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Association of Baseline Neutrophil to Lymphocyte and Platelet to Lymphocyte Ratios with Relapse in Sarcoidosis: A Single Center Retrospective Study

Güzide Tomas[1], **Şeyma Başlılar**[1], **Mustafa Düger**[2]

1 Department of Pulmonology, Sultan 2. Abdülhamid Han Training and Research Hospital, Istanbul, Türkiye

2 Department of Pulmonology, Istanbul Medipol Mega University Hospital, Istanbul, Türkiye

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Abstract

Background: Sarcoidosis is a heterogeneous multisystem granulomatous disease characterized by variable clinical course and relapse potential. Current ATS, BTS, and ERS guidance highlights the need for accessible biomarkers that may support clinical assessment and longitudinal follow up. Inflammatory hematologic indices such as neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) have been investigated as potential markers of disease activity in sarcoidosis. This study aimed to evaluate the association of baseline NLR and PLR values with clinical phenotype and relapse in sarcoidosis patients.

Methods: In this single-center retrospective study, adult patients followed with a diagnosis of sarcoidosis between January 2014 and June 2024 were reviewed. Patients with concomitant infection at diagnosis, HIV infection, active malignancy, hematologic disease, coexisting tuberculosis, or missing clinical/laboratory data were excluded. Baseline complete blood count parameters were used to calculate NLR and PLR values. Relapse status during follow-up was recorded, and laboratory parameters at relapse were additionally evaluated in relapsing patients. Group comparisons, ROC analyses, and multivariate logistic regression analyses were performed to evaluate the association between inflammatory indices and relapse.

Results: A total of 198 patients were included, and relapse occurred in 32 patients (16.2%). Patients with relapse had significantly higher baseline NLR (median 2.6 vs 2.1, p=0.003) and PLR (median 208.6 vs 132.3, p<0.001) values compared with non-relapsing patients. In relapsing patients, both NLR and PLR increased significantly during relapse compared with baseline values (NLR 6.7 vs 2.6, p<0.001; PLR 393.6 vs 208.6, p=0.004). ROC analysis demonstrated modest discriminative ability for relapse, with AUC values of 0.669 for NLR and 0.715 for PLR. In multivariate logistic regression analysis, advanced radiological stage (Stage 2–4), higher baseline NLR, and higher baseline PLR were independently associated with relapse.

Conclusions: Baseline and relapse-time NLR and PLR values were significantly elevated in sarcoidosis patients who developed relapse. Among these indices, PLR demonstrated better discriminative performance than NLR. Although these biomarkers should not be considered standalone predictive tools, they may provide supportive information in the clinical assessment and longitudinal monitoring of sarcoidosis patients. Prospective multicenter studies are needed to validate their clinical applicability.

Keywords: Sarcoidosis; Neutrophil to Lymphocyte Ratio; Platelet to Lymphocyte Ratio; Biomarkers

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Correspondence / Yazışma Adresi: *Güzide Tomas, Department of Pulmonology, Sultan 2. Abdülhamid Han Training and Research Hospital, Istanbul, Türkiye e-mail: guzide.tomas@hotmail.com*

Sarkoidozda Başlangıç Nötrofil/Lenfosit ve Trombosit/Lenfosit Oranlarının Nüks ile İlişkisi: Tek Merkezli Retrospektif Çalışma

Öz

Amaç: Sarkoidoz, değişken klinik seyir ve nüks potansiyeli ile karakterize heterojen, multisistemik granülomatöz bir hastalıktır. Güncel ATS, BTS ve ERS rehberleri, klinik değerlendirme ve uzun dönem izleme katkı sağlayabilecek erişilebilir biyobelirteçlere olan ihtiyacı vurgulamaktadır. Nötrofil lenfosit oranı (NLO) ve trombosit lenfosit oranı (TLO) gibi inflamatuvar hematolojik indeksler, sarkoidozda hastalık aktivitesinin potansiyel belirteçleri olarak araştırılmıştır. Bu çalışmada, başlangıç NLO ve TLO değerlerinin sarkoidoz hastalarında klinik fenotip ve nüks ile ilişkisini değerlendirmeyi amaçladık.

Yöntemler: Bu tek merkezli retrospektif çalışmada, Ocak 2014 ile Haziran 2024 tarihleri arasında sarkoidoz tanısıyla izlenen erişkin hastalar incelendi. Tanı sırasında eşlik eden enfeksiyonu bulunan, HIV enfeksiyonu olan, aktif malignitesi, hematolojik hastalığı veya eşlik eden tüberkülozu bulunan ya da klinik/laboratuvar verileri eksik olan hastalar çalışma dışı bırakıldı. Başlangıç tam kan sayımı parametreleri kullanılarak NLO ve TLO değerleri hesaplandı. İzlem sürecindeki nüks durumu kaydedildi ve nüks gelişen hastalarda nüks sırasındaki laboratuvar parametreleri ayrıca değerlendirildi. İnflamatuvar indeksler ile nüks arasındaki ilişkiyi değerlendirmek amacıyla grup karşılaştırmaları, ROC analizleri ve çok değişkenli lojistik regresyon analizleri yapıldı.

Bulgular: Toplam 198 hasta çalışmaya dahil edildi ve 32 hastada (%16,2) nüks gelişti. Nüks gelişen hastalarda başlangıç NLO (medyan 2,6'ya karşı 2,1; p=0,003) ve TLO (medyan 208,6'ya karşı 132,3; p<0,001) değerleri, nüks gelişmeyen hastalara göre anlamlı derecede yüksekti. Nüks gelişen hastalarda hem NLO hem de TLO değerleri, nüks döneminde başlangıç değerlerine kıyasla anlamlı olarak arttı (NLO 6,7'ye karşı 2,6; p<0,001; TLO 393,6'ya karşı 208,6; p=0,004). ROC analizinde nüks açısından mütevazı düzeyde ayırt edici performans saptandı ve NLO için AUC değeri 0,669, TLO için ise 0,715 olarak bulundu. Çok değişkenli lojistik regresyon analizinde ileri radyolojik evre (Evre 2–4), yüksek başlangıç NLO ve yüksek başlangıç TLO değerlerinin nüks ile bağımsız olarak ilişkili olduğu gösterildi.

Sonuç: Nüks gelişen sarkoidoz hastalarında başlangıç ve nüks dönemindeki NLO ve TLO değerleri anlamlı derecede yüksek bulundu. Bu indeksler arasında TLO, NLO'ya kıyasla daha iyi ayırt edici performans gösterdi. Bu biyobelirteçler tek başına prediktif araçlar olarak değerlendirilmemekle birlikte, sarkoidoz hastalarının klinik değerlendirilmesi ve uzun dönem izlemlerinde destekleyici bilgi sağlayabilir. Klinik uygulamadaki yerlerinin doğrulanabilmesi için prospektif çok merkezli çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Sarkoidoz; Nötrofil Lenfosit Oranı; Trombosit Lenfosit Oranı; Biyobelirteçler.

INTRODUCTION

The clinical course of sarcoidosis is marked by considerable variability, posing ongoing challenges for diagnosis, monitoring, and long-term management. While some patients experience spontaneous remission, others develop a chronic or relapsing disease course that may result in progressive organ impairment. This unpredictability has fueled sustained interest in identifying objective markers capable of reflecting disease activity and anticipating clinical outcomes[1].

Sarcoidosis is characterized by granulomatous inflammation with the potential to involve multiple organ systems. Although pulmonary parenchyma and intrathoracic lymph nodes are most frequently affected, extrapulmonary manifestations are common and substantially contribute to disease burden and clinical heterogeneity[2]. The wide spectrum of organ involvement and disease severity underscores the complexity of sarcoidosis and highlights limitations in current approaches to prognostic assessment.

Recognizing this complexity, major respiratory societies have issued guidance that prioritizes individualized evaluation and management. The American Thoracic Society (ATS) and the European Respiratory Society (ERS) recommend a comprehensive diagnostic approach, with management decisions tailored according to organ involvement, symptom burden, and estimated risk of progression[3]. Similarly, the British Thoracic Society (BTS) emphasizes patient-centered care and structured, individualized follow-up strategies in its clinical statement on pulmonary

sarcoidosis[4]. Despite these recommendations, practical tools that reliably quantify systemic inflammatory activity and predict relapse remain limited.

Several conventional biomarkers, including serum angiotensin-converting enzyme (ACE) and soluble interleukin-2 receptor (sIL-2R), have been evaluated as potential indicators of disease activity. However, their application in routine clinical practice is constrained by variable sensitivity and specificity, limiting their usefulness as standalone prognostic tools. Consequently, there is a persistent need for simple, accessible, and cost-effective biomarkers that can assist clinicians in disease monitoring and risk stratification[1].

In this context, inflammatory indices derived from routine complete blood count parameters have emerged as attractive candidates. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) reflect shifts across different immune cell populations and have been proposed as surrogate markers of systemic immune activation. These indices have demonstrated potential relevance in a variety of inflammatory and granulomatous diseases[5]. In sarcoidosis, observational studies have suggested associations between elevated NLR and PLR values and disease activity, extent of organ involvement, and clinical outcomes. Nevertheless, available evidence remains inconsistent, and their relationship with relapse during longitudinal follow-up has not been firmly established[6]. Given the continued lack of accessible prognostic biomarkers highlighted in current sarcoidosis guidelines, further investigation of NLR and PLR is warranted. Therefore, the present study aimed to evaluate the clinical significance of baseline neutrophil to lymphocyte and platelet-to-lymphocyte ratios in patients with sarcoidosis and to examine their association with relapse during follow up.

METHODS

Adult patients of both sexes who were followed with a diagnosis of sarcoidosis in a pulmonology clinic between January 2014 and June 2024 were retrospectively reviewed. Approval for the study was granted by the local ethics committee (approval no: 2024-9). Potentially eligible patients were identified through structured screening of medical records. Sarcoidosis was diagnosed on the basis of compatible clinical and radiological features, histopathological evidence of non-caseating granulomas when available, and exclusion of other granulomatous disorders.

A total of 303 patients with a diagnosis of sarcoidosis were initially screened through the electronic hospital database. After exclusion of patients with concomitant infection at diagnosis, coexisting tuberculosis, HIV infection, active malignancy, hematologic disease, or missing clinical/laboratory data, 198 patients were included in the final analysis.Baseline laboratory assessments included erythrocyte sedimentation rate, C-reactive protein (CRP), serum calcium, albumin, and complete blood count parameters (neutrophil, lymphocyte, monocyte, and platelet counts). The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were calculated from these values. Baseline laboratory measurements were obtained at the time of diagnosis before initiation of systemic treatment whenever available. In patients who developed relapse, laboratory measurements obtained at the time relapse was recognized were additionally recorded, and NLR and PLR were recalculated accordingly. Patients were categorized based on extrapulmonary involvement, treatment requirement, and relapse status, and intergroup comparisons were performed. Relapse was defined as the re-emergence or progression of

clinical symptoms and/or radiological findings compared with previous evaluations, accompanied by laboratory evidence of inflammatory activity when available, and considered clinically significant enough to require initiation or intensification of treatment by the treating pulmonology team. Only disease reactivation occurring after a period of clinical stability or remission was considered relapse. Clinical and radiological evaluations were performed by experienced pulmonologists at a tertiary referral center. The study protocol was approved by the Health Sciences University Süreyyapaşa Chest Diseases and Thoracic Surgery Training and Research Hospital Scientific Research Ethics Committee on 13 June 2024 (approval number: 2024-9). Due to the retrospective nature of the study, the requirement for informed consent was waived. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for MacOS, version 30.0 (IBM Corp., Armonk, NY, USA). Categorical variables were presented as number and percentage [n (%)], while continuous variables were expressed as mean ± standard deviation or median (interquartile range, IQR) according to data distribution. Normality of continuous variables was assessed using the Kolmogorov–Smirnov test.

Comparisons between patients with and without relapse were performed using Student's t-test for normally distributed continuous variables and the Mann–Whitney U test for non-normally distributed continuous variables. Categorical variables were compared using the Chi-square test or Fisher's exact test when expected cell counts were low.

In patients who experienced relapse, baseline and relapse laboratory parameters were compared using the Wilcoxon signed-rank test due to non-normal distribution of the data.

Receiver operating characteristic (ROC) analysis was performed to evaluate the discriminative performance of baseline biomarkers for relapse. The area under the curve (AUC) and optimal cut-off values were determined using the Youden index.

Multivariate logistic regression analysis was performed to identify factors independently associated with relapse. Due to the limited number of events, only a restricted number of clinically relevant variables that would not result in overfitting were included in the model.

A two-sided p-value <0.05 was considered statistically significant for all analyses.

RESULTS

A total of 198 patients with sarcoidosis were included in the final analysis. Over the follow-up period, relapse occurred in 32 patients (16.2%), whereas 166 patients (83.8%) remained free of relapse. A comparison of demographic and clinical characteristics according to relapse status is presented in Table 1.

No statistically significant differences were observed between patients with and without relapse with respect to age, sex, smoking history, duration of follow-up, or diagnostic modality (all $p>0.05$). In contrast, radiological staging differed markedly between groups ($p<0.001$), with a greater proportion of Stage 2 and Stage 4 disease among patients who experienced relapse. While overall extrapulmonary involvement did not vary significantly, involvement of organ systems categorized as "other" was more frequently observed in the relapse group ($p=0.007$). The need for treatment was substantially higher among patients with relapse than among those without relapse (96.9% vs. 28.9%, $p<0.001$). Mortality rates were comparable between the two groups.

Significant differences were also noted in baseline laboratory parameters (Table 1). Patients who developed relapse exhibited higher median levels of CRP, serum calcium, NLR, and PLR at baseline (all $p\leq0.003$). Conversely, baseline albumin and lymphocyte counts were significantly lower in the relapse group ($p<0.001$ and $p=0.006$,

respectively). Median baseline NLR values were significantly increased in patients with relapse compared with relapse-free patients [2.6 (1.9–4.8) vs. 2.1 (1.6–2.8), p=0.003]. Similarly, baseline PLR values were substantially higher in the relapse group [208.6 (127.1–308.5) vs. 132.3 (100–173.3), p<0.001].

Table I: Baseline demographic and clinical features stratified by relapse status

Variable	Total (n=198)	No Relapse (n=166)	Relapse (n=32)	p-value
Sex, n (%)				0.702
Male	74 (37.4)	63 (38.0)	11 (34.4)	
Female	124 (62.6)	103 (62.0)	21 (65.6)	
Age, years (mean ± SD)	51 ± 15	50 ± 15	54 ± 13	0.197
Smoking status, n (%)				0.791
Never smoker	168 (84.8)	142 (85.5)	26 (81.3)	
Current smoker	26 (13.1)	21 (12.7)	5 (15.6)	
Former smoker	4 (2.0)	3 (1.8)	1 (3.1)	
Pack-years (mean ± SD)	13.8 ± 8.5	13.3 ± 8.3	15.8 ± 9.7	0.529
Radiological stage, n (%)				<0.001
Stage 0	19 (9.6)	18 (10.8)	1 (3.1)	
Stage 1	81 (40.9)	74 (44.6)	7 (21.9)	
Stage 2	81 (40.9)	61 (36.7)	20 (62.5)	
Stage 3	13 (6.6)	12 (7.2)	1 (3.1)	
Stage 4	4 (2.0)	1 (0.6)	3 (9.4)	
Follow-up duration, years (mean ± SD)	4.8 ± 2.7	4.7 ± 2.7	5.4 ± 2.7	0.137
Diagnostic method, n (%)				0.389
EBUS	116 (58.6)	100 (60.2)	16 (50.0)	
Transbronchial biopsy	12 (6.1)	9 (5.4)	3 (9.4)	
Mediastinoscopy	20 (10.1)	15 (9.0)	5 (15.6)	
Peripheral biopsy	15 (7.6)	11 (6.6)	4 (12.5)	
Not specified	35 (17.7)	31 (18.7)	4 (12.5)	
Extrapulmonary involvement, n (%)	59 (29.8)	47 (28.3)	12 (37.5)	0.298
Skin	21 (35.6)	18 (38.3)	3 (25.0)	0.509
Eye	21 (35.6)	17 (36.2)	4 (33.3)	1.000
Neurologic	5 (8.5)	4 (8.5)	1 (8.3)	1.000
Cardiac	4 (6.8)	3 (6.4)	1 (8.3)	1.000
Other	23 (39.0)	14 (29.8)	9 (75.0)	0.007
Hypercalciuria, n (%)	10 (5.6)	6 (4.1)	4 (12.5)	0.084
Serum ACE, U/L (median, IQR)	56 (36–84.5)	56 (37–77)	56.5 (36–101.5)	0.411
Urinary calcium, mg/day (mean ± SD)	113 ± 102.2	106.5 ± 98.4	142.4 ± 115.1	0.082
CRP, mg/L (median, IQR)	3 (2–9.3)	3 (2–6)	14.1 (2–46)	<0.001
ESR, mm/h (median, IQR)	20 (11–31)	20 (12–30)	20 (11–43)	0.671
Serum calcium, mg/dL (median, IQR)	9.6 (9.2–10.1)	9.5 (9.1–10.0)	9.7 (9.4–10.4)	0.040
Albumin, g/dL (mean ± SD)	4.1 ± 0.5	4.2 ± 0.4	3.5 ± 0.4	<0.001
Neutrophils, ×10⁹/L (median, IQR)	4.1 (3.3–5.3)	4.2 (3.3–5.2)	3.9 (3.3–5.5)	0.872
Lymphocytes, ×10⁹/L (mean ± SD)	2.3 ± 1.5	2.4 ± 1.6	1.6 ± 0.8	0.006
Monocytes, ×10⁹/L (median, IQR)	0.5 (0.4–0.6)	0.5 (0.4–0.6)	0.6 (0.4–0.8)	0.009
NLR (median, IQR)	2.1 (1.6–2.9)	2.1 (1.6–2.8)	2.6 (1.9–4.8)	0.003
Platelets, ×10⁹/L (median, IQR)	259.5 (226–315)	258 (226–306)	266 (226.5–381.5)	0.308
PLR (median, IQR)	136.4 (104.4–186.5)	132.3 (100–173.3)	208.6 (127.1–308.5)	<0.001
Treatment required, n (%)	79 (39.9)	48 (28.9)	31 (96.9)	<0.001
Mortality, n (%)				0.162
Alive	197 (99.5)	166 (100)	31 (96.9)	
Deceased	1 (0.5)	0 (0)	1 (3.1)	

Abbreviations: SD, standard deviation; IQR, interquartile range; EBUS, endobronchial ultrasound; ACE, angiotensin-converting enzyme; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio. Note: Other

extrapulmonary involvement included less common organ manifestations such as testicular, hepatic, splenic, renal, musculoskeletal, and other non specific extrapulmonary involvement

Comparison of Baseline and Relapse Laboratory Parameters

Among patients who experienced relapse, laboratory parameters at baseline and at the time of relapse were compared (Table 2). At relapse, CRP, serum calcium, neutrophil count, monocyte count, NLR, platelet count, and PLR were all significantly higher compared to baseline values (all p≤0.026). Albumin levels were significantly lower during relapse compared with baseline (p=0.015).

Table II: Laboratory findings at baseline and at relapse in patients who experienced relapse

Variable	Baseline	Relapse	p-value
CRP, mg/L (median, IQR)	14.1 (2–46)	87 (53–102)	<0.001
ESR, mm/h (median, IQR)	20 (11–43)	33 (26–49)	0.067
Serum calcium, mg/dL (median, IQR)	9.7 (9.4–10.4)	10.9 (10.0–11.1)	<0.001
Albumin, g/dL (median, IQR)	3.6 (3.5–3.8)	3.1 (2.5–3.9)	0.015
Neutrophils, ×10⁹/L (median, IQR)	3.9 (3.3–5.5)	8.1 (6.9–8.9)	<0.001
Lymphocytes, ×10⁹/L (median, IQR)	1.4 (1.0–1.9)	1.1 (1.0–1.3)	0.055
Monocytes, ×10⁹/L (median, IQR)	0.6 (0.4–0.8)	0.9 (0.6–1.0)	0.007
NLR (median, IQR)	2.6 (1.9–4.8)	6.7 (5.3–8.6)	<0.001
Platelets, ×10⁹/L (median, IQR)	266 (226.5–381.5)	427.5 (289.5–462.0)	0.026
PLR (median, IQR)	208.6 (127.1–308.5)	393.6 (211.2–472.1)	0.004

Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IQR, interquartile range; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio.

Although sedimentation rate and lymphocyte count showed a trend toward increase and decrease, respectively, these changes did not reach statistical significance.

Notably, median NLR increased from 2.6 (1.9–4.8) at baseline to 6.7 (5.3–8.6) at relapse (p<0.001), while median PLR increased from 208.6 (127.1–308.5) to 393.6 (211.2–472.1) (p=0.004).

Receiver operating characteristic (ROC) analysis was performed to assess the discriminative performance of baseline biomarkers for relapse (Table 3, Figure 1). Baseline NLR demonstrated a statistically significant discriminative ability for relapse, with an area under the curve (AUC) of 0.669 (95% CI: 0.561–0.776; p=0.002). An optimal cut-off value of >4.22 yielded a sensitivity of 34.4% and a specificity of 97.0%.

Table III: ROC analysis of baseline NLR and PLR for discrimination of relapse in sarcoidosis

Biomarker	AUC (95% CI)	p-value	Cut-off value	Sensitivity (%)	Specificity (%)
NLR	0.669 (0.561–0.776)	0.002	>4.22	34.4	97.0
PLR	0.715 (0.607–0.822)	<0.001	>236.6	46.9	92.2

Abbreviations: AUC, area under the curve; CI, confidence interval; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; ROC, receiver operating characteristic.

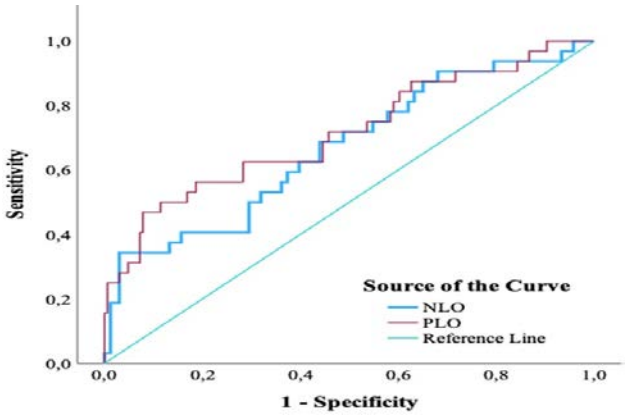

Figure 1. ROC curves of NLR and PLR for predicting relapse in sarcoidosis.

Baseline PLR showed a higher discriminative performance compared to NLR, with an AUC of 0.715 (95% CI: 0.607–0.822; p<0.001). At a cut-off value of >236.6, PLR demonstrated a sensitivity of 46.9% and a specificity of 92.2%.

The results of the multivariate logistic regression analysis evaluating independent factors associated with relapse in patients with sarcoidosis are presented in Table 4. In the NLR model, no significant association was observed between relapse and either age or sex, whereas advanced-stage disease (Stage 2–4) was independently associated with relapse development (OR=3.035; p=0.015). In addition, higher baseline NLR levels were independently associated with an increased likelihood of relapse (OR=1.457; p=0.002).

In the PLR model, age was found to be independently associated with relapse, with each 1-year increase in age corresponding to approximately a 3% increase in relapse risk (OR=1.033; p=0.038). Similarly, advanced-stage disease was identified as an independent risk factor for relapse (OR=3.181; p=0.015). Elevated baseline PLR levels were also independently associated with relapse development (OR=1.013; p<0.001). These findings suggest that baseline NLR and PLR values may contribute to clinical assessment in identifying sarcoidosis patients at higher risk for relapse (Table 4).

Table IV: Multivariate logistic regression analysis for predictors of relapse in sarcoidosis

Variables	NLR Model OR (95% CI)	p-value	PLR Model OR (95% CI)	p-value
Age	1.020 (0.991–1.049)	0.178	1.033 (1.002–1.065)	**0.038**
Sex				
Male	Reference	–	Reference	–
Female	1.311 (0.525–3.275)	0.562	0.676 (0.261–1.752)	0.420
Radiological stage				
Stage 0–1	Reference	–	Reference	–
Stage 2–4	3.035 (1.241–7.419)	0.015	3.181 (1.246–8.119)	**0.015**
NLR	1.457 (1.142–1.858)	0.002	–	–
PLR	–	–	1.013 (1.007–1.018)	<0.001

Abbreviations: OR, odds ratio; CI, confidence interval; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio.

Discussion: In this retrospective cohort analysis including 198 patients with sarcoidosis, we found that baseline neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) values were significantly higher among individuals who experienced relapse during follow-up compared with those who remained relapse-free. Furthermore, both indices showed a marked increase at the time of relapse, suggesting that they may reflect heightened systemic inflammatory activity and increased disease burden. These observations are in line with prior evidence indicating that hematologic inflammatory markers can serve as indirect indicators of immune system activation in sarcoidosis as well as in other inflammatory disorders.

The clinical relevance of NLR in sarcoidosis has been explored in several studies. Elevated NLR values at the time of diagnosis have been associated with more advanced radiological stages and have been proposed as a potential tool for distinguishing active disease from stable clinical states, supporting its possible role in disease monitoring[5]. In addition, a systematic review examining the diagnostic utility of NLR reported a relationship between increased NLR levels and radiological severity, particularly in cases with pulmonary involvement, although its overall diagnostic specificity was found to be limited[6]. Other investigations have demonstrated that patients with chronic or active sarcoidosis tend to exhibit reduced lymphocyte counts

accompanied by higher NLR values compared with those in remission, further emphasizing the association between NLR and disease activity[7].

The role of PLR in sarcoidosis has also attracted increasing attention. Comparative studies evaluating hematologic indices in sarcoidosis patients and healthy controls have consistently shown higher NLR and PLR values in affected individuals, with elevations correlating with radiological stage and systemic inflammatory load[8]. Notably, PLR has often demonstrated superior discriminative capacity relative to NLR in identifying inflammatory conditions, which may be attributed to the complex interactions between platelets and immune cells within granulomatous inflammatory processes[8]. Moreover, studies assessing comprehensive inflammatory profiles in sarcoidosis have suggested that combining hematologic ratios with conventional markers such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) may enhance the identification of active disease phases, underscoring the multifactorial nature of systemic inflammation in this condition[5].

Although an ideal biomarker for routine sarcoidosis monitoring has not yet been established, the findings of the present study, supported by ROC analysis, indicate that readily obtainable blood count–derived indices may offer clinically meaningful information. Both NLR and PLR demonstrated statistically significant discriminatory ability for relapse, with PLR showing higher specificity. These results are consistent with observations in other pulmonary and inflammatory diseases, in which increased NLR and PLR values have been linked to disease progression and unfavorable clinical outcomes[6]. The strengths of this study include the relatively large sample size, structured longitudinal follow-up, and standardized laboratory measurements. However, several limitations should be acknowledged. The retrospective design introduces the potential for selection bias, and detailed data regarding pulmonary function testing and immunomodulatory treatment strategies were unavailable for a subset of patients. In addition, although NLR and PLR were associated with relapse, the optimal threshold values identified in this study require confirmation in prospective investigations involving broader and more diverse populations.

Interpretation of inflammatory hematologic indices in sarcoidosis should be made cautiously, as several clinical factors may influence NLR and PLR values independently of disease activity. Corticosteroid treatment, immunomodulatory therapies, concomitant inflammatory disorders, and subclinical infections may alter circulating leukocyte and platelet profiles, potentially affecting the predictive performance of these biomarkers. Although multivariate analyses were performed in the present study to minimize the impact of confounding variables, residual confounding cannot be completely excluded because of the retrospective design. Recent studies have similarly emphasized that hematologic inflammatory indices should be interpreted as supportive rather than definitive markers of disease activity in sarcoidosis and other chronic inflammatory disorders[9-11].

Another important finding of the present study is the relatively high specificity but modest sensitivity of the identified NLR and PLR cut-off values. These findings suggest that elevated baseline PLR and NLR values may be more useful for identifying patients at increased relapse risk who may benefit from closer clinical follow-up rather than serving as standalone screening tools. In particular, patients with PLR values above the identified threshold (>236.6) may warrant more careful longitudinal monitoring in terms of clinical symptoms, radiological progression, and

treatment response. However, given the single-center nature of this study, caution should be exercised when generalizing these threshold values to broader patient populations. Larger prospective multicenter studies involving ethnically and clinically diverse cohorts are needed to validate the reproducibility and clinical applicability of these findings[12-14].

Although ROC analyses demonstrated statistically significant discriminative performance for both NLR and PLR, the modest AUC values and relatively low sensitivity levels suggest that these biomarkers should not be considered standalone predictive tools for clinical decision-making. Nevertheless, given their low cost and easy accessibility, they may serve as supportive biomarkers in clinical assessment and follow up.

Due to the limited number of relapse events in the present study, inclusion of a large number of covariates in the same multivariate model could have adversely affected model stability. Therefore, only a limited number of clinically relevant variables were included in the regression analyses. Finally, although statistically significant cut-off values for NLR and PLR were identified through ROC analysis, these thresholds require validation in prospective, multicenter studies before they can be applied in routine clinical practice.

Another important limitation is the single center design of the study, which may restrict the generalizability of the findings to different healthcare settings and patient populations. Since inflammatory biomarkers such as NLR and PLR may be influenced by demographic characteristics, ethnicity, comorbidities, and treatment practices, the identified cut-off values may not be universally applicable across all sarcoidosis cohorts. Therefore, external validation through large prospective multicenter studies involving diverse populations is necessary before these biomarkers can be routinely incorporated into clinical practice.

Limitations: This study has several limitations that should be acknowledged. First, its retrospective design may be associated with selection bias and limits the ability to establish causal relationships between inflammatory indices and relapse in sarcoidosis. Second, the study was conducted at a single center, which may limit the generalizability of the findings to broader and more diverse patient populations.

Third, detailed data regarding pulmonary function tests, imaging based activity assessments, and immunomodulatory treatment regimens were not available for all patients, which may have influenced the evaluation of disease activity and relapse. In addition, potential confounding factors that could affect neutrophil to lymphocyte and platelet to lymphocyte ratios such as subclinical infections, comorbid inflammatory conditions, or medication use could not be fully controlled.

CONCLUSION

In conclusion, baseline and relapse-time neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios were significantly higher in sarcoidosis patients who developed relapse. Among these indices, PLR demonstrated better discriminative performance than NLR for predicting relapse. Although their predictive performance alone may not be sufficient for standalone clinical decision-making, these inexpensive and easily accessible hematologic indices may provide supportive information for risk stratification and longitudinal monitoring of sarcoidosis patients. Further prospective, multicenter studies involving larger and more diverse populations are needed to validate their prognostic utility before routine clinical implementation.

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Conflict of Interest: The author(s) declare that there is no financial conflict of interest related to this article.

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