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Original Article *Özgün Araştırma*

ENHANCING DIAGNOSTIC ACCURACY IN POLYCYSTIC OVARY SYNDROME USING NOVEL INFLAMMATORY INDICES

Polikistik Over Sendromunda Tanısal Doğruluğun Yeni İnflamatuar İndekslerle Artırılması

Funda BULUT ARIKAN[1] **Nevin SAĞSÖZ**[2]

[1] *Department of Physiology, Faculty of Medicine, Kırıkkale University, KIRIKKALE, TÜRKİYE*
[2] *Department of Obstetrics and Gynecology, Faculty of Medicine, Kırıkkale University, KIRIKKALE, TÜRKİYE*

ABSTRACT

Objectives: Polycystic ovary syndrome (PCOS) is characterized by a complicated and incompletely understood pathophysiology. This study investigates the role of inflammation in its pathophysiology, compares the diagnostic performance of inflammatory indices, and assesses the clinical utility of novel biomarkers.

Material and Methods: This retrospective study included 30 patients with PCOS and 32 healthy controls. Inflammatory indices including neutrophil to lymphocyte ratio (NLR), monocyte to lymphocyte ratio (MLR), neutrophil to monocyte ratio (NMR), platelet to lymphocyte ratio (PLR), platelet large cell ratio (PLCR), mean platelet volume to lymphocyte ratio (MPVLR), systemic immune inflammation index (SII), systemic inflammation response index (SIRI), multi-inflammatory index (MII), and monocyte to high density lipoprotein ratio (MHR) were calculated. Receiver operating characteristic (ROC) curve analysis evaluated their diagnostic performance. Biochemical, hormonal, hematological, and inflammatory parameters were measured using ELISA and an automated analyzer.

Results: Inflammatory indices SII (p=0.006), SIRI (p=0.022), MII (p=0.013), and MHR (p=0.003) were significantly higher in patients, while PLCR was lower (p=0.024). Biochemical parameters CRP (p=0.027), insulin (p=0.021), and LDL (p=0.027) were elevated, HDL decreased (p=0.035). ROC analysis identified MHR as the most accurate biomarker (AUC=0.747, 100% specificity), followed by CRP (AUC=0.726) and MII (AUC=0.713). SII and SIRI showed moderate but relevant accuracy. All were statistically significant (p< 0.05).

Conclusion: The present study highlights the potential of inflammation-based indices particularly MHR, MII, SII, SIRI, and CRP as valuable biomarkers in PCOS diagnosis. MHR showed the strongest diagnostic performance (100% specificity), while CRP and MII also demonstrated good accuracy. SIRI's high sensitivity supports its role in early detection, and both SII and SIRI may serve as complementary markers. Overall, the results underscore the significance of inflammation in PCOS and support the clinical utility of these markers. PCOS influences hematological and biochemical parameters as well as inflammatory indices.

Keywords: *PCOS, inflammatory indices, diagnostic accuracy.*

ÖZ

Amaç: Polikistik over sendromu (PCOS), kompleks ve hâlen tam olarak aydınlatılamamış bir patofizyoloji ile karakterizedir. Bu çalışma, PCOS'un patofizyolojisinde inflamasyonun rolünü araştırmayı, inflamatuar indekslerin tanısal performanslarını karşılaştırmayı ve yeni biyobelirteçlerin klinik kullanım değerini değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntemler: Bu retrospektif çalışmaya, 30 PCOS hastası ve 32 sağlıklı kontrol birey dâhil edilmiştir. Nötrofil/lenfosit oranı (NLR), monosit/lenfosit oranı (MLR), nötrofil/monosit oranı (NMR), platelet/lenfosit oranı (PLR), büyük platelet oranı (PLCR), ortalama platelet hacmi/lenfosit oranı (MPVLR), sistemik immün-inflamasyon indeksi (SII), sistemik inflamasyon yanıt indeksi (SIRI), multi inflamatuar indeks (MII) ve monosit/yüksek yoğunluklu lipoprotein oranı (MHR) gibi inflamatuar indeksler hesaplanmıştır. Tanısal performansları, ROC eğrisi analizi ile değerlendirilmiştir. Biyokimyasal, hormonal, hematolojik ve inflamatuar parametreler ELISA ve otomatik analizör kullanılarak ölçülmüştür.

Bulgular: SII (p=0,006), SIRI (p=0,022), MII (p=0,013) ve MHR (p=0,003) değerleri hasta grubunda anlamlı olarak yüksek bulunurken; PLCR değeri anlamlı şekilde düşüktü (p=0,024). Biyokimyasal parametrelerden CRP (p=0,027), insülin (p=0,021) ve LDL (p=0,027) düzeyleri artmış; HDL düzeyi ise azalmıştı (p=0,035). ROC analizinde, MHR en yüksek tanısal doğruluk gösteren biyobelirteç olarak tanımlandı (AUC=0,747, %100 özgüllük), bunu CRP (AUC=0,726) ve MII (AUC=0,713) izledi. SII ve SIRI, orta düzeyde ancak anlamlı tanısal doğruluk gösterdi. Tüm bulgular istatistiksel olarak anlamlıydı (p<0,05).

Sonuç: Bu çalışma, özellikle MHR, MII, SII, SIRI ve CRP gibi inflamasyon temelli indekslerin PCOS tanısında değerli biyobelirteçler olabileceğini ortaya koymaktadır. MHR, %100 özgüllük ile en güçlü tanısal performansı göstermiştir. CRP ve MII de yüksek doğruluk oranlarıyla dikkat çekmiştir. SIRI'nin yüksek duyarlılığı, erken tanıda önemli bir belirteç olabileceğini desteklemektedir. Hem SII hem de SIRI, tamamlayıcı tanı araçları olarak değerlendirilebilir. Genel olarak, elde edilen sonuçlar inflamasyonun PCOS üzerindeki önemini vurgulamakta ve bu indekslerin klinik kullanım potansiyelini desteklemektedir. PCOS, hematolojik ve biyokimyasal parametreler kadar inflamatuar indeksleri de etkilemektedir.

Anahtar Kelimeler: *PCOS, inflamatuar indeksler, tanısal doğruluk*

Correspondence / Yazışma Adresi: **Dr. Funda BULUT ARIKAN**
Department of Physiology, Faculty of Medicine, Kırıkkale University, KIRIKKALE, TÜRKİYE
Phone / Tel: +905331402676 **E-mail** / E-posta: funbulut@kku.edu.tr.
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INTRODUCTION

Polycystic ovary syndrome (PCOS) is a complex and heterogeneous ovarian dysfunction disorder characterized by menstrual dysfunction, androgen excess, and infertility, as well as metabolic abnormalities including obesity and insulin resistance. It is a common endocrine disorder primarily affecting women of reproductive age.[1] PCOS affects an estimated 6–13% of women in this population, yet approximately 70% of these individuals remain undiagnosed worldwide.[2] Although the exact pathogenesis of PCOS has not been fully elucidated, chronic low-grade inflammation, characterized by the simultaneous expression of proinflammatory and anti-inflammatory cytokines and a multifaceted immunological interplay, is considered a key factor in disease initiation and progression.[1,3]

Therefore, this study aims to investigate inflammatory markers in patients with PCOS, a condition in which inflammation plays a crucial etiological role, including neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), neutrophil-to-monocyte ratio (NMR), platelet-to-lymphocyte ratio (PLR), platelet-large cell ratio (PLCR), mean platelet volume (MPV), MPV-to-lymphocyte ratio (MPVLR), systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), multi-inflammatory index (MII), and monocyte-to-high-density lipoprotein ratio (MHR). The neutrophil-to-lymphocyte ratio (NLR) is a widely used parameter for assessing inflammatory status, calculated by dividing the absolute neutrophil count by the absolute lymphocyte count.[4] It holds significant prognostic value in various infectious and inflammatory diseases,[5,6] cardiovascular diseases,[7] and multiple cancer types.[8] Other inflammatory indices used to evaluate inflammation include the MLR and NMR.[9–11] One study reported the utility of MLR as an inflammation marker in patients with vitiligo.[9] Another study suggested that elevated MLR, combined with high serum white blood cell (WBC), C-reactive protein (CRP), and lymphocyte levels, could aid in differentiating parapneumonic effusion and thoracic empyema.[10]

Additional commonly used inflammatory markers include PLR, MPV, and MPVLR. As integrative reflections of thrombotic and inflammatory pathways, PLR, MPV, and MPVLR have demonstrated prognostic significance in various diseases, including cancer, sepsis, and multisystem inflammatory syndrome.[12–16] Increasing evidence indicates that platelets play a crucial role in the pathophysiology of sepsis.[12] Platelet activation is induced by inflammatory and coagulation responses in sepsis and damaged endothelial cells, and these activated platelets can exacerbate coagulation disorders and systemic inflammatory reactions.[17] Consequently, elevated PLR has been proposed as an indicator of a heightened host thrombotic/inflammatory response.[12,13]

In this study, SII, SIRI, MII, and MHR will also be evaluated in patients with PCOS. The SII is a recently developed marker reflecting systemic inflammatory response, with elevated levels associated with various diseases and malignancies.[18,19] One study specifically identified a relationship between SII and PCOS.[18] SIRI represents the balance between inflammatory response and immune status and was first used to predict survival outcomes in pancreatic cancer patients undergoing chemotherapy.[18,20]

MHR, another parameter under investigation, is a novel composite predictor that reflects the balance between monocyte-driven inflammation and oxidative stress and HDL cholesterol levels. It has been suggested that MHR has superior predictive power for clinical outcomes compared to monocyte count or HDL cholesterol concentration alone.[21]

MII is an integrated biomarker calculated as the product of NLR and CRP, used to evaluate systemic inflammatory status. Recent studies have explored its prognostic and diagnostic utility in various pathological conditions, including musculoskeletal disorders, malignancies, cardiovascular diseases, COVID-19, and neurological disorders.[22–24]

MATERIALS AND METHODS

Study Population

This controlled, retrospective study was conducted with a total of 62 volunteers (30 patients and 32 controls). Demographic and clinical data of patients aged 20 to 45 years, diagnosed with PCOS between January 2020 – August 2024 at the Department of Obstetrics and Gynecology clinic of Kırıkkale University Faculty of Medicine Hospital, which obtained from the hospital's electronic database. The diagnosis of PCOS was established based on the Rotterdam criteria, which require at least two of the following three features: (1) clinical and/or biochemical hyperandrogenism (HA), (2) oligo- or anovulation, and (3) polycystic ovarian morphology (PCOM) via ultrasound (Rotterdam ESHRE/ASRM, 2003). Polycystic ovary morphology was defined as ≥12 follicles (2–9 mm) and/or ovarian volume ≥10 cm³ in at least one ovary. Detection in a single ovary was sufficient for diagnosis.

Inclusion and Exclusion Criteria

Healthy Controls Inclusion Criteria: Absence of PCOS, endocrine disorders, malignancy, and pregnancy; no use of anti-inflammatory or hormonal medications within the past 6 months.

Healthy Controls Exclusion Criteria: Presence of PCOS, endocrine disorders, malignancy, or pregnancy; use of relevant medications in the past 6 months.

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PCOS Patients Inclusion Criteria: Diagnosis based on at least two Rotterdam criteria; no endocrine disorders, malignancy, or pregnancy; no recent use of medications affecting inflammation.

Ethical Considerations

All necessary ethical approvals for the study were obtained from the Non-Interventional Clinical Research Ethics Committee of Kırıkkale University (Date: 16.10.2024, Decision No: 2024.01.02). The study was conducted in accordance with relevant ethical guidelines and the principles outlined in the Declaration of Helsinki.

Statistical Analyses

All data were analyzed using IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, NY, USA). The Shapiro–Wilk test was employed to assess the normality of data distribution. Based on the results of the normality test, differences in means between the patient and control groups were analyzed using either the independent samples t-test or the Mann–Whitney U test. To evaluate the diagnostic performance of the inflammatory markers, Receiver Operating Characteristic (ROC) curve analysis was performed. The Area Under the Curve (AUC) was calculated to assess the model's discriminatory power. The optimal cut-off value was determined using the Youden index, which identifies the threshold that maximizes the sum of sensitivity and specificity (Youden index = sensitivity + specificity − 1). A p-value of <0.05 was considered statistically significant. Depending on the distribution of the data, Pearson's or Spearman's two-tailed correlation analysis was applied to assess relationships between variables.

Laboratory Parameters

For biochemical analyses, venous blood samples were collected between the 2nd and 5th days of the menstrual cycle following a 12-hour fasting period. All samples were processed in the same laboratory under standardized procedures. The biochemical parameters analyzed in this study included: C-reactive protein (CRP), follicle-stimulating hormone (FSH), luteinizing hormone (LH), thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxine (FT4), glucose, insulin, HbA1c, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides, total cholesterol, hemoglobin, red cell distribution width (RDW), platelet distribution width (PDW), hematocrit (HCT), white blood cell count (WBC), neutrophil count, lymphocyte count, monocyte count, platelet count, mean platelet volume (MPV), plateletcrit (PCT), PLCR, mean corpuscular volume (MCV), and mean corpuscular hemoglobin (MCH).

Biochemical parameters (CRP, FSH, LH, TSH, FT3, FT4, insulin, HbA1c) were measured using Roche Elecsys electrochemiluminescence immunoassays (ECLIA) on the Roche cobas e801 analyzer (Roche Diagnostics GmbH, Mannheim, Germany). Lipid profiles (LDL, HDL, triglycerides, total cholesterol) and glucose were measured using enzymatic colorimetric methods on a Roche cobas c702 clinical chemistry analyzer with manufacturer-supplied reagents**.** Complete blood count parameters were measured using the Mindray BC6800 hematology analyzer.

Systemic inflammation indices were calculated as follows:

NLR = Neutrophil count / Lymphocyte count, MLR = Monocyte count / Lymphocyte count

PLR = Platelet count / Lymphocyte count, NMR = Neutrophil count / Monocyte count

MPVLR = Mean platelet volume / Lymphocyte count, LMR = Lymphocyte count / Monocyte count, SII = Platelet count × Neutrophil count / Lymphocyte count, SIRI = Neutrophil count × Monocyte count / Lymphocyte count, MHR = Monocyte count / HDL-C, MII = NLR × CRP

RESULTS

Comparative analyses in Tables 1 and 2 revealed significant differences in biochemical, hormonal, hematological, and inflammatory parameters. Inflammatory indices SII (p=0.006), SIRI (p=0.022), MII (p=0.013), and MHR (p=0.003 were significantly higher in the PCOS group, while PLCR was lower (p=0.024). Other indices (NLR, MLR, PLR, MPVLR, LMR) showed no significant differences (p>0.05). CRP (p=0.027) and insulin (p=0.021) levels were significantly higher in patients, indicating increased inflammation and insulin resistance. LDL was also elevated (p=0.027), while HDL was lower (p=0.035). Glucose, HbA1c, and total cholesterol showed no significant differences (p>0.05). No significant differences were observed in TSH, FT3, FT4, FSH, or LH levels. WBC (p=0.010), neutrophil (p=0.043), and monocyte (p=0.011) counts were significantly higher in patients, while HCT (p=0.007), MCV (p=0.027), and MPV (p=0.034) were lower. RDW, PDW, hemoglobin, and platelet count showed no significant differences. Comprehensive correlation analyses evaluated associations between systemic inflammation indices and hematological, lipid, glucose metabolism, thyroid, and reproductive markers. Significant correlations were observed between inflammation indices and several inflammatory parameters. SII showed a strong positive correlation with several key markers, including neutrophils (r=0.681, p<0.001), NLR (r=0.798, p<0.001), PLR (r=0.604, p<0.001), MLR (r=0.450, p<0.001), and CRP (r=0.456, p=0.003). SII was also positively correlated with SIRI (r=0.668, p<0.001) and MII (r=0.603, p<0.001), while it had a negative correlation with LMR (r=—

0.450, p<0.001) and MPV (r=–0.275, p=0.032). SIRI demonstrated strong positive correlations with neutrophils (r=0.846, p<0.001), NLR (r=0.823, p<0.001), MLR (r=0.805, p<0.001), and monocytes (r=0.736, p<0.001). In contrast, SIRI was strongly negatively correlated with LMR (r=–0.805, p<0.001).

Table 1: Comparison of demographic, biochemical, hormonal, and hematological parameters

Category	Parameters	Control (Mean ± SD)	Patient (Mean ± SD)	p-value
Demographic	Age (years)	26.5±6.3	28.1±5.4	0.29
Biochemical	Glucose (mg/dL)	87.86±8.06	85.31±9.15	0.26
	Insulin (µIU/mL)	11.4 ±6.36	18.06±8.30	**0.021***
	HbA1c (%)	5.16±0.35	5.39±0.29	0.055
	LDL (mg/dL)	87.65±26.90	105.78±25.35	**0.027***
	HDL (mg/dL)	60.94±16.72	52.00±17.53	**0.035***
	Triglyceride (mg/dL)	94.11±41.17	116.48±42.79	0.08
	Total Cholesterol (mg/dL)	166.17±24.73	182.80±31.48	0.055
Hormonal	FSH (mIU/mL)	7.53±7.58	6.11±2.89	0.36
	LH (mIU/mL)	8.15±6.32	9.28±5.78	0.48
	TSH (µIU/mL)	2.18±1.10	1.82±0.88	0.16
	FT3 (pg/mL)	3.12±0.54	3.31±0.72	0.27
	FT4 (ng/dL)	1.25±0.13	1.21±0.20	0.49
Hematological	Hemoglobin (g/dL)	13.01±0.92	12.94±1.53	0.81
	RDW (%)	13.97±1.46	14.08±1.80	0.79
	PDW (fl)	15.90±0.74	15.99±0.33	0.53
	HCT (%)	40.80±2.46	38.48±3.97	**0.007***
	WBC (10^3/µL)	7.68±2.12	9.63±3.38	**0.010***
	Neutrophil (10^3/µL)	4.86±2.01	6.29±3.04	**0.043***
	Lymphocyte (10^3/µL)	2.30±0.64	2.54±0.79	0.20
	Monocyte (10^3/µL)	0.48±0.14	0.59±0.18	**0.011***
	Platelet (10^3/µL)	297.81±64.7	318.97±71	0.22
	MPV (fl)	13.60±17.81	9.82±0.88	0.25
	PCT (%)	0.29±0.05	0.31±0.05	0.14
	P-LCR (%)	30.26±9.44	25.30±6.38	**0.024***
	MCV (fl)	87.59±6.34	84.11±5.54	**0.027***
	MCH (pg)	27.96±2.32	28.12±2.72	0.80

HbA1c: Hemoglobin A1c; LDL: Low-Density Lipoprotein; HDL: High-Density Lipoprotein; Triglyceride: Triglycerides; Total Cholesterol: Total Cholesterol; FSH: Follicle-Stimulating Hormone; LH: Luteinizing Hormone; TSH: Thyroid-Stimulating Hormone; FT3: Free Triiodothyronine; FT4: Free Thyroxine; Hemoglobin: Hemoglobin; RDW: Red Cell Distribution Width; PDW: Platelet Distribution Width; HCT: Hematocrit; WBC: White Blood Cell Count; Neutrophil: Neutrophil Count; Lymphocyte: Lymphocyte Count; Monocyte: Monocyte Count; Platelet: Platelet Count; MPV: Mean Platelet Volume; PCT: Plateletcrit; P-LCR: Platelet Large Cell Ratio; MCV: Mean Corpuscular Volume; MCH: Mean Corpuscular Hemoglobin
*p<0.05

Table 2: Comparison of inflammatory indices between the control and patient groups

Parameters	Control (Mean ± SD)	Patient (Mean ± SD)	p-value
NLR	2.51±2.52	2.66±1.57	0.78
MLR	0.23±0.14	0.24±0.08	0.66
PLR	127.30±38.21	134.48±42.97	0.49
NMR	10.40±2.72	10.84±3.85	0.60
MPVLR	5.03±2.13	4.19±1.23	0.07
LMR	5.23±1.84	4.51±1.40	0.10
SII	582.13±26	814.02±36	**0.006***
SIRI	1.34±1.87	1.65±1.51	**0.022***
MII	9.59±16.5	19.54±23.41	**0.013***
MHR	0.0085±0.003	0.0126±0.005	**0.003****
CRP (mg/L)	3.45±3.919	7.80±7.364	**0.027***

NLR: Neutrophil-to-Lymphocyte Ratio; MLR: Monocyte-to-Lymphocyte Ratio; PLR: Platelet-to-Lymphocyte Ratio; NMR: Neutrophil-to-Monocyte Ratio; MPVLR: Mean Platelet Volume-to-Lymphocyte Ratio; LMR: Lymphocyte-to-Monocyte Ratio; SII: Systemic Immune-Inflammation Index; SIRI: Systemic Inflammation Response Index; MII: Multi-Inflammatory Index; MHR: Monocyte-to-HDL Ratio; CRP: C-Reactive Protein. *p<0.05, *p<0.005

MII showed a very strong positive correlation with CRP (r=0.918, p<0.001) and moderate correlations with NLR (r=0.608, p<0.001), MLR (r=0.460, p=0.001), and neutrophils (r=0.523, p<0.001).MHR was strongly associated with monocytes (r=0.783, p<0.001) and MLR (r=0.559, p<0.001), and negatively with HDL (r=–0.713, p<0.001) and LMR (r=–0.559, p<0.001).

Hematological and Derived Inflammation Indices Correlations; Several inflammation indices exhibited expected correlations. For example, NLR and MLR

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were positively correlated (r=0.658, p<0.001), while LMR was negatively correlated with MLR (r=–1.000, p<0.001), consistent with their inverse definitions. Hemoglobin showed negative correlations with NLR (r=–0.375, p=0.045) and MLR (r=–0.450, p=0.014).

Platelet Related Parameters; PDW showed significant positive associations with MPV (r=0.725, p<0.001), PLCR (r=0.742, p<0.001), and neutrophils (r=0.488, p=0.009), and a negative correlation with platelet count (r=–0.609, p=0.001). PLCR correlated strongly with MPV (r=0.992, p<0.001).

According to the ROC analysis results, MHR demonstrated the highest AUC value (0.747) and distinguished itself as the most specific biomarker with perfect specificity at 100%. CRP and MII also exhibited robust diagnostic accuracy, reflected by their high AUC values (0.726 and 0.713, respectively) and well-balanced sensitivity and specificity. SII and SIRI exhibited moderate yet clinically relevant diagnostic performance, demonstrating sensitivities of 62.1% and 82.8% alongside specificities of 75.0% and 57.1%, respectively, underscoring their potential utility as supportive biomarkers. Notably, all biomarkers achieved statistically significant results with p> 0.05 (Table 3, Figure 1).

The findings suggest that the patient group with PCOS may have a higher inflammatory state and an increased cardiovascular risk burden.

Table 3: ROC Analysis results ıncluding AUC, cutoff values, sensitivity, and specificity

Variables	AUC ± SE	95% Confidence Interval (Lower - Upper)	Cutoff	p-value	Sensitivity (%)	Specificity (%)
SII	0.702±0.068	0.568-0.835	618.5	0.003**	62.1	75.0
SIRI	0.676±0.073	0.533-0.819	0.92	0.016*	82.8	57.1
MII	0.713±0.080	0.557-0.869	8.98	0.008*	69.6	78.3
MHR	0.747±0.077	0.597-0.897	0.015	0.001**	44.4	100.0
CRP	0.726±0.082	0.565-0.887	4.81	0.006*	68.2	84.2

AUC: Area Under Curve, *p<0.05, *p<0.005

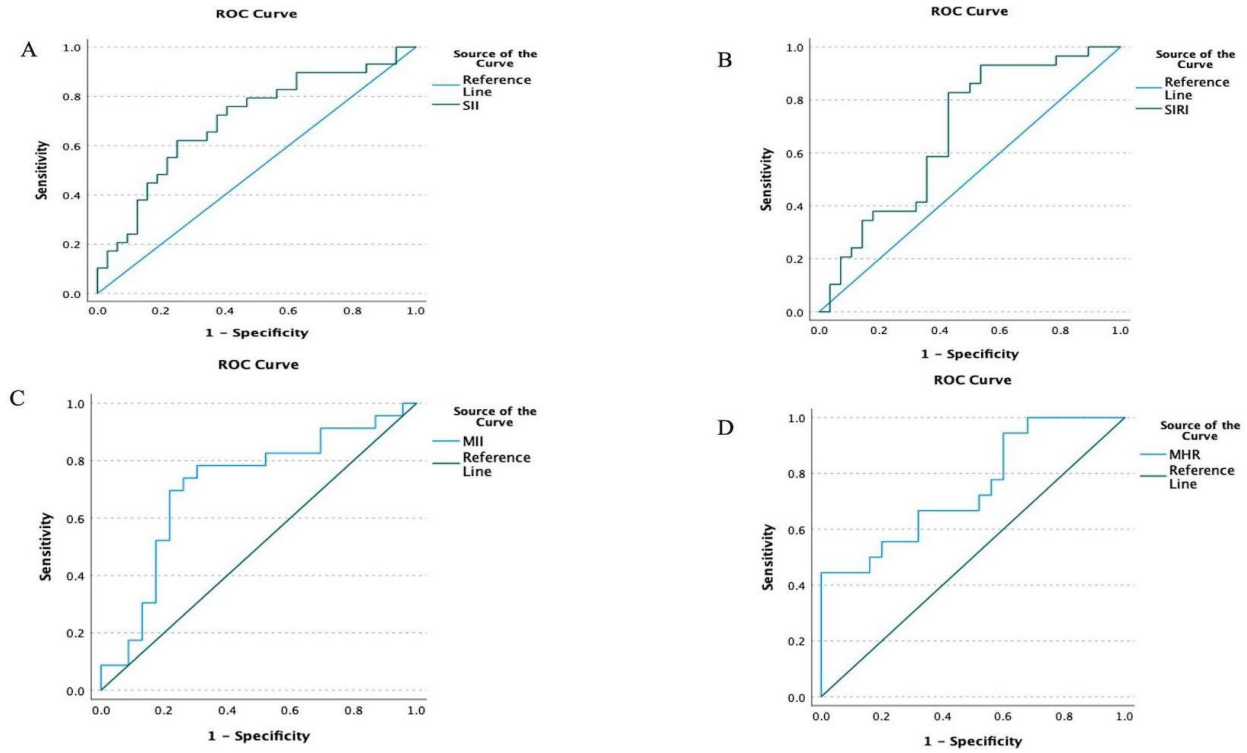

Figure 1: ROC curves for A; Systemic immune-inflammation index (SII), B; Systemic inflammation response index (SIRI), C; Multi-inflammatory index (MII), D; Monocyte to HDL Ratio (MHR)

DISCUSSION

The pathogenesis of PCOS remains incompletely understood, but growing evidence underscores the significant role of inflammation in its development.[25] Chronic low-grade inflammation, characterized by complex interactions between proinflammatory and anti-inflammatory cytokines, appears to play a crucial role in both the initiation and progression of the disorder.[3] The present findings support this view, demonstrating that women with PCOS exhibit elevated levels of key inflammatory markers, including the SII, SIRI, MII, MHR, and CRP.

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Normal female reproductive function depends on the precise regulation of the hypothalamic-pituitary-gonadal (HPG) axis. Disruptions in this axis can lead to ovulatory dysfunction, contributing to reproductive impairment and reduced fertility. Inflammatory processes and oxidative stress may further disrupt this balance by altering the LH/FSH ratio, thereby promoting hyperandrogenism, anovulation, and infertility, key endocrine features of PCOS. [1,25] As the leading cause of anovulatory infertility, PCOS remains a major contributor to female reproductive dysfunction worldwide.[2]

These findings highlight the potential diagnostic and prognostic value of inflammatory biomarkers in PCOS. Given the strong link between inflammation and PCOS pathogenesis, future studies should investigate whether targeted anti-inflammatory strategies could improve reproductive and metabolic outcomes in affected women.

While limited studies have investigated inflammatory indices in PCOS patients, our findings align with emerging evidence in this field. Recent research has demonstrated significantly elevated SII and SIRI levels in PCOS patients compared to controls, with SIRI identified as an independent predictor of PCOS diagnosis.[26] Notably, SIRI may serve not only as a diagnostic marker but also as a potential tool for phenotypic stratification in PCOS.

The clinical relevance of these inflammatory markers is further supported by reproductive outcomes. A study of 966 PCOS patients undergoing IVF revealed that lower SII levels were associated with higher embryo and blastocyst formation rates, suggesting that elevated SII may adversely affect assisted reproductive outcomes in PCOS women.[27]

The monocyte-to-HDL ratio (MHR) has recently emerged as a novel biomarker reflecting inflammation and oxidative stress. [21,28] Our findings corroborate this association, demonstrating statistically significant elevations in monocyte and LDL levels alongside reduced HDL in PCOS patients. Consistent with our results, previous studies have reported higher MHR values in PCOS patients compared to controls, supporting its potential as a useful predictive marker for PCOS.[29,30]

To our knowledge, this study is the first to investigate MII in PCOS, finding significantly elevated levels in patients. As a composite biomarker combining NLR and CRP, MII has shown diagnostic value in other diseases such as cancer and stroke.[22–24] Elevated MII in PCOS suggests its potential as a marker for assessing systemic inflammation in this population. These findings underscore the role of inflammation in PCOS and the potential clinical utility of these indices for diagnosis and prognosis. Further research should assess whether targeting these markers can improve PCOS management. The present study revealed no statistically significant differences in NLR, MLR, PLR, or LMR between study groups. These findings are consistent with the work of Can et al. [31], who similarly reported no significant differences in NLR levels between PCOS patients and control subjects. In a related study, Taşkömür et al. [32] observed that while normal-weight PCOS patients exhibited significantly higher NLR compared to overweight controls, no significant intergroup differences were detected in PLR values.

Contrary to our results, Wang et al.[33] demonstrated significantly elevated neutrophil counts and NLR in PCOS patients relative to controls. Their findings suggested that relative neutrophilia and elevated NLR may serve as potentially effective, sensitive, and specific prognostic markers for PCOS, while also providing insights into the characteristic chronic low-grade inflammatory mechanisms associated with the disorder. Similarly, Özay et al.[34] reported statistically significant increases in both NLR and PLR among PCOS patients, proposing these hematological indices as valuable markers for detecting inflammatory processes in PCOS. This study also found elevated monocyte, neutrophil, and leukocyte counts in the patient group. As key players in phagocytosis, monocytes and neutrophils promote inflammation by releasing pro-inflammatory cytokines such as IL-1, IL-6, and TNF-α. [35] Their accumulation can increase oxidative stress and inflammation, potentially affecting platelets and endothelial cells. This may activate procoagulant pathways, contributing to hypertension, atherosclerosis, cardiovascular disease, and immune-related thrombotic disorders.[28,36] These immune system imbalances transform PCOS from a reproductive disorder into a systemic condition affecting multiple organ systems.[27,37] The immunological disturbances not only impair ovulation, endometrial receptivity, and follicular development but also predispose patients to obesity, diabetes, microbial dysbiosis, cardiovascular diseases, thyroid disorders, hypertension, and NAFLD. Consequently, women with PCOS exhibit greater susceptibility to inflammatory diseases compared to healthy individuals.[27,37]

In the present study, elevated insulin, CRP, and LDL levels, along with reduced HDL and decreased HCT, MPV, MCV, and PLCR in PCOS patients, support its classification as a multisystem disorder with wide-ranging metabolic effects. Consistent with our findings, Almaeen et al.[38] observed lower HCT, MPV, and MCV in PCOS patients. Similarly, prior studies reported increased neutrophil, monocyte, and leukocyte levels in PCOS versus controls.[30,34] However, Sucu et al. reported no significant differences in neutrophil, monocyte, or leukocyte counts between PCOS and control groups.[39]

In the present study, P-LCR and MPV markers of platelet activity were significantly lower in PCOS patients compared to controls. This contrasts with Sucu et al., who reported elevated PLCR, PDW, and MPV. Notably, research on platelet indices in PCOS remains limited. The ROC analysis results revealed that MHR emerged as the most specific biomarker with the highest discriminative power, demonstrating 100% specificity. CRP and MII showed excellent balanced sensitivity and specificity with robust diagnostic performance, suggesting significant potential for clinical applications. Both SII and SIRI may function as supportive and complementary diagnostic markers. Notably, SIRI exhibits a high sensitivity rate (82.8%), allowing for the effective identification of most cases.

To our knowledge, this study is the first to investigate MII in PCOS, alongside rarely studied indices like SII, SIRI, and MHR. Findings offer new insights into PCOS-related inflammation and its potential clinical relevance. This study confirms the key role of inflammation in PCOS, evidenced by elevated SII, SIRI, MII, MHR indices, and CRP levels. Among these, MHR emerged as the most powerful discriminative biomarker, demonstrating the highest AUC (0.747) and 100% specificity, highlighting its potential as a strong diagnostic tool. With its excellent specificity rate, MHR is particularly suitable for use in situations where false-positive results are highly costly. CRP and MII showed balanced sensitivity and specificity with strong discriminative power, highlighting their significant clinical diagnostic potential. Similarly, SII and SIRI may be considered as supportive or complementary biomarkers. Notably, the high sensitivity of SIRI may confer a significant advantage in the context of early diagnosis.

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