FSH ratio, Thyroid profile, Total Testosterone, HOMA-IR, Lipid profile, C-Reactive Protein (CRP), WBC, Neutrophils, Lymphocytes, M/HDL ratio, N/L ratio were noted for all the participants. Taking BMI 25 kg/m^2 as the reference, both control group and cases group was divided into two sub groups. The control group was divided into sub groups, Group A and Group B. Group A includes 53 subjects which is normal BMI group and Group B includes 47 subjects in the High-BMI group. Similarly, the case group was divided into sub groups, Group C and Group D. Group C consists of 67 cases (normal BMI group) and 33 cases in the Group D (high BMI group). All the baseline, hormonal, biochemical and inflammatory parameters were compared among the groups and sub groups.

2.1. Inclusion criteria

Women of reproductive age group diagnosed with PCOS diagnostic criteria (established at the ESHRE/ASRM seminar in Rotterdam in 2003),[14] that is, the diagnosis of PCOS meets at least the following two conditions: (1) Clinical and/or biochemical Hyperandrogenemia; (2) Oligomenorrhea or anovulation; (3) Ultrasound examination of polycystic ovaries (≥12 follicles, 2-10mm in size).

2.2. Exclusion criteria

Women with preexisting cardiovascular diseases, other causes for irregular menstruation or excess androgens such as hyperprolactinemia, Cushing's syndrome, delayed congenital adrenal hyperplasia, pregnancy, and breastfeeding, known Type 1 or Type 2 diabetes, anu other chronic or acute infection (within 30 days), who are on contraceptives and/or anti-androgen therapy (within 6 months) were excluded from the study.

Baseline data like age, past history, menarche time, anthropometric data such as BMI, waist circumference (WC), systolic blood pressure (SBP), diastolic blood pressure (DBP), smoking rate; Hormonal profile such as follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin (P), estradiol (E2), total testosterone (TT), thyroid-stimulating hormone (TSH), free triiodothyronine (FT3); free thyroxine (FT4); fasting insulin level (INS), triglycerides (TGL), total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), inflammatory markers like, C-reactive protein (CRP), white blood cells (WBC), neutrophils Cells (N), lymphocytes (L),

monocytes (M), neutrophils/lymphocytes ratio (N/L ratio), monocytes/high-density lipoproteins ratio (M/H ratio)

Blood sample was collected from all the study subjects 2-3 days after normal menstruation. Patients with amenorrhea took blood when no dominant egg hold was determined under ultrasound. The subjects fasting elbow median venous blood from the morning was collected by vacuum blood collection and sent to the central clinical laboratory of our hospital for processing and testing.

Hormone level detection was done by Chemiluminescence detection (Roche COBAS E 411), Biochemical parameters were analyzed on Vitros 250 and BA 400 automated biochemistry analyzers. Insulin resistance (HOMA-IR) index= fasting insulin (μIU/ml) × fasting blood glucose (mmol/L)/22.5 Inflammatory markers like WBC, lymphocytes, neutrophils, monocytes were determined using five-part Horiba automatic hematology analyzer.

2.3. Statistical analysis

All the data was sorted by Excel and analyzed using SPSS 20.0. The counting data were expressed in the form of example or %, while the measurement data are expressed in mean and standard deviation and analyzed by student t-test. Spearman correlation analysis was used for correlation analysis. The receiver operating characteristic curve (ROC) and area under the curve (AUC) are used to judge the ability of M/HDL ratio and N/L ratio, and the combination of the two to diagnose PCOS patients. AUC>0.5 is of predictive value, P<0.05 indicates that the difference is statistically significant.

3. Results

Comparison of clinical indexes between PCOS group and healthy control group Comparing the basic information of PCOS group and CON group, it was found that age, menarche time, WC, blood pressure (BP), smoking rate and infertility years were not statistically significant (P>0.05), indicating that the subjects of the two groups were comparable. Compared with CON group, the levels of BMI, BLH, LH/FSH, TT, HOMA-IR, TGL, LDL, Monocytes, N/L ratio and M/HDL ratio in PCOS group were increased significantly and the level of HDL was decreased (P < 0.05). (Table 1)

Taking BMI=25kg/m2 as the boundary, the control group and the case group are divided into two subgroups: Normal-BMI and High-BMI, namely Group A, Group B, Group C, and Group D. Comparing group B with group A and group D with group C: WC, HOMA-IR, TGL, LDL, CRP, WBC are all increased (P<0.05), HDL is decreased (P<0.05), indicating these indicators are correlated with BMI. However, compared with group B and group D, both LDL and CRP were increased (P<0.05), indicating that LDL and CRP were also related to PCOS disease; compared group C with group A and group D with group B: LH, LH/FSH, TT, HOMA-IR, Monocytes, N/L ratio, M/HDL ratio all increased (P<0.05), indicating that these indicators are related to PCOS disease. However, compared group B with group A: both HOMA-IR and Monocytes were increased (P<0.05), indicating that they were also related to BMI. Then N/L ratio and M/HDL ratio can be used as specific inflammatory markers of PCOS disease. (Table 2)

Through spearman correlation analysis between specific inflammatory indexes MHR and NLR and hormone levels LH, LH/FSH and TT in PCOS group, the results showed that MHR was positively correlated with LH (r=0.523, p<0.001, Figure 1 A), TT (R=0.559, P<0.001, Figure 1 C) significantly, while MHR was not correlated with LH/FSH (r=0.104, P>0.05, Figure 1 B); N/L ratio was positively correlated with LH (r=0.631, P<0.001, Figure 1 D), TT (r=0.592, P<0.001, Figure 1 F), there was no correlation between NLR and LH/FSH (r=0.077, P>0.05, Figure 1 E). The results showed that M/HDL ratio and N/L ratio were related to the abnormal hormone level expression of PCOS. (Figure 1)

The diagnostic value of M/HDL ratio, N/L ratio and the combination of the two in PCOS infertility patients In all PCOS patients, the ROC curve of M/HDL ratio showed that the area under the curve was 0.705 (95%CI: 0.631-0.779). According to the Youden index, the cut-off value was 10.139. When M/HDL ratio >10.139 was used as the basis for the diagnosis of PCOS, the sensitivity and specificity were 75.2% and 71.4% respectively. The ROC curve of N/L ratio shows that the area under the ROC curve is 0.692 (95%CI: 0.617-0.766). According to the Youden index, the critical value is 1.7. When N/L ratio >1.7 was used as the basis for the diagnosis of PCOS, the sensitivity and specificity were 75.2% and 66.3% respectively. The ROC curve of the combination of MHR and NLR showed that the area under the curve was 0.729 (95%CI: 0.659-0.800), and the sensitivity and specificity were 75.2% and 71.4% respectively (Figure 2). It shows that the combination of the two to diagnose PCOS has more diagnostic value.

4. Discussion

Polycystic ovary syndrome (PCOS) is a complex multifactorial disease, which is a difficult problem that plagues the fertility of women of childbearing age. Infertility patients with PCOS are usually obese, and studies have shown that obesity may be the cause of the clinical symptoms of PCOS.[13] This is consistent with our study. Compared with the control group with tubal infertility during the same period, the BMI of the PCOS group was higher significantly. We compared the basic information of the two groups of patients in the PCOS group and the control group and found that: age, menarche time, BMI, WC, blood pressure (BP), smoking rate and years of infertility were

Table 1: Comparison of indicators between the two groups of infertility patients

Parameter	PCOS Case Group (N=100)	Control Group (N=100)	P value
Age (years)	31.09±3.16	31.27±2.91	
Menarche time	13.58±2.43	14.06±1.87	
BMI (kg/m2)	25.94±3.78	23.8±3.59	0.031
WC (cm)	82.59±16.20	77.74±10.03	
SBP (mmHg)	119.18±14.97	114.43±11.74	
DBP (mmHg)	74.77±11.02	71.75±6.22	
Smoking rate (%)	0	0	
Infertility years	4.54±2.0	3.98±2.38	
FSH (mIU/ml)	6.21±1.31	6.41±1.55	
LH (mIU/ml)	8.53±4.98	5.66±3.58	0.001
LH/FSH ratio	1.22±0.94	0.81±0.67	0.043
Prolactin (ng/ml)	17.59±8.71	16.24±5.65	
E2 (pg/ml)	36.39±14.49	37.07±14.40	
TT (ng/ml)	0.37±0.17	0.24±0.11	0.004
TSH (uIU/ml)	3.77±1.56	2.95±1.06	
FT3 (pmol/L)	4.58±1.37	4.24±1.26	
FT4 (pmol/L)	14.09±8.51	13.97±9.42	
HOMA-IR	3.05±2.37	2.25±1.50	0.005
TGL (mg/dL)	158.05±133.79	109.43±65.6	0.001
CHO (mg/dL)	207.42±43.30	191.66±34.41	
LDL (mg/dL)	122.55±36.73	114.82±27.45	0.015
HDL (mg/dL)	50.26±8.89	53.35±10.44	0.045
CRP (mg/L)	4.83±3.03	3.47±2.28	
WBC (×109/L)	7.98±2.28	7.22±2.19	
Neutrophils (×109/L)	4.81±1.58	4.24±1.45	
Lymphocytes (×109/L)	2.38±0.76	2.27±1.05	
Monocytes (×109/L)	0.61±0.18	0.51±0.20	0.001
M/HDL ratio	1.94±1.06	1.54±0.92	0.004
N/L ratio	11.46±7.73	8.77±5.46	0.005

not statistically significant (P>0.05), indicating that the subjects in the two groups were comparable and can be used for the following analysis. However, compared with the control group, the LH, LH/FSH, TT, HOMA-IR, TGL, LDL, Monocytes, N/L ratio, and M/HDL ratio levels in the PCOS group were increased significantly, the HDL level was decreased (P<0.05). It shows that these indicators may be involved in the pathophysiological process of PCOS, but it can not be ruled out whether the changes of these indicators are induced by obesity.

In recent years, more and more infertile patients with normal weight have been diagnosed with PCOS, so it is particularly important to find the group specific index of PCOS. Because we divided PCOS group and con group into two subgroups, normal BMI and high BMI, with BMI=25kg/m2 as the boundary. This can effectively match BMI and eliminate the interference caused by obesity. Studies have found that insulin resistance plays an important role in the of PCOS and genetic susceptibility.[15] Obese patients are prone to lipid distribution disorder and insulin resistance.[16]

Therefore, this insulin resistance in PCOS patients will lead to the increase of triglyceride (TGL) and the decrease of high-density lipoprotein (HDL), resulting in vascular atherosclerosis and hypertension.[17–19] Moreover, the over accumulated adipose tissue in obese PCOS patients secretes many adipokines, such as adiponectin, tumor necrosis factor-α (TNF-α), monocyte chemoattractant protein-1 (MCP-1), etc. These factors cause the activation of the nuclear transcription factor-κB (NF-κB) system and promote the inflammatory response.[20] CRP is an acute phase protein and can also be used as a sensitive marker of systemic inflammation. Previous studies have shown that its concentration is significantly increased in patients with PCOS and is positively correlated with BMI.[21] This is consistent with our results: the increase in WC, HOMA-IR, TG, LDL, CRP, WBC, Monocytes (P<0.05), the decrease in HDL (P<0.05) are related to BMI. Abnormal hypothalamic-pituitary-ovarian or adrenal axis is the pathophysiological factor of PCOS. The disorder of gonadotropin-releasing hormone (GnRH) secretion mode leads to the relative increase in the release of sex hormones.[22] Ovarian estrogen is the cause of the abnormal feedback mechanism, which leads to an increase in the release of LH.[23] Although there are no significant differences in FSH, they also have a downward trend. Studies have shown that: the ratio between

Table 2: Comparison of indicators between PCOS group and control group with different BMI

Parameter	Group A	Group B	P value	Group C	Group D	P value	P value	P value
Age (years)	30.57±3.01	31.51±3.21		31.25±3.01	31.31±2.72			
Menarche time	13.86±2.01	13.45±1.98		13.94±1.65	14.11±1.37			
BMI (kg/m2)	21.66±2.10	27.97±2.40	0.001	21.87±1.940	28.00±2.21	0.001		
WC (cm)	71.46±8.13	89.58±14.10	0.009	71.29±4.62	84.53±4.51	0.013		
SBP (mmHg)	113.18±8.97	117.23±15.07		110.92±7.97	112.18±8.34			
DBP (mmHg)	72.05±6.22	75.77±7.07		70.83±6.02	71.99±5.74			
Smoking rate (%)	0	0		0	0			
Infertility years	3.61±1.68	4.41±2.10	0.033	3.76±2.36	4.10±2.42			
FSH (mIU/ml)	6.55±1.49	6.04±1.18		6.62±1.53	6.04±1.50			
LH (mIU/ml)	9.14±5.24	8.22±4.84		5.90±3.67	5.26±3.40		0.009	0.006
LH/FSH ratio	1.36±0.52	1.19±0.72	0.048	0.78±0.50	0.83±0.51		0.021	0.035
Prolactin (ng/ml)	18.17±7.94	16.52±7.67		17.35±6.09	15.71±6.83			
E2 (pg/ml)	39.82±15.95	34.59±13.42		35.19±14.17	38.06±13.71			
TT (ng/ml)	0.37±0.19	0.37±0.15		0.23±0.11	0.25±0.12		0.001	0.007
TSH (uIU/ml)	2.28±1.16	2.01±1.06		2.19±1.21	1.98±0.94			
FT3 (pmol/L)	4.20±0.85	4.34±1.25		4.05±0.98	4.21±1.16			
FT4 (pmol/L)	14.39±5.42	13.82±6.21		13.80±8.19	14.27±7.46			
HOMA-IR	2.60±2.29	3.34±2.39	0.033	1.67±1.01	2.76±1.68	0.021	0.028	0.041
TGL (mg/dL)	100.12±42.53	181.63±154.16	0.001	90.37±57.60	129.36±71.77	0.001		
CHO (mg/dL)	182.19±38.60	210.76±42.46	0.015	187.67±32.04	192.39±37.83			0.045
LDL (mg/dL)	110.01±37.06	128.92±35.13	0.006	110.40±26.63	121.98±27.02	0.001		0.048
HDL (mg/dL)	52.88±9.26	48.64±8.49	0.023	54.81±10.42	49.48±8.11	0.017		
CRP (mg/L)	2.80±2.14	4.94±2.79	0.001	2.71±1.67	3.99±2.44	0.002		0.039
WBC (×109/L)	7.31±2.13	8.14±1.42	0.021	7.13±1.96	7.48±2.10	0.048		
Neutrophils (×109/L)	4.26±1.52	4.84±1.10	0.012	4.15±1.24	4.32±1.25			0.042
Lymphocytes (×109/L)	2.31±0.62	2.44±0.63		2.15±0.91	2.32±0.74			
Monocytes (×109/L)	0.57±0.14	0.63±0.26	0.023	0.50±0.19	0.52±0.18		0.038	0.013
M/HDL ratio	11.27±6.13	11.83±5.26		8.56±4.17	8.89±4.09		0.001	0.002
N/L ratio	1.90±0.47	2.06±0.75		1.50±0.55	1.61±0.76		0.042	0.039

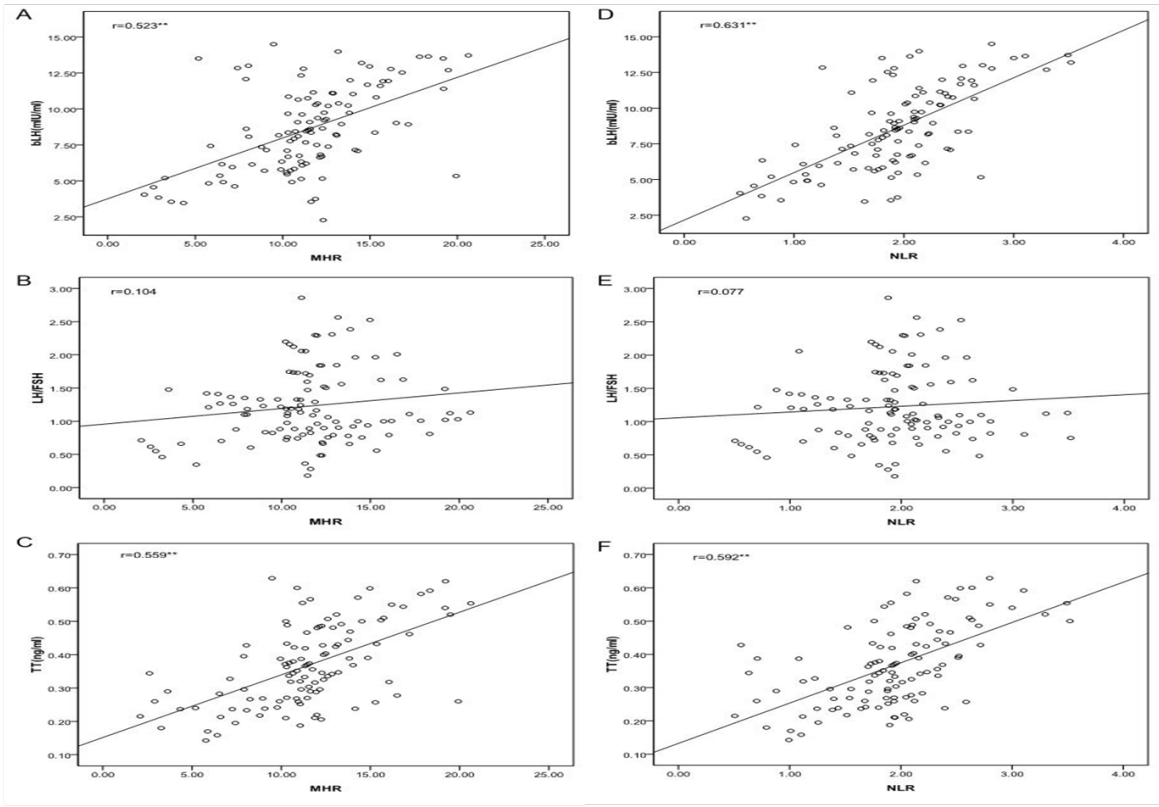

Fig. 1: Correlation of MHR and NLR with BLH, LH/FSH and TT respectively. * is P<0.05, ** is P < 0.01

LH/FSH is usually between 1-2. In women with polycystic ovary disease, it can be as high as two or three.[24] Although LH/FSH did not reach 2 in our study, we confirmed that the increase in LH/FSH (P<0.05) is related to PCOS disease. Through research, we found that LH, LH/FSH, TT, NLR and M/HDL ratio can be used as specific indicators of PCOS disease (Table 2).

It has been found that chronic low-grade inflammatory response runs through the whole pathological process of PCOS and plays an important role in the occurrence and development of PCOS. NLR and MHR are new composite inflammatory indexes related to leukocytes,[25,26] both of which are the ratio of two inflammatory indexes, avoiding the influence of factors such as blood volume on the absolute value. They are more stable and more clinical significance than a single index.

Neutrophils are one of the important leukocyte subsets involved in and controlling inflammatory response, their increase is often related to the occurrence, progress and severity of inflammatory response.[27,28] Lymphocytes are an important part of the body's immune function. During inflammatory reaction, their proliferation function is damaged and apoptosis is accelerated. At the same time, the stress of catecholamine and cortisol hormone in the body is increased, which can lead to further reduction of lymphocytes.[29] Therefore, NLR is an inflammatory index reflecting these two important systems at the same time and has good clinical value. It has been studied that the increase of inflammatory factor levels in PCOS patients changes their original negative correlation with Anti-Müllerian hormone (AMH) levels and induces increased testosterone synthesis.[30] Hyperandrogenemia reduces the levels of estradiol and progesterone in gonadotropin hypothalamic cells and enhances excessive secretion of gonadotropin releasing hormone and LH hypersecretion.[31] Our results also confirmed this point. The results of this study showed that the inflammatory index N/L ratio in the PCOS group was positively correlated with the hormone levels LH and TT. Monocytes are the source of various inflammatory cytokines and participate in the occurrence and development of inflammatory reactions. Activated monocytes can recognize various inflammatory cells and inflammatory factors.[32] HDL-C can remove excess cholesterol, inhibit the formation of foam cells, thereby preventing the occurrence of atherosclerosis. It can also inhibit the production of various chemokines, thereby inhibiting the activation of monocytes and related inflammatory reactions. In addition, it can play an anti-inflammatory and antioxidant effect by hindering the migration of macrophages and LDL-C molecule oxidation.[33] Therefore, the increase of MHR reflects the enhancement of tissue inflammation and the decrease of anti-inflammatory and antioxidant capacity. It

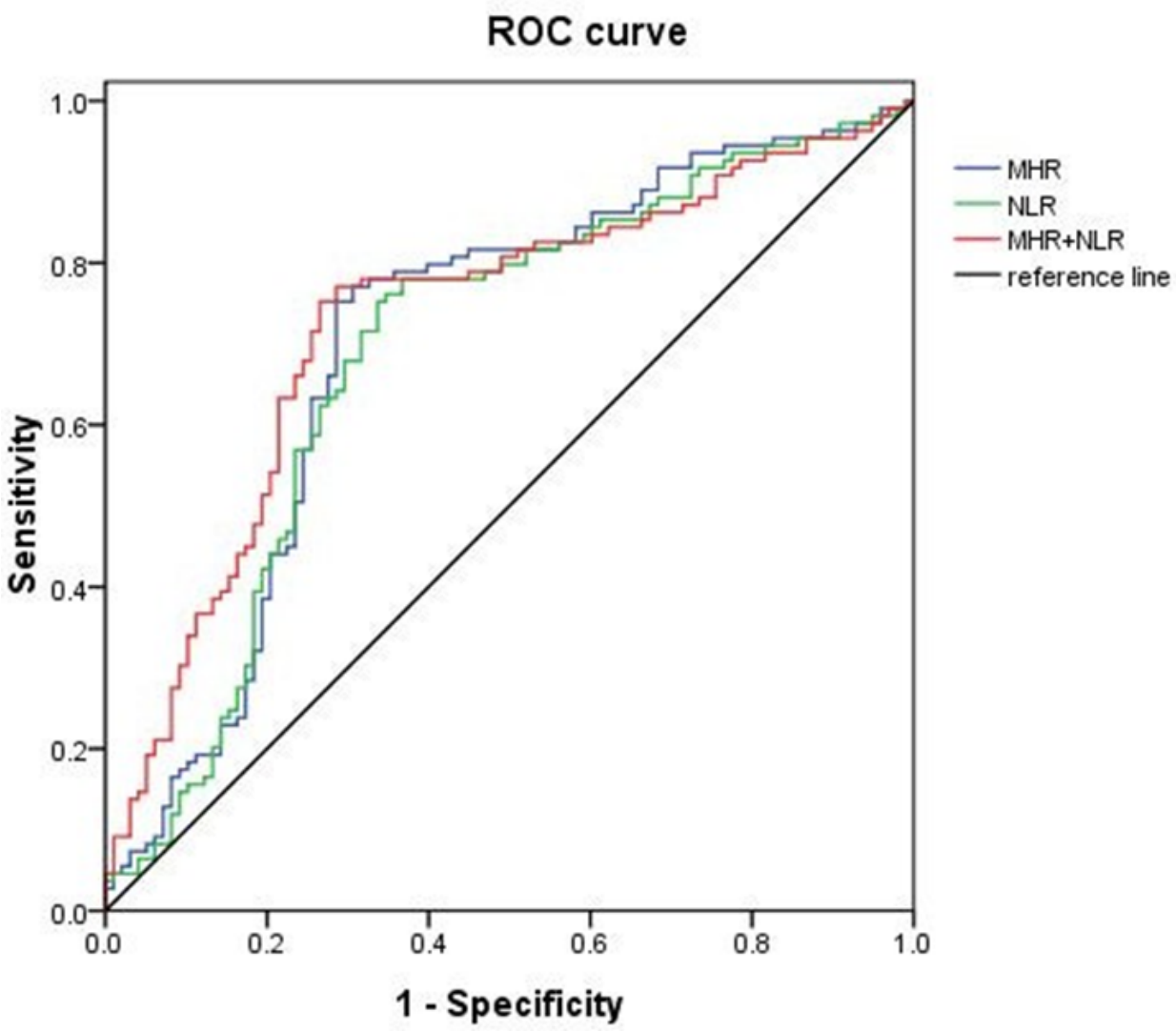

Fig. 2: ROC curve of MHR, NLR and the combination of the two

can also reflect the condition of blood lipids, which is an ideal indicator of inflammation. Studies have shown that the endocrine, blood glucose and lipid metabolism disorders in PCOS patients will be worse than those in the normal control group, and the impact of LH and LH/FSH will increase.[34] And the high level of androgen in the blood circulation of PCOS patients can inhibit the negative feedback of estrogen and progesterone on the pulse release of LH, which has become one of the potential reasons for the increase of LH secretion and the change of LH/FSH ratio. Our results also confirmed this point. The results of this study showed that the inflammatory index M/HDL ratio in the PCOS group was positively correlated with the hormone levels LH and TT respectively. It shows that chronic inflammation can cause endocrine disorders in PCOS. However, there is no correlation between N/L ratio and M/HDL ratio and LH/FSH in this study. This may be due to the small sample size of this study, and the disorder of the gonadotropin-releasing hormone (GnRH) secretion pattern in PCOS led to an increase in the release of LH and FSH,[35] resulting in the insignificant correlation between LH/FSH and inflammatory indexes. It is necessary to expand the sample size for research.

Since NLR and MHR can be used as a specific indicator of PCOS disease, we found through the ROC curve that MHR>10.139 or NLR>1.7 have diagnostic value for PCOS. The area under the ROC curve of MHR and NLR for the diagnosis of PCOS is 0.705 (95% CI: 19 0.631-0.779) and 0.692 (95% CI: 0.617-0.766). The combination of the two has higher predictive value, and the area under the ROC curve for diagnosing PCOS is 0.729 (95%CI: 0.659-0.800). In conclusion, MHR and NLR are not chronic inflammatory indicators caused by obesity but caused by PCOS disease itself. MHR and NLR can affect hormone levels and can be

used as important diagnostic markers for PCOS.

5. Source of Funding

None.

6. Conflict of Interest

None.

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