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Research Article

Prognostic value of the LDH-to-albumin ratio in mycosis fungoides: a retrospective case–control study

Mikozis fungoideste LDH/albumin oranının prognostik değeri: retrospektif olgu-kontrol çalışması

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Abstract

Aim: Mycosis fungoides (MF) is the most common type of primary cutaneous T-cell lymphoma with a variable clinical course. This study aimed to evaluate the prognostic value of the lactate dehydrogenase-to-albumin ratio (LAR) in predicting advanced-stage disease in MF patients.

Material and Methods: A retrospective case–control study included 92 patients with MF and 94 healthy controls. Clinical and laboratory data were collected from medical records. LAR and other inflammatory indices were calculated. Group comparisons and receiver operating characteristic (ROC) analyses were performed.

Results: Patients with MF had significantly higher LAR, LDH, CRP, ESR, CAR, and SII values, and lower albumin levels than controls ($p<0.05$). LAR correlated positively with disease stage ($r=0.614$) and LDH ($r=0.956$), and negatively with albumin ($r=-0.598$). ROC analysis demonstrated that LAR had the best discriminative ability for advanced disease (AUC 0.877; 95% CI 0.816–0.939).

Conclusion: LAR is a promising and easily obtainable biomarker for identifying advanced-stage MF. Incorporating LAR into clinical assessments may improve risk stratification and support more individualized management. Prospective multicenter studies are warranted to validate these findings and confirm its prognostic utility.

Keywords: mycosis fungoides, lactate dehydrogenase, serum albumin, biomarkers, prognosis

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Öz

Amaç: Mycosis fungoides (MF), değişken klinik seyirli en yaygın primer kutanöz T hücreli lenfomadır. Güvenilir prognostik biyobelirteçlerin belirlenmesi, risk sınıflaması ve bireyselleştirilmiş hasta yönetimi açısından önemlidir. Bu çalışmada, LDH/albumin oranının (LAR) MF hastalarında ileri evre hastalığı öngörmedeki prognostik değerinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Retrospektif olgu-kontrol çalışmasına 92 MF hastası ve 94 sağlıklı kontrol dahil edilmiştir. Klinik ve laboratuvar verileri elektronik kayıtlardan elde edilmiştir. LAR ve diğer inflamatuvar indeksler hesaplanmış; grup karşılaştırmaları ve ROC analizleri yapılmıştır.

Bulgular: MF hastalarında LAR, LDH, CRP, ESR, CAR ve SII değerleri anlamlı olarak yüksek, albumin düzeyleri ise düşük bulunmuştur ($p<0.05$). LAR, klinik evre ($r=0.614$), LDH ($r=0.956$) ve albumin ($r=-0.598$) ile anlamlı korelasyon göstermiştir. ROC analizi, LAR'ın ileri evre hastalığı ayırt etmede en yüksek doğruluğa sahip olduğunu göstermiştir (AUC 0.877; %95 GA 0.816–0.939).

Sonuç: LAR, MF'de ileri evre hastalığın belirlenmesinde umut verici, kolay erişilebilir bir biyobelirteçtir. Klinik değerlendirmelere LAR'ın dahil edilmesi, risk sınıflamasını geliştirebilir ve bireyselleştirilmiş tedavi yaklaşımlarına katkı sağlayabilir. Bulguların doğrulanması için ileriye dönük çok merkezli çalışmalar gereklidir.

Anahtar Kelimeler: mikozis fungoides, laktat dehidrogenaz, serum albümin, biyobelirteçler, prognoz

Introduction

Mycosis fungoides (MF) is the most common type of primary cutaneous T-cell lymphoma, typically exhibiting an indolent course, although progressive forms may also occur. The clinical course of MF is highly variable; while some patients may experience limited patches and plaques for many years, others may progress to develop tumoral lesions, lymph node involvement, and visceral dissemination [1]. Therefore, the identification of prognostic biomarkers that can predict disease progression is crucial for risk stratification and the implementation of personalized treatment strategies in MF management.

The lactate dehydrogenase-to-albumin ratio (LAR), calculated by dividing Lactate dehydrogenase (LDH) levels by albumin levels, has been associated with poor prognosis in several malignancies, including colorectal cancer, bladder cancer, breast cancer, nasopharyngeal carcinoma, and diffuse large B-cell lymphoma [2-7]. LAR is an easily calculable parameter in clinical practice and has emerged as a potential prognostic biomarker. However, there is a paucity of data in the literature regarding the prognostic role of LAR specifically in patients with MF.

In this study, we aimed to evaluate the potential prognostic value of the LAR in predicting advanced-stage disease in patients with MF. We believe that the data obtained from this study may contribute to clinical follow-up and risk stratification in the management of patients with MF.

Material and Methods

This study was conducted among patients diagnosed with MF who were followed at the Chronic Disease Outpatient Clinic, Department of Dermatology, Ankara Etlik City Hospital. A total of 92 MF patients who had not received any topical treatment within the past month or systemic treatment within the past three months, and who had no active infection, additional inflammatory disease, or concomitant malignancy, with sufficient follow-up duration and complete medical records, were included in the study. The control group consisted of 94 age- and sex-matched individuals who were completely healthy, with no history of acute or chronic diseases or malignancy.The study was designed and conducted in a retrospective, cross-sectional design.

Data including age, sex, age at MF diagnosis, disease duration (months), laboratory parameters, and clinical staging were retrospectively obtained from the hospital's electronic medical records and patient files. Clinical staging of MF patients was performed according to the European Organisation for Research and Treatment of Cancer (EORTC) TNM classification, and patients were categorized as early stage (IA-IIA) and advanced stage (IIB and above).

All laboratory measurements were obtained as part of routine clinical care and retrieved retrospectively from the hospital's electronic medical records. All analyses were performed in the same hospital laboratory using standardized analytical platforms and protocols, ensuring consistency across participants.

The recorded parameters included albumin (g/dL), LDH (U/L), C-reactive protein (CRP, mg/L), erythrocyte sedimentation rate (ESR, mm/hour), platelet count (10^3/μL), absolute neutrophil count (10^3/μL), and absolute lymphocyte count (10^3/μL).Based on these data, the following calculated inflammatory indices were derived:

- LDH/Albumin Ratio (LAR): Calculated by dividing the LDH value (U/L) by the albumin value (g/dL).
- CRP/Albumin Ratio (CAR): Calculated by dividing the CRP value (mg/L) by the albumin value (g/dL).
- Neutrophil/Lymphocyte Ratio (NLR): Determined by dividing the absolute neutrophil count (10^3/μL) by the absolute lymphocyte count (10^3/μL).
- Platelet/Lymphocyte Ratio (PLR): Determined by dividing the platelet count (10^3/μL) by the absolute lymphocyte count (10^3/μL).
- Systemic Inflammation Index (SII): Calculated using the formula: [neutrophil count (10^3/μL) × platelet count (10^3/μL)] / lymphocyte count (10^3/μL).

The study was and approved by the Ankara Etlik City Hospital Clinical Research Ethics Committee (AESH-BADEK-2025-298). All procedures were conducted in accordance with the Declaration of Helsinki and local regulatory guidelines. Informed consent obtained from patients.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version 26.0. The normality of distribution for continuous variables was assessed using the Shapiro-Wilk test. For non-normally distributed data, the Mann-Whitney U test was used for intergroup comparisons. Categorical variables were analyzed using the chi-square test. Spearman correlation analysis was conducted to assess correlations between the parameters. To determine the predictive value of the parameters for advanced-stage disease, Receiver Operating Characteristic (ROC) curve analysis was performed, and Area Under the Curve (AUC), cut-off values, sensitivity, and specificity were calculated. A p-value <0.05 was considered statistically significant.

Results

A total of 186 participants, including 92 patients and 94 controls, were included in the study. There was no significant difference between the groups in terms of age and sex distribution. The age and sex distributions of the study groups, along with the clinical staging data of the patient group, are summarized in table 1.

Table 1. Demographic and staging data of the study group.

Parameter	Patient Group	Control Group
Number of cases	92	94
Mean age ± SD (years)	53.08 ± 13.43	46.71 ± 12.37
Median age (IQR) (years)	54 (44.5–61)	48 (39–55)
Sex (male)	43 (46.7%)	44 (46.8%)
Sex (female)	49 (53.3%)	50 (53.2%)
Disease duration mean ± SD (months)	64.07 ± 75.41	-
Disease duration median (IQR) (months)	36 (18–78)	-
Number of patients according to stages		
Stage 1A T1a T1b	14 1	-
Stage 1B T2a T2b	2 10	-
Stage 2A	45	-
Stage 2B	15	-
Stage 3A	4	-
Stage 3B	1	-

A statistically significant difference was identified in LAR between the patient and control groups. However, there was no significant association between LAR and gender, age, age at disease onset, or disease duration (p>0.05). In the patient group, LAR, LDH, CRP, ESR, CAR, and SII values were significantly higher compared to the control group, while albumin levels were significantly lower (p<0.05). No significant differences were observed in NLR and PLR between the groups (Table 2).

Table 2. Comparison of clinical parameters between patient and control groups.

Parameter	Patient Median	Control Median	p	Effect Size (r)
CRP (mg/L)	3.52	2.18	**0.0001**	0.28
ESR (mm/h)	8.0	6.00	**0.0005**	0.26
Albumin (g/dL)	44.25	46.80	**0.0000**	0.42
LDH (U/L)	205.00	183.00	**0.0000**	0.35
CAR	0.30	0.11	**0.0000**	0.43
NLR	1.95	1.84	0.2393	0.09
PLR	127.98	110	0.0508	0.14
SII	528.23	405.3	**0.0018**	0.23
LAR	4.55	3.90	**0.0000**	0.45

Abbrev.: CRP: C-reactive protein, ESR: Erythrocyte Sedimentation Rate, LDH: Lactate Dehydrogenase, CAR: CRP/Albumin Ratio, NLR: Neutrophil/Lymphocyte Ratio, PLR: Platelet/Lymphocyte Ratio, SII: Systemic Inflammation Index, LAR: LDH/Albumin Ratio

When examining the correlation of LAR with other parameters, a strong positive correlation was identified with clinical stage (r=0.614) and LDH levels (r=0.956), while a strong negative correlation was observed with albumin levels (r=-0.598). A borderline, low-level positive correlation was noted between LAR and SII (r=0.202). For other parameters, including CRP, sedimentation, beta-2 microglobulin, CAR, NLR, and PLR, only low or very low correlations with LAR were observed, and these were not statistically significant (p>0.05). These findings are summarized in table 3.

When early-stage and advanced-stage patients were compared, albumin, LDH, and the LAR showed statistically significant differences between the two groups (p<0.001). In contrast, no significant differences were observed between early and advanced stages in terms of ESR, CRP, CAR, NLR, PLR, and SII values (p>0.05) (Table 4).

Table 3. Correlation of LDH/albumin ratio with clinical and laboratory parameters.

Parameter	r	p
Clinical Stage	0.614	<0.001
Disease Duration	0.084	0.427
CRP	0.07	0.510
ESR	0.009	0.930
Albumin	0.598	<0.001
LDH	0.956	<0.001
Beta-2 Microglobulin	0.061	0.565
CAR	0.135	0.199
NLR	0.052	0.622
PLR	0.053	0.619
SII	0.202	0.053

Abbrev.: CRP: C-reactive protein, ESR: Erythrocyte Sedimentation Rate, LDH: Lactate Dehydrogenase, CAR: CRP/Albumin Ratio, NLR: Neutrophil/Lymphocyte Ratio, PLR: Platelet/Lymphocyte Ratio, SII: Systemic Inflammation Index

Table 4. Comparison of clinical parameters between early and advanced stages.

Parameter	Early Stage (Mean ± SD, Median)	Advanced Stage (Mean ± SD, Median)	p
CRP (mg/L)	4.6 ± 4.94, 3.23	5.24 ± 3.97, 3.95	0.242
ESR (mm/hr)	11.99 ± 9.95, 8.0	13.45 ± 11.74, 7.5	0.909
Albumin (g/dL)	44.76 ± 2.91, 44.8	39.1 ± 4.16, 39.0	<0.001
LDH (U/L)	209.4 ± 56.6, 189.5	285.75 ± 63.7, 284.0	<0.001
Beta-2 Microglobulin (mg/L)	4.27 ± 18.86, 1.97	2.4 ± 0.74, 2.22	0.83
CAR	0.1 ± 0.11, 0.07	0.14 ± 0.11, 0.11	0.81
NLR	34.98 ± 279.9, 1.8	3.14 ± 1.83, 2.77	0.7
PLR	131.89 ± 47.32, 127.14	161.5± 80.06, 133.1	0.242
SII	547.5 ± 237.2, 498.0	703.1 ± 345.5, 635.6	0.34
LAR	4.71 ± 1.4, 4.38	7.36 ± 1.61, 7.52	<0.001

Abbrev.: CRP: C-reactive protein, ESR: Erythrocyte Sedimentation Rate, LDH: Lactate Dehydrogenase, CAR: CRP/Albumin Ratio, NLR: Neutrophil/Lymphocyte Ratio, PLR: Platelet/Lymphocyte Ratio, SII: Systemic Inflammation Index, LAR: LDH/Albumin Ratio

ROC analysis showed that albumin and LDH had good discriminative ability in distinguishing advanced-stage disease, with lower albumin and higher LDH values indicating advanced disease. Among the evaluated parameters, the highest discriminative performance was observed. The identified cut-off values may be applied in clinical practice to predict advanced-stage disease with high accuracy (Table 5).

Table 5. ROC Analysis results.

Parameter	AUC (95% CI)	p	Cut-off
Albumin	0.854 (0.789–0.920)	<0.0001	≤ 41.1 g/dL
LDH	0.829 (0.756–0.902)	<0.0001	≥ 253 U/L
LAR	0.877 (0.816–0.939)	<0.0001	≥ 6.01

Abbrev.: LAR: LDH/Albumin Ratio

Discussion

In patients with MF, both clinical presentation and laboratory findings are important in assessing prognosis and guiding treatment decisions. The findings of our study suggest that the LAR may serve as a simple and accessible biomarker to help identify patients with advanced-stage disease. To our knowledge, this is the first study to specifically demonstrate the prognostic value of LAR in predicting advanced-stage disease in MF. Incorporating LAR into clinical assessments could potentially support risk stratification and contribute to more individualized management strategies in this patient population.

In recent years, the role of inflammation-based biomarkers in predicting prognosis across various malignancies has been increasingly investigated [2,8,9]. LDH, a marker of tissue injury and tumor burden, is a well-established adverse prognostic factor in MF and other malignancies [10,11]. Albumin, a negative acute-phase reactant reflecting nutritional and inflammatory status, is associated with worse outcomes

when low [12]. Against this background, composite indices that integrate these signals, such as the LAR, may provide incremental prognostic information by simultaneously capturing tumor burden and the host inflammatory–nutritional reserve, thereby helping to identify patients who may have more aggressive disease biology. Our findings are consistent with recent studies in other lymphomas, supporting the notion that LAR reflects both tumor burden and host status. Importantly, our data extend these observations to MF, where evidence has previously been lacking. For example, in a large cohort, ROC-derived cut-offs of LDH (≥301 U/L) and albumin (<38 g/L) were both significantly associated with poorer overall survival and progression-free survival; however, the LAR (≥6) provided superior prognostic discrimination (AUC 0.653) compared with either marker alone [4]. Similarly, in ENKTL, a high LAR (>5.4) was identified as an independent poor prognostic factor, further supporting the concept that this composite index integrates tumor burden and host status more effectively than single parameters [13].

In parallel with this composite-marker concept, several other inflammation-based indices have been explored in MF, including NLR, PLR, CRP, and the SII. While some reports suggest associations with advanced disease or poorer outcomes, findings across cohorts have been inconsistent and proposed cut-offs vary [14–17]. In our cohort, NLR and PLR did not differ significantly, and although CAR and SII were higher in patients than controls, they did not discriminate advanced disease. These discrepancies may reflect the biology of cutaneous T-cell lymphomas where peripheral blood inflammatory indices can be less sensitive than markers of tissue injury or nutritional status as well as potential confounding from intercurrent infection, medication exposure, sample size, and the cross-sectional design. Importantly, although LDH and albumin are individually recognized as prognostic markers in MF, our data demonstrate that their composite, the LAR, provides superior discriminative ability for advanced-stage disease, with an AUC of 0.877 compared with either marker alone. This suggests that LAR captures both tumor burden and the host nutritional–inflammatory status more effectively than single parameters, thereby offering incremental prognostic value beyond established markers. While healthy controls were included to highlight the biological distinction, the clinically relevant finding was the ability of LAR to differentiate early- from advanced-stage MF. Nevertheless, external validation in larger, multicenter cohorts and integration into multifactor prognostic scores will be essential before LAR can be adopted in routine practice.

If validated, LAR could be incorporated as an adjunctive laboratory marker alongside clinical examination and TNMB staging. In practice, a higher LAR might prompt closer surveillance, earlier staging work-up, or more frequent follow-up. For instance, an elevated LAR in an early-stage patient might justify more frequent clinical visits or early imaging to rule out progression. Interpretation should, however, account for potential confounders that may alter LDH or albumin independently of lymphoma activity such as hepatic dysfunction, nephrotic protein loss, malnutrition, acute infection, hemolysis, muscle injury, and corticosteroid use as well as pre-analytical variation and inter-laboratory differences. Until externally validated, center-specific thresholds and standardized reporting are advisable. Incorporating LAR into future prognostic models may facilitate earlier detection of disease progression and enhance clinical decision-making.

Limitations of the study

Limitations include the retrospective, single-center design; reliance on cross-sectional measurements; and the absence of survival endpoints such as overall survival (OS) and progression-free survival (PFS), which precludes definitive conclusions about long-term outcomes. The number of advanced-stage cases was also limited, which may affect precision. These factors support cautious interpretation and underscore the need for external validation. Strengths include the use of routinely available laboratory measures and a well-defined control group.

In conclusion, prospective, multicenter cohorts are needed to derive and externally validate robust cut-offs, to test whether LAR adds incremental prognostic value over established factors such as stage, LDH, blood involvement, and beta-2 microglobulin using multivariable modeling and decision-analytic approaches, and to evaluate longitudinal changes in LAR as a marker of treatment response or impending progression. Subgroup analyses, particularly in patients with folliculotropic MF, erythroderma, or Sézary syndrome, may further clarify the prognostic performance of LAR and define clinical contexts where it offers the greatest utility. Overall, our findings highlight the potential of LAR as a practical, inexpensive biomarker that may complement existing staging systems, although further validation is essential before routine clinical adoption

Declaration of conflicting interests

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Ethics approval

The study was reviewed and approved by the Ankara Etlik City Hospital Clinical Research Ethics Committee (AESH-BADEK-2025-298).

Authors' contribution

All authors contributed significantly to the study. G.T.A. was responsible for the study design, data analysis, and interpretation. F.K. contributed to study design and data collection. S.P.K. reviewed and approved the final version of the manuscript. All authors read and approved the final version and share equal responsibility for the content.

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