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Diagnostic value of hemoglobin and neutrophil-to-lymphocyte ratio in Behcet Disease

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Abstract

The purpose of our study was to investigate the diagnostic value of NLR, hemoglobin (HB) and combine NLR with HB in the BD patients.

Sixty-seven patients with BD were diagnosed in the rheumatology or dermatology between June 2015 and June 2019; 92 matching healthy physical examiners were included in our study. SPSS was used for statistical analysis.

Compared with the healthy control, NLR was increased ($P < .001$), while the HB level was decreased ($P < .001$) in the patients of BD. In addition, ESR and CRP were increased in BD patients. NLR has no relationship with CRP and ESR, while the HB levels were negatively correlated with CRP and ESR ($r = -0.293$, $P = .046$; $r = -0.431$, $P = .002$). ROC curve analysis revealed the AUC of NLR and HB were 0.797 and 0.798 ($P < .001$). When combined NLR with HB, the AUC was 0.897 ($P < .001$). Besides, logistic regression analysis demonstrated that NLR and HB were independent risk factors in the BD patients.

We observed that the diagnostic value of NLR, HB and combined NLR with HB in the BD patients were high, particularly when combine NLR with HB. NLR and HB were independent risk factors in the BD patients. In addition, HB levels related to the disease activity of BD patients.

Abbreviations: AUC = the area under the ROC curve, BD = Behcet Disease, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, HB = hemoglobin, NLR = neutrophil to lymphocyte Ratio, RA = rheumatoid arthritis, ROC = operating characteristic curve, SLE = systemic lupus erythematosus.

Keywords: Behcet disease, hemoglobin, neutrophil to lymphocyte ratio (NLR)

1. Introduction

Behcet disease (BD) is a complicated, chronic, systemic vasculitis disease that can affect a variety of organs.[1] Characteristics of BD are recurrent oral, genital mucosal ulcers, uveitis, and skin lesions, In addition, neurological, cardiovascular, gastrointestinal, and musculoskeletal systems can be involved.[2] The global prevalence of BD ranges from 0.1/1000 to 1/10000.[3] The diagnosis of BD based on an international standard and the details of this standard were listed in Table 1.[4] In general, BD is a sporadic disease, although it has the highest incidence on the Silk Road and BD was first described by Hulusi Behcet in 1937.[5]

As being generally known, BD is an inflammatory disease. This raises the question of whether inflammation markers can be helpful in identifying BD patients. The neutrophil to lymphocyte Ratio (NLR) has been suggested as a predictor of several conditions, such as autoimmune disease,[6] cardiovascular disease,[7] hypertension,[8] and malignancies.[9] Previous studies have illuminated that the hemoglobin (HB) may be employed as an indicator in active inflammatory disease. HB level has been found to be significantly reduced in rheumatoid arthritis (RA)[10] and systemic lupus erythematosus (SLE).[11] However, to the best of our knowledge, the predictive value of the HB level in BD remains unclear. Despite the fact that the value of NLR in the BD patients has been studied before, we were the first to reveal the relation between the NLR and HB in BD.

2. Patients and methods

From June 2015 to June 2019, there were 112 BD patients that visited the rheumatology or dermatology in our hospital. Forty-five BD patients with hematological diseases, infectious diseases, malignancies, other autoimmune diseases or chronic disease and patients treated for nearly 3 months such as corticosteroids and immunosuppressive treatments which can effect on the hemogram and anemia were excluded in our study. Thus, in this study, we studied the clinical and hematology features of these 67 qualified BD patients. Furthermore, only 50 patients measured the erythrocyte sedimentation rate (ESR) and 47 BD patients detected for C-reactive protein (CRP). In addition, the control group was 92 gender and age appropriate individuals who underwent health check-up in the same hospital. The Ethics Committee of the First Affiliated Hospital of Guangxi Medical University gave permission to our study.

Sixty-seven patients and 92 healthy subjects' fasting blood were collected before admitted to hospital. Routine blood tests were evaluated using the Beckman Coulter LH 780 blood

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Table 1

The international diagnostic criteria of Behcet disease patients and point scores ≥4 indicates Behcet diagnosis.

Symptom	Point scores
Ocular lesions	2
Genital aphthosis	2
Oral aphthosis	2
Skin lesions	1
Neurological manifestations	1
Vascular manifestations	1
Positive pathergy test	1

analyzer (Beckman Coulter, Brea, CA). NLR (neutrophils to lymphocytes ratio) was calculated on the basis of the blood cell counts. ESR was tested by automatic Analyser Minitor-100 (Electa Lab S.r.l; Forli, Italy) and CRP was measured using Automatic Biochemical Analyser 7600-120 (Hitachi High Technologies, Japan).

3. Statistical analysis

We used SPSS for statistical analysis (version 24.0, Chicago, IL) and $P < .05$ (2-tailed) was thought to be statistically significant. The Kolmogorov-Smirnov test was used to determine whether the data were normal distribution. The student *t* test was applied to normal distribution samples and described by (mean ± standard deviation) while non-normal distribution samples were analyzed by Mann–Whitney *U* test and represented by median and interquartile range (IQR). Correlation analysis was used by the spearman approach. Diagnostic value of NLR, HB and the combination of NLR and HB was calculated by operating characteristic curve (ROC) and the area under the ROC curve (AUC). In addition, logistic analysis was generated to determine independent risk factors for BD.

4. Results

The incidence of clinical features of BD patients were displayed in Table 2, it revealed that the incidence of oral ulcers, genital ulcers and skin lesions were high when compared with other clinical features and the differences in the incidence of clinical characteristics of BD patients may be due to regional or ethnic differences. As showed in Table 3, age and sex have no statistical difference between the 2 parameters. White blood cell count, NLR, neutrophils, monocytes, platelets, ESR, CRP were significantly elevated while the HB level, red blood cell count were markedly decreased in total BD patients compared with healthy controls.

Table 2

The incidence of clinical features in Behcet disease patients.

Clinical features (n = 112)	Incidence
Oral ulcers	93.75%
Genital ulcers	70.54%
Skin lesions	42.86%
Eye affection	30.36%
Vasculitis	2.68%
NeuroBehçet	0.89%
Joint affection	8.93%
Gastrointestinal ulcer	4.46%
Embolism	2.68%
Epifolliculitis	1.79%

Table 3

Comparison of demographic and laboratory parameters of patients with Behcet disease and healthy controls.

	Behcet patients	Healthy controls	*P* value
Sex (male/female)	42/25	50/42	.29
age	32 (26∼40)	36.5 (27∼48)	.06
WBC	8.84 ± 3.23	6.59 ± 1.20	<.001
RBC	4.5 ± 0.83	4.90 ± 0.67	.004
NEU	5.2 (4.1∼7.4)	3.6 (2.94∼4.24)	<.001
LYM	1.88 ± 0.76	2.24 ± 0.51	<.001
MONO	0.68 (0.54∼0.92)	0.46 ± 0.18	<.001
PLT	274.5 (224.3∼359.05)	248.85 (220.08∼299.4)	.012
NLR	3.27 (1.85∼4.77)	1.66 (1.3∼1.91)	<.001
HB	125 (109.2∼136)	142.9 (129.43∼153.93)	<.001
ESR	30.5 (10∼48)	13 (7∼19)	<.001
CRP	24.74 (8.29∼55.35)	<10	

CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, HB = hemoglobin, LYM = lymphocyte, MONO = monocyte, NEU = neutrophil, NLR = neutrophil-to- lymphocyte ratio, PLT = platelet, RBC = red blood cell, WBC = white blood cell.

This study demonstrated that the HB levels were negatively correlated with ESR and CRP with $r = -0.431$, $P = .002$; $r = -0.293$, $P = .046$, respectively. Furthermore, NLR was uncorrelated with ESR and CRP with $r = 0.11$, $P = .448$; $r = 0.156$, $P = .294$ (Table 4, Figs. 2–3).

Logistic regression analysis was used to determine whether laboratory indicators were independent risk factors in BD patients. The results demonstrated that NLR and HB were independent predictive factors in BD patients with EXP (B) = 3.129; 95% CI = 1.954–5.009; $P < .001$; EXP (B) = 0.921; 95% CI = 0.891–0.952; $P < .001$, respectively (Table 5).

ROC was carried out to calculate the cutoff value of NLR and HB to predict BD, and it revealed that the cutoff value of NLR, HB were 2.61 and 136, respectively. The AUC value of NLR was 0.797, $P < .001$, with sensitivity = 62.69%; specificity = 94.57%. For HB, the AUC value was 0.798,

Table 4

Correlation analysis of experimental indexes with neutrophil to lymphocyte Ratio and hemoglobin.

	NLR		HB	
	r	*P*	*r*	*P*
Age	–0.035	.78	0.174	.16
WBC	0.541	<.001	0.153	.22
NEU	0.736	<.001	0.161	.19
LYM	–0.677	<.001	0.173	.16
PLT	0.108	.39	–0.147	.24
ESR	0.11	.45	–0.431	.002
CRP	0.156	.29	–0.293	.046

CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, HB = hemoglobin, LYM = lymphocyte, NEU = neutrophil, NLR = neutrophil-to- lymphocyte ratio, PLT = platelet, WBC = white blood cell.

Table 5

Logistic regression analysis between neutrophil to lymphocyte Ratio, hemoglobin and patients with Behcet disease.

Variables	Exp (B)	*P* value	95%CI
NLR	3.129	<.001	1.954–5.009
Hemoglobin	0.921	<.001	0.891–0.952

95%CI = 95% confidence interval, NLR = neutrophil-to- lymphocyte ratio.

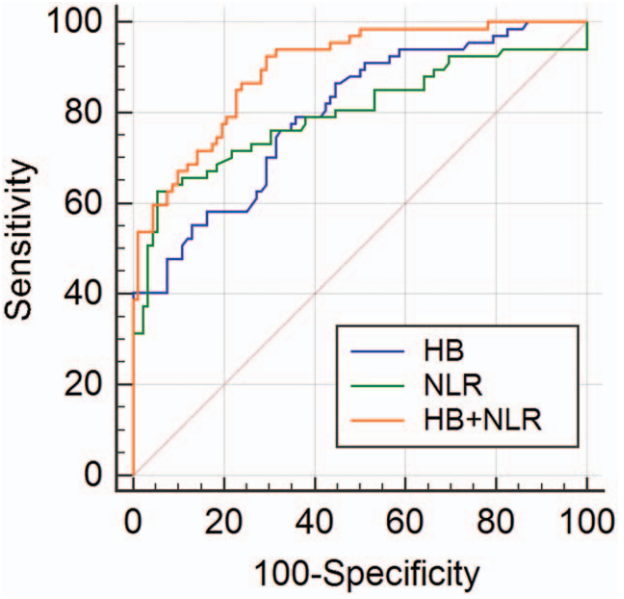

Figure 1. The operating characteristic curve curve of NLR, hemoglobin and the combination of NLR and hemoglobin. NLR = neutrophil to lymphocyte Ratio.

$P < .001$, with sensitivity = 76.12%, specificity = 67.39%. The AUC value of NLR+HB was 0.897, $P < .001$, with sensitivity = 92.50%; specificity = 70.70% (Fig. 1).

5. Discussion

This study demonstrated that NLR was increased but HB was decreased in BD patients. Another key finding was that HB levels were negatively correlated with ESR and CRP, while NLR has no correlation with ESR and CRP. Furthermore, NLR and HB were independent predictive factors for BD. NLR and HB are easily detectable and applicable laboratory parameters, these findings indicate that NLR and HB maybe predictive factors for BD and reflect inflammatory response and disease activity in BD patients.

BD is an inflammatory disease, which the exact cause is unclear.[12] Numerous studies have demonstrated that BD maybe relate to genetics, infection, immune factors and inflammatory mediators. M De Menthon revealed that BD has familial predisposition and significantly correlated with human leucocyte antigen (HLA-B51).[13] Besides, M Studd found that infectious factors also relate to BD.[14]

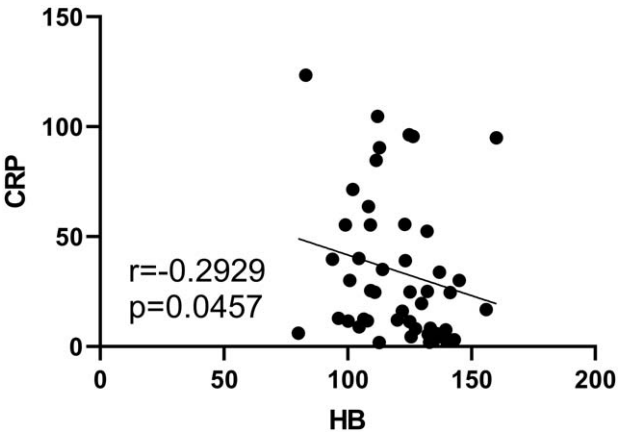

Figure 2. The correlation between hemoglobin and C-reactive protein levels in patients with BD.

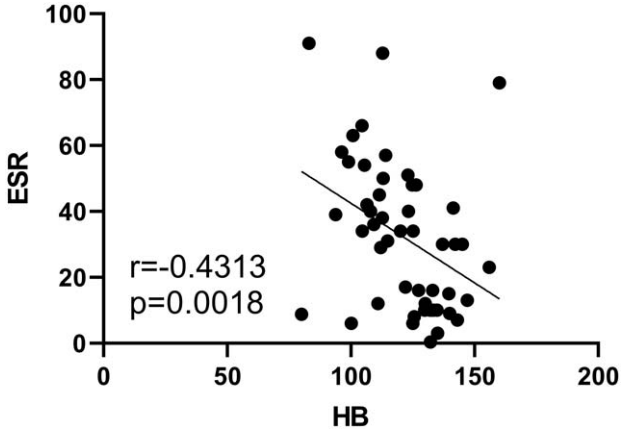

Figure 3. The correlation between erythrocyte sedimentation rate and hemoglobin in patients with BD.

As an inflammatory index, NLR has been studied in many inflammatory diseases. The value of NLR in SLE patients were significantly elevated when compared with healthy controls and has high diagnostic value with sensitivity 0.574; specificity 0.926.[15] Furthermore, Katipoglu et al demonstrated that NLR as an indicator of inflammation was higher in Keratoconus patients with sensitivity71.4% and specificity55%.[16] In a study conducted by Tas et al, they found that NLR may be a helpful index in making precancerous pathologies of the cervix patients with sensitivity71% and specificity60%.[17]

BD have many clinical features and could lead to varying degrees of dysfunction.[2] In a study by Yuksel et al, NLR in the patients with BD was higher than healthy controls.[18] In another study, Alan S et al suggest that NLR can be one of the diagnostic criterions for BD.[19] In addition, Ozturk et al found that NLR was correlated with inflammatory activity in BD.[20] This study identified that NLR was significantly elevated in BD patients when compared with the healthy control. Consistent with the previous studies, our results further confirmed that NLR combine with HB has higher diagnostic effectiveness.

Anemia is common in BD.[21] Low HB levels have been found to be an indicator of inflammatory disease. Previous studies reported that low HB levels was significantly related to the activity of RA[22,23] and the HB level was increased after starting targeted RA treatment.[24] Besides, Yu et al proved that the HB level of SLE patients is significantly lower than that of the healthy control group, which can be used as a marker for predicting SLE.[11]

In conclusion, this study certifies that NLR is increase and the HB levels is reduce in the BD patients and the HB levels inversely associate with BD. In addition, we find that NLR and HB are independent predictive factors in BD patients and combine NLR with HB has higher diagnostic efficiency when compare with NLR and HB alone. We assume that HB can cause DB inflammation or served as the result of BD activity.

However, this is a retrospective analysis and more and larger researches are needed to confirm whether NLR binding to HB is a useful biomarker for the diagnosis of the patients with BD.

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