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ORIGINAL RESEARCH

Diagnostic Value of Neutrophil-to-Lymphocyte and Platelet-to-Lymphocyte Ratios in HLA-B27-Associated Acute Anterior Uveitis

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Objective: To evaluate the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) as inflammatory markers in patients with HLA-B27-associated acute anterior uveitis (AAU) compared to healthy controls.

Methods: This retrospective case-control study included 42 patients diagnosed with HLA-B27-associated AAU and 42 age- and sex-matched healthy controls. Ocular findings, uveitis activity, and hematologic parameters were extracted from medical records. The NLR and PLR were calculated and compared between groups to assess their diagnostic value.

Results: Both NLR and PLR were significantly elevated in the HLA-B27 AAU group (Mean ± SD: 3.46 ± 2.08 and 171.53 ± 88.44) compared to controls (1.59 ± 0.61 and 123.94 ± 48.67, respectively) ($p < 0.001$ and $p = 0.003$). White blood cell count (WBC), neutrophil count, and platelet count were also significantly higher in the AAU group. Receiver operating characteristic (ROC) curve analysis showed that NLR had an area under the curve (AUC) of 0.798, with 71.4% sensitivity and 88.1% specificity, while PLR had an AUC of 0.679, with 64.3% sensitivity and 71.4% specificity.

Conclusion: Patients with HLA-B27-associated AAU exhibited significantly higher NLR and PLR compared to controls. These hematologic markers reflect systemic inflammation but are not disease specific. NLR and PLR may serve as an adjunctive indicator in patients presenting with clinical signs of active HLA-B27 AAU.

Keywords: neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, NLR, PLR, HLA-B27, HLA-B27 AAU, acute anterior uveitis, AAU

Introduction

Uveitis is a leading cause of ocular morbidity, contributing to 5–10% of global visual impairment.[1] Among its various forms, acute anterior uveitis (AAU) is the most prevalent, accounting for 28–50% of all uveitis cases.[2] HLA-B27-associated AAU is the most frequently identifiable subtype, with approximately 50% of AAU cases positive for HLA-B27.[2] This condition is characterized by intraocular inflammation localized to the anterior segment and may lead to recurrent episodes, complications, and long-term visual impairment. Up to 10% of affected individuals may experience severe vision loss or legal blindness.[3] Beyond its ocular manifestations, HLA-B27-associated AAU is linked to systemic inflammatory diseases, including ankylosing spondylitis, reactive arthritis, and psoriatic arthritis. While diagnosis primarily relies on clinical presentation, with HLA-B27 testing serving as a confirmatory tool, although turnaround times vary depending on laboratory techniques.

The neutrophil-to-lymphocyte ratio (NLR) serves as a simple and effective metric for quickly evaluating a subject's inflammatory status, as it closely correlates with C-reactive protein (CRP) levels.[4,5] A complete blood count (CBC) is used to calculate both the NLR and the platelet-to-lymphocyte ratio (PLR). The NLR is determined by dividing the

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neutrophil count by the lymphocyte count, while the PLR is calculated by dividing the platelet count by the lymphocyte count.

Recent studies have explored the role of NLR in various ocular conditions, including thyroid-related orbitopathy (TRO),[6] pterygium,[7] non-arteritic anterior ischemic optic neuropathy (NAION),[8] and idiopathic AAU.[9] A positive correlation between CRP and NLR levels has been identified in idiopathic AAU,[9] further supporting the role of NLR as an inflammatory marker. However, there is currently limited research specifically investigating NLR in HLA-B27-associated AAU. Given its potential as an accessible and cost-effective biomarker, evaluating the relationship between NLR, PLR, and active HLA-B27-associated AAU may provide valuable insight into its diagnostic utility. This study aims to evaluate the relationship between NLR and PLR levels in patients with active HLA-B27-associated AAU compared to healthy control subjects.

Methods

This case-control study was approved by the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University (IRB No. 0603/66, COA No. 1228/2023). As this was a retrospective chart review with anonymized data, the requirement for informed consent was waived. Patient data confidentiality was strictly maintained, and the study was conducted in accordance with the tenets of the Declaration of Helsinki. Data were collected from electronic medical records of patients diagnosed with HLA-B27-associated AAU who visited uveitis clinic, Chulalongkorn Memorial Hospital, Bangkok, Thailand, between January 1, 2015, and December 31, 2022.

Eligible cases included laboratory-confirmed active HLA-B27 AAU patients aged ≥18 years who underwent a comprehensive ophthalmologic evaluation. The diagnosis was established per the Standardization of Uveitis Nomenclature II (SUN II) classification and confirmed via serological HLA-B27 testing.[10]

Patients were excluded if they had any of the following conditions: hematologic diseases, HIV infection, active local (ocular or non-ocular) or systemic infections during the current episode of uveitis at the time of CBC collection. Infectious uveitis was ruled out in all cases through appropriate laboratory testing, and patients with a positive treponemal test for syphilis, clinical suspicion of tuberculosis, or evidence of latent infectious causes were excluded in accordance with the SUN II classification criteria for HLA-B27 AAU. Patients with a history of chemotherapy or radiotherapy, cancer, pregnancy, or recent ophthalmic surgery or laser procedures (within three months prior to the CBC test) were also excluded. Additional exclusions included patients with cardiovascular disease, including coronary artery disease, acute coronary syndromes, and arterial hypertension. Patients who had received blood transfusions within three months prior to the CBC test or were using systemic steroids were also excluded.

The control group comprised randomly selected healthy individuals, matched by age and sex, who were sourced from the annual check-up clinic at Chulalongkorn Memorial Hospital, Bangkok, Thailand. These subjects had their electronic medical records recorded within the period of January 1, 2015, to December 31, 2022. Each control subject had a CBC test performed in the same calendar year as their age- and sex-matched HLA-B27 case.

We measured the counts of neutrophils, lymphocytes, platelets, red blood cells, and white blood cells (WBC) as part of the CBC analysis. Additionally, the PLR and NLR were calculated by dividing the platelet count by the lymphocyte count and the neutrophil count by the lymphocyte count, respectively.

Data analysis was performed using STATA/SE for Mac version 18.0 (StataCorp, TX). Clinical and demographic characteristics were categorized into continuous and categorical variables. Where appropriate, groups were compared using the unpaired *t*-test, with statistical significance defined as a P-value of less than 0.05.

The accuracy of NLR and PLR was assessed, and the optimal cutoff threshold was determined using receiver operating characteristic (ROC) analysis. The Liu method was employed to estimate the most suitable cutoff point by maximizing the product of sensitivity and specificity.

Results

Among 42 patients with HLA-B27 AAU, males were more commonly affected (66.67%), with a mean age of 47.48 ± 13.78 years (Table 1). Most cases were unilateral. Severe inflammation (3+ to 4+ cells) was observed in half of the cases, and four patients developed hypopyon. Ocular complications were noted in three patients, including ocular hypertension

Table 1 Characteristics of Patients with HLA-B27 AAU

Characteristic	HLA B-27 Anterior Uveitis (N=42)
Age (years, mean ± SD) Male, n (%)	47.48 ± 13.78 28 (66.67%)
Symptom onset to CBC test (days, mean ± SD)	7.24 ± 5.02
Right eye involvement, n (%) Bilateral involvement, n (%)	20 (47.62%) 2 (4.76%)
Degree of anterior chamber cell, n (%) 0.5+ 1+ 2+ 3+ 4+	 6 (14.29%) 9 (21.43%) 6 (14.29%) 9 (21.43%) 12 (28.57%)
Hypopyon, n (%)	4 (9.52%)
Complication, n (%) Ocular hypertension CME	3 (7.14%) 2 (4.76%) 1 (2.38%)
HLA-B27-associated disease, n (%) Ankylosing spondylitis Reactive arthritis	7 (16.67%) 6 (14.29%) 1 (2.38%)

(n = 2) and cystoid macular edema (n = 1). Seven patients had systemic HLA-B27-associated diseases, predominantly ankylosing spondylitis (n = 6).

A comparison of CBC parameters and inflammatory biomarkers between HLA-B27 AAU patients and healthy controls is summarized in Table 2. NLR was significantly higher in HLA-B27 AAU patients (3.46 ± 2.08) compared to controls (1.59 ± 0.61, P < 0.001). Similarly, PLR was significantly elevated in the AAU group (171.53 ± 88.44) compared to controls (123.94 ± 48.67, P = 0.003). Additionally, WBC, neutrophil count (PMN), and platelet count were significantly higher in AAU patients (P < 0.001 for WBC and PMN, P = 0.008 for Plt), whereas lymphocyte counts (LYM) showed no significant difference between groups (P = 0.21).

Table 2 Comparison of CBC Parameters & Inflammatory Biomarkers

Variable	HLA-B27 AAU (N=42)	Control (N=42)	Mean Difference (95% CI)	P-value
Hemoglobin (g/dL)	14.12 ± 1.34	14.23 ± 1.35	0.11 (−0.48, 0.69)	0.716
Hematocrit (%)	42.67 ± 3.56	43.18 ± 3.86	0.58 (−1.11, 2.12)	0.533
WBC (×10³/μL)	9.31 ± 3.02	6.60 ± 1.29	−2.72 (−3.72, −1.71)	<0.001*
Neutrophils (×10³/μL)	6.47 ± 2.47	3.55 ± 0.82	−2.92 (−3.72, −2.13)	<0.001*
Lymphocytes (×10³/μL)	2.18 ± 0.99	2.42 ± 0.76	−0.24 (−0.14, 0.62)	0.21
Platelets (×10³/μL)	320.83 ± 90.89	274.21 ± 64.89	−46.62 (−80.90, −12.34)	0.008*
NLR	3.46 ± 2.08	1.59 ± 0.61	−1.86 (−2.53, −1.20)	<0.001*
PLR	171.53 ± 88.44	123.94 ± 48.67	−45.8 (−78.57, −16.60)	0.003*

Notes: *$p < 0.05$, indicating statistical significance.

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Table 3 Association of NLR, PLR, and WBC with Anterior Chamber Inflammation Severity

Clinical Finding	NLR (Mean ± SD)	PLR (Mean ± SD)	WBC (×10³/μL) (Mean ± SD)
Anterior chamber cell			
0.5+	3.20 ± 1.08	185.73 ± 84.47	8.75 ± 2.07
1+	2.69 ± 2.48	163.54 ± 101.56	7.45 ± 2.79
2+	2.65 ± 1.06	152.19 ± 68.64	9.57 ± 3.43
3+	3.90 ± 2.15	161.75 ± 68.64	10.60 ± 3.28
4+	4.23 ± 2.03	187.43 ± 97.30	9.91 ± 2.28
Anterior chamber flare			
1+	3.34 ± 2.18	158.80 ± 32.14	9.95 ± 4.21
2+	3.09 ± 1.03	128.18 ± 35.80	9.46 ± 2.46
3+	2.85 ± 0.42	152.90 ± 19.54	7.30 ± 0.96

In subgroup analysis, patients with HLA-B27-associated systemic diseases (n = 7) showed no significant differences in NLR (mean difference: 2.85, 95% CI: −0.10 to 5.80, P = 0.057) or PLR (mean difference: 134.54, 95% CI: −0.89 to 269.97, P = 0.051) when compared to matched healthy controls. Additionally, an analysis of inflammatory markers across different grades of anterior chamber inflammation revealed no significant correlation between clinical severity and levels of NLR, PLR, or WBC counts (Table 3).

ROC curve analysis was conducted to assess the diagnostic performance of NLR and PLR in distinguishing HLA-B27 AAU patients from controls (Figure 1). Using the Liu method, optimal cut-off values of 2.11 for NLR and 133.61 for PLR were determined (Figure 2). At these thresholds, NLR demonstrated a sensitivity of 71.4% (95% CI: 55.4–84.3) and specificity of 88.1% (95% CI: 74.4–96.0), while PLR showed a sensitivity of 64.3% (95% CI: 48.0–78.4) and specificity of 71.4% (95% CI: 55.4–83.4). The diagnostic performance metrics computed from the best cut-off values are summarized in Table 4. The area under the curve (AUC) for NLR was 0.798 (95% CI: 0.713–0.883), indicating moderate to good discrimination, whereas PLR had a lower AUC of 0.679 (95% CI: 0.578–0.779).

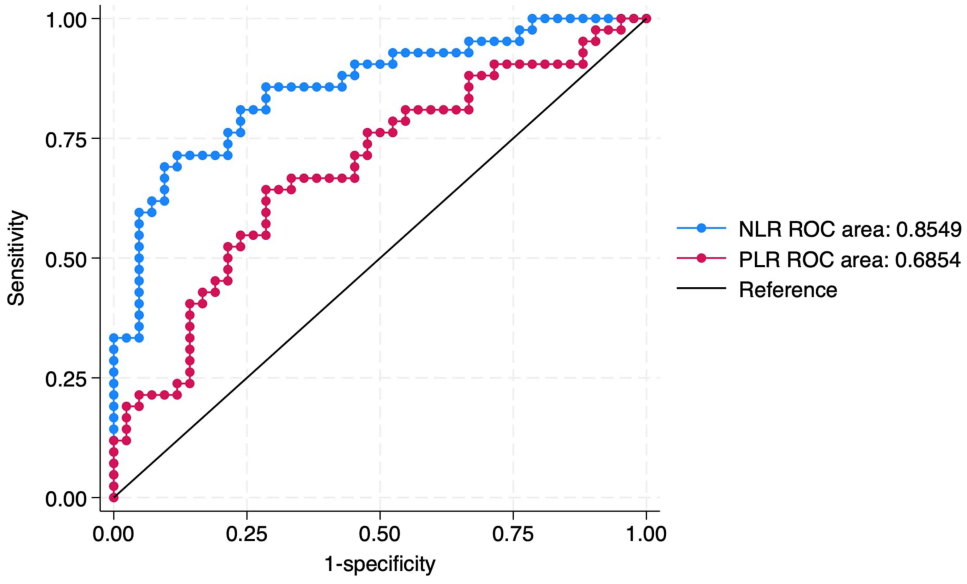

Figure 1 ROC curve analysis for discrimination between controls and HLA-B27 AAU groups.

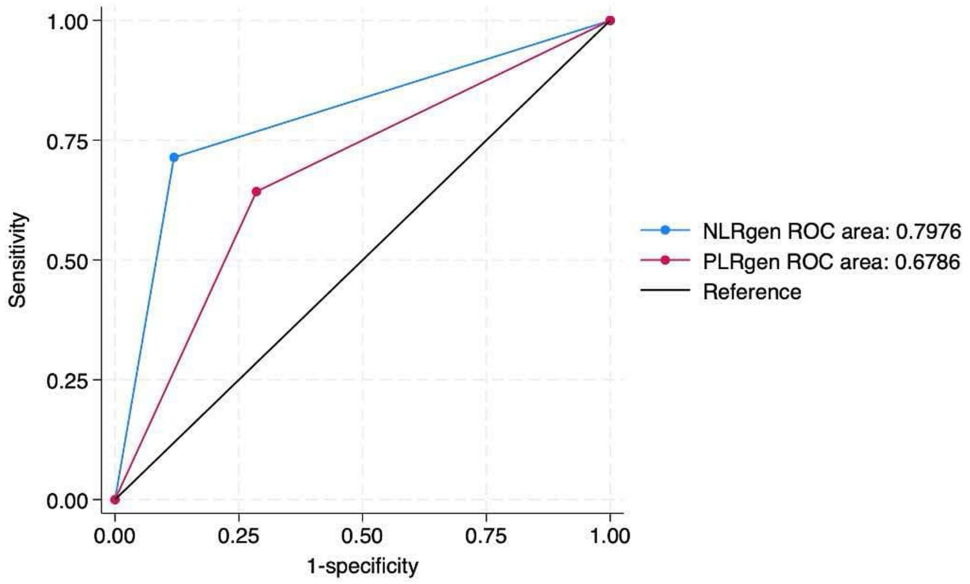

Figure 2 ROC curve analysis for optimal cut-off value in distinguishing HLA-B27-associated AAU from controls.

Discussion

Access to HLA-B27 testing may be limited in certain healthcare settings due to factors such as cost, availability, and long turnaround times. In contrast, NLR and PLR are inexpensive, rapid, and easily obtained through routine blood tests, offering a practical alternative for preliminary evaluation in various clinical environments. Our findings demonstrate that NLR and PLR are significantly elevated in patients with active HLA-B27 AAU compared to healthy controls. A cut-off value of 2.11 for NLR and 133.61 for PLR was identified to differentiate patients from controls, both demonstrating good sensitivity and specificity.

The observed elevation in NLR and PLR suggests the presence of subclinical systemic inflammation in the early stages of active AAU, potentially preceding or coinciding with disease onset. The mean time from symptom onset to CBC testing in our cohort was 7.24 ± 5.02 days, which reflects the typical interval at which patients presented for evaluation and laboratory work-up.

Table 4 Summary of Statistical Parameters at the Optimal Cut-off Value

Metric	NLR (95% CI)	PLR (95% CI)
Sensitivity	71.4% (55.4–84.3)	64.3% (48–78.4)
Specificity	88.1% (74.4–96)	71.4% (55.4–83.4)
Likelihood ratio (+)	6 (2.58–14)	2.08 (1.31–3.3)
Likelihood ratio (-)	0.324 (0.199–0.53)	0.462 (0.276–0.772)
Odd ratio	18.5 (5.99–56.7)	4.5 (1.81–11.2)
Positive predictive value	85.7% (69.7–95.2)	69.2% (52.4–83)
Negative predictive value	75.5% (61.1–86.7)	66.7% (51–80)
AUC	0.798 (0.713–0.883)	0.679 (0.578–0.779)

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The interplay between Th17-mediated inflammation, neutrophil activation, and systemic immune dysregulation provides a plausible explanation for the elevated NLR observed in our study. A key driver of this inflammation is the Th17 cell pathway, which plays a crucial role in the pathogenesis of autoimmune diseases, including HLA-B27-associated AAU. Th17 cells secrete pro-inflammatory cytokines such as IL-17, IL-6, and TNF-α, which actively promote neutrophil recruitment and activation.[11,12] This mechanism is particularly relevant in HLA-B27-associated diseases, as increased IL-17 has been implicated in ankylosing spondylitis and associated uveitis.[13,14] Elevated IL-17 levels contribute to systemic neutrophilia, leading to an increase in NLR.[12,15] Additionally, IL-17 enhances neutrophil survival and prolongs their inflammatory activity, contributing to persistent inflammation even in the absence of overt infection.[16]

Recent studies on uveitis support the utility of NLR and PLR as inflammatory markers. Kurtul et al reported higher NLR and PLR values in noninfectious uveitis, with cut-offs of 1.95 and 99.2, respectively.[17] Demir et al observed elevated NLR (cut-off: 2.49) and PLR (cut-off: 111.7) in idiopathic acute anterior uveitis.[18] Both studies demonstrated that NLR exhibited better sensitivity and specificity than PLR. Additionally, Ozgonul et al demonstrated that NLR and PLR levels were significantly elevated in patients with idiopathic acute anterior uveitis compared to controls, with cut-offs of 1.51 and 99.55, respectively.[9] While this overlap exists, it is important to note that idiopathic and HLA-B27-associated AAU are clinically and immunopathologically distinct. HLA-B27 associated AAU is frequently linked to systemic inflammatory disorders, particularly spondyloarthropathies, and is characterized by a different immune response profile, notably Th17-mediated inflammation. Ozgonul et al also found a positive correlation between CRP levels and NLR ($r = 0.461$, $p = 0.002$), further supporting the inflammatory role of NLR in uveitis.[9]

Avcı et al also reported that NLR and PLR were significantly higher in Behcet's disease patients experiencing anterior uveitis compared to those without an active episode, reinforcing their potential as markers of inflammation.[19] Similarly, a study by Kim et al evaluating inflammatory markers in HLA-B27-associated uveitis found that while CRP and the CRP/albumin ratio were significantly elevated during the uveitic phase, NLR and PLR did not significantly differ between active and resolved phases.[20] This finding may limit the utility of NLR and PLR for monitoring treatment response over time. These observations suggest that although NLR and PLR may serve as inflammatory indicators in some forms of uveitis, their longitudinal utility may vary depending on the underlying etiology and disease course.

The statistical analysis of NLR and PLR cut-off values highlights the superior diagnostic performance of NLR in distinguishing HLA-B27-associated AAU from healthy controls. NLR demonstrated a higher specificity (88.1%) compared to PLR (71.4%), indicating better accuracy in correctly identifying non-diseased individuals. Additionally, NLR had a higher positive likelihood ratio (6.0 vs 2.08) and a lower negative likelihood ratio (0.324 vs 0.462), reinforcing its stronger ability to confirm or exclude disease presence. The odds ratio for NLR (18.5) was significantly higher than that of PLR (4.5), suggesting that an elevated NLR is a much stronger predictor of HLA-B27 AAU.

Importantly, while NLR's positive predictive value (PPV = 85.7%) suggests a strong ability to confirm disease presence, it must be interpreted with caution when applied outside the study setting. PPV is highly dependent on disease prevalence, which is relatively high in a tertiary care center where patients with suspected HLA-B27 AAU are more commonly referred. In lower-prevalence settings, such as primary care or general ophthalmology clinics, the PPV would be lower, reducing the certainty that a positive NLR truly indicates disease. This underscores the need for clinicians to consider pre-test probability and local disease prevalence when applying NLR as a diagnostic marker. Additionally, the area under the curve (AUC) for NLR (0.798) was superior to PLR (0.679), confirming its better overall diagnostic accuracy. While both markers reflect systemic inflammation, these findings suggest that NLR is a more reliable and clinically useful biomarker than PLR for the presumptive diagnosis of HLA-B27 AAU.

This study has several limitations. First, the sample size was relatively small, which may limit the generalizability of the findings. Second, the retrospective design introduces the possibility of selection bias and limits control over potential confounders. Third, we did not include a comparison group of patients with other forms of uveitis, such as HLA-B27-negative AAU or Behcet's disease, which precludes evaluation of the specificity of NLR and PLR in distinguishing HLA-B27 AAU from other inflammatory eye conditions. Lastly, we did not collect longitudinal data, so we were unable to assess dynamic changes in NLR and PLR over the disease course or in response to treatment. Future studies should explore longitudinal changes in NLR and PLR in relation to disease activity and treatment response, as well as compare

these markers across various forms of uveitis, to assess their potential role in monitoring inflammation and their broader diagnostic utility.

Conclusion

Our study demonstrates that NLR and PLR are significantly elevated in patients with HLA-B27- AAU compared to healthy controls, supporting their potential utility in distinguishing active disease from healthy individuals. The identified NLR cut-off value showed good sensitivity and specificity, suggesting its role as a presumptive diagnostic marker for active HLA-B27 AAU. While both markers reflect systemic inflammation, their diagnostic role is nonspecific and should be interpreted within the appropriate disease context and setting. These findings further emphasize the systemic inflammatory nature of HLA-B27 AAU and the potential role of readily available hematologic indices in its assessment.

Disclosure

The authors declare there are no conflicts of interest related to this study.

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