The European Research Journal 2022;8(6):777-782 Original Article

DOI: 10.18621/eurj.1090380 *Rheumatology*

C-reactive protein to albumin ratio in Behçet's disease

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ABSTRACT

Objectives: This study aims to evaluate the relationship between C-reactive protein (CRP)/albumin ratio (CAR) and other hematological parameters in Behçet's disease (BD).

Methods: A total of 200 participants (100 BD patients and 100 healthy control) were recruited from the rheumatology outpatient clinic in this cross-sectional study. Laboratory tests were conducted to measure complete blood count, erythrocyte sedimentation rate (ESR), CRP, albumin, CAR, neutrophil to lymphocyte ratio (NLR), and platelet to lymphocyte ratio (PLR). Laboratory findings of BD patients and healthy controls were compared and evaluated. BD Activity scores (Behçet's Disease Current Activity Form [BDCAF]) were calculated.

Results: In the BD group, there were 42 male and 58 female participants with a mean age of 42.49 ± 13.15 years and in the healthy control group, 44 male and 56 female participants with a mean age of 44.90 ± 10.98 years. NLR, CRP, ESR and CAR values were significantly higher in patient group than in the healthy controls ($p < 0.05$). BDCAF score varied between 0 and 4 with a mean of 1.55 ± 0.64. A statistically significant correlation was observed between BDCAF and CRP, ESR and CAR ($p < 0.0001$).

Conclusions: In this study, a significant correlation was found between CAR and BDCAF, NLR, CRP, albumin and ESR. CAR can be useful in the diagnosis and following of BD patients.

Keywords: Albumin, Behçet's disease, C-reactive protein, C-reactive protein/albumin ratio

Behçet's disease (BD) is a systemic vasculitis with mucocutaneous, articular, ocular, vascular, neurological and gastrointestinal involvements, which may be seen alone or in combination in patients [1]. Etiology of the disease, which is also known as Behcet syndrome is not fully known [2].

The diagnosis of the disease and response to treatment are evaluated with clinical symptoms. There is no specific laboratory test for the diagnosis and follow up of BD. Although the specificity values of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are low, they are the most frequently used tests [3]. Previous studies have examined the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) in different rheumatological diseases [3-8]. High CRP and low albumin are associated with inflammation. CAR has been shown to be associated with inflammation in some studies. Recent studies of the CRP/albumin ratio (CAR) have reported that it could be a marker of disease activity in rheumatological diseases [9-16]. Only one study could be found in literature related to CAR in BD patients. In this study, patients with Behçet's uveitis were evaluated [15].

The aim of this study was to investigate the relationship between CAR and other laboratory and clinical parameters in patients with BD.

Received: *March 19, 2022;* ***Accepted:*** *August 4, 2022;* ***Published Online:*** *September 8, 2022*

How to cite this article: *Ünal Enginar A. C-reactive protein to albumin ratio in Behçet's disease. Eur Res J 2022;8(6):777-782. DOI: 10.18621/eurj.1090380*

e-ISSN: 2149-3189

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METHODS

This cross-sectional study included BD patients who presented at the Rheumatology Clinic between October 2021 and December 2021, and healthy individuals as a control group. The clinical and laboratory data were obtained retrospectively from the hospital database.

The study included 100 patients diagnosed with BD according to the Behcet Disease International Working Group Diagnostic Criteria [17] and 100 age and gender-matched individuals. Exclusion criteria were defined as age < 18 years or > 65 years, pregnancy or breast-feeding, the presence of a malignant disease, other chronic inflammatory disease, active hepatitis, or chronic liver or kidney disease.

A record was made for all the study subjects of age, gender, neutrophil, lymphocyte, platelets, albumin, CRP, ESR, NLR, PLR, and CAR values. NLR is calculated as the ratio of neutrophil count to lymphocyte count, PLR as the ratio of platelet count to lymphocyte count, and CAR as the ratio of CRP to albumin.

The drugs used by the patients in the BD group and the BD involvements were recorded. To evaluate disease activity, the Behçet's Disease Current Activity Form (BDCAF) was completed. This form is scored in 12 clinical categories (headache, oral ulceration, genital ulceration, erythema nodosum, skin pustules, arthralgia, arthritis, nausea or vomiting or abdominal pain, diarrhea or hematochezia, eye, nervous system and major vessel involvement). According to this scale, values of ≥ 2 show disease activity [18]. A Turkish version of BDCAF has been tested and validated [19].

The normal ranges were accepted as 0–5 mg/L for CRP, 35–52 g/L for albümin and 0-20 mm/h for ESR. Neutrophil, lymphocyte, and platelet counts were recorded as 10^3 u/L.

The study protocol was approved by the Ethics Committee of Necmettin Erbakan University (decision no: 2022/3573).

Statistical Analysis

The SAS version 9.4 was used for statistical analysis. While evaluating the study data, descriptive statistics, including the mean, standard deviation, median, frequency, ratio, minimum and maximum values were obtained. The Kolmogorov-Smirnov test was conducted to check the normality distribution of independent data. Since the data were found to be normally distributed, the independent t-test was used for the comparative analysis. The chisquare test was used for the analysis of qualitative independent data. Pearson correlation coefficient (rs) was used for correlations between parametric data. Statistical significance was accepted as $p < .05$.

RESULTS

Evaluation was made of 100 BD patients, comprising 58 (58%) females and 42 (42%) males with a mean age of 42.49 ± 13.15 years, and 100 healthy control group subjects, comprising 56 (56%) females and 44 (44%) males with a mean age of 44.90 ± 10.98 years. No statistically significant difference was determined between the groups in respect of age and gender (p = 0.16 and p = 0.78, respectively). Involvements in the BD patients were determined as mucocutaneous in 94 (94%) patients, arthritis in 12 (12%), ocular in 26 (26%), vascular in 5 (5%), and neurological in 1 (1%).

Drugs being taken by the patients in the BD group were recorded as colchicine (89.58%), azathioprine (27.08%), low-dose steroids (6.25%), sulphasalazine (4.17%), and tumor necrosis factor (TNF) inhibitors (6.25%). In 4 patients who had previously used colchicine, the drugs were terminated on patient request. None of these patients had any complaints. The disease activity index of the BD patients evaluated with the BDCAF was determined to be mean 1.55 ± 0.64. The NLR, CRP, CAR and ESR values were significantly higher in the BD patient group than in the healthy control group (p = 0.022, p = 0.013, p = 0.011 and $p < 0.001$, respectively) (Table 1).

A statistically significant correlation was determined between CAR and the BCDAF score, neutrophil count, NLR, CRP, albumin, and ESR ($p < 0.0001$). The correlation between CAR and lymphocyte count and PLR was statistically significant but weaker ($p < 0.05$) (Table 2).

A statistically significant correlation was observed between BDCAF and CRP, ESR, CAR ($p < 0.0001$). The correlation between BDCAF and neutrophil and lymphocyte count was statistically significant but weaker ($p < 0.05$) (Table 3).

Table 1. Demographic, clinical and laboratory parameters of the BD patients and healthy subjects

n = 200	Behçet disease (n = 100)	Control (n = 100)	*p* value
Age (years)	42.49 ± 13.15	44.90 ± 10.98	0.16
Sex			
Female	58 (58.00%)	56 (56.00%)	0.78
Male	42 (42.00%)	44 (44.00%)	
BDCAF	1.55 ± 0.64		
Neutrophil (×10^3 µ/L)	4.49 ± 1.81	4.08 ± 1.26	0.06
Lymphocyte (×10^3 µ/L)	2.24 ± 0.74	2.32 ± 0.66	0.41
NLR	2.20 ± 1.22	1.87 ± 0.73	**0.022****
Platelet (×10^3 µ/L)	270.27 ± 67.55	273.69 ± 65.12	0.72
PLR	132.19 ± 51.26	125.24 ± 39.61	0.28
CRP (mg/L)	4.08 ± 6.70	2.34 ± 1.77	**0.013****
Albumin (g/L)	45.35 ± 2.83	46.10 ± 2.62	0.05
CAR	0.09 ± 0.16	0.05 ± 0.04	**0.011****
ESR (mm/h)	17.80 (15.24)	9.92 (8.40)	**< 0.001*****
Mucocutanous, n (%)			
+	94 (94.00)		
-	06 (6.00%)		
Arthritis, n (%)			
+	12 (12.00%)		
-	88 (88.00%)		
Ocular, n (%)			
+	26 (26.00%)		
-	74 (74.00%)		
Vascular, n (%)			
+	05 (5.00%)		
-	95 (95.00%)		
Neurological, n (%)			
+	01 (1.00%)		
-	99 (99.00%)		
Colchicine, n (%)			
+	86 (89.58%)		
-	10 (10.42%)		
Azathioprine, n (%)			
+	26 (27.08%)		
-	70 (72.92%)		
Steroid, n (%)			
+	06 (6.25)		
-	90 (93.75)		
Sulphasalazinei, n (%)			
+	04 (4.17)		
-	92 (95.83)		
TNF inhibitors, n (%)			
+	06 (6.25)		
-	90 (93.75)		

Data are shown as mean±standard deviation or n (%). BDCAF = Behçet's Disease Current Activity Form, NLR = neutrophil to lymphocyte ratio, PLR = platelet to lymphocyte ratio, CRP = C-reactive protein, CAR = C-reactive protein to albumin ratio, ESR = erythrocyte sedimentation rate, TNF = tumor necrosis factor

Table 2. C-reactive protein/albumin ratio and its correlation with other clinical parameters

		CAR
BDCAF	r	0.40998
	p value	**< 0.0001**
Neutrophil	r	0.31384
	p value	**< 0.0001**
Lymphocyte	r	-0.16240
	p value	**0.0216**
NLR	r	0.45205
	p value	**< 0.0001**
Platelet	r	-0.03510
	p value	0.6217
PLR	r	0.15288
	p value	**0.0307**
CRP	r	0.99782
	p value	**< 0.0001**
Albumin	r	-0.28275
	p value	**< 0.0001**
ESR	r	0.52936
	p value	**< 0.0001**

BDCAF = Behçet's Disease Current Activity Form, NLR = neutrophil to lymphocyte ratio, PLR = platelet to lymphocyte ratio, CRP = C-reactive protein, CAR = C-reactive protein to albumin ratio, ESR = erythrocyte sedimentation rate

Table 3. BDCAF and its correlation with other clinical parameters

		BDCAF
Neutrophil	r	0.22197
	p value	**0.0264**
Lymphocyte	r	0.04289
	p value	0.6718
NLR	r	0.14016
	p value	0.1643
Platelet	r	0.20258
	p value	**0.0432**
PLR	r	0.14788
	p value	0.1420
CRP	r	0.41355
	p value	**< 0.0001**
Albumin	r	-0.10776
	p value	0.2859
CAR	r	0.40998
	p value	**< 0.0001**
ESR	r	0.53736
	p value	**< 0.0001**

BDCAF = Behçet's Disease Current Activity Form, NLR = neutrophil to lymphocyte ratio, PLR = platelet to lymphocyte ratio, CRP = C-reactive protein, CAR = C-reactive protein to albumin ratio, ESR = erythrocyte sedimentation rate

DISCUSSION

BD may involve all types and sizes of vessels, and very different clinical tables may develop. There is no specific laboratory test for BD either in diagnosis or follow up. ESR and CRP are the most frequently used tests [20]. In a previous study of BD patients, a relationship was reported between elevated ESR and CRP and newly developed erythema nodosum, superficial thrombophlebitis or joint involvement. In the same study, a correlation was also determined between BDCAF score and ESR and CRP values [21]. However, there may be false positives and false negatives in these tests [20]. Therefore, clinicians continue to seek a practical, inexpensive and easy-to-apply test. There are studies in literature related to NLR and PLR in BD, just as in different rheumatological diseases [5-8]. In the current study, NLR was determined to be higher in the BD patients than in the control group. Hammad *et al*. [5] reported that NLR was higher in active BD patients than in non-active BD patients, and that both NLR and PLR were correlated with the BDCAF score. In a meta-analysis and another study, NLR was determined to be higher in active BD patients [6, 7], and PLR was found to be higher in active BD patients in another previous study [8]. Hou and Guan [3] reported that disease duration (≤ 60 months), NLR (≥ 2), CRP (≥ 10 mg/L), ESR (≥ 20mm/h), and albumin globulin ratio (< 1.5) were risk factors in BD patients independently of disease activity.

Recent studies have been conducted related to CAR in rheumatological diseases such as axial spondyloarthropathy, ANCA-related vasculitis, rheumatoid arthritis, Behcet uveitis, relapsing poly-

chondritis, and Kawasaki disease [9-16]. To the best of our knowledge, there is only one study in the literature related to CAR and BD. In that study, Kim *et al* examined 50 patients with BD-related uveitis and 52 patients with HLA-B27-related uveitis. A correlation was determined between CAR and the severity of ocular inflammation, and it was reported that CAR could be useful in respect of acute flare-ups in patients with chronic uveitis [15]. In a study by Bozkurt *et al*. [16], the CAR values were determined to be higher in 35 non-infective uveitis patients than in the healthy control group. CAR and CRP were reported to increase with activation and the severity of uveitis. Only 7 BD patients were included in that study [16]. In the current study, the NLR, CRP, CAR, and ESR values were determined to be higher in the BD patients than in the healthy control group. Moreover, a statistically significant correlation was determined between CAR and the BDCAF score, neutrophil count, lymphocyte count, NLR, PLR, CRP, albumin, and ESR. Thus, it can be said that CAR may be a more effective marker in BD patients than the evaluation of CRP alone as a positive acute phase protein, or albumin alone as a negative acute phase protein.

Limitations

There were some limitations to this study, primarily the retrospective design and relatively low number of patients. As the majority of BD patients in the study had low disease activity, no comparisons could be made with BD patients with high disease activity. That comorbidities and other factors such as diet were not evaluated could also be considered a limitation.

CONCLUSION

In conclusion, it was observed from the results of this study that CAR is a parameter that could be used in the diagnosis and follow up of BD patients. Nevertheless, there is a need for further studies to support these findings.

Authors' Contribution

Study Conception: AÜE; Study Design: AÜE; Supervision: AÜE; Funding: AÜE; Materials: AÜE; Data Collection and/or Processing: AÜE; Statistical Analysis and/or Data Interpretation: AÜE; Literature Review: AÜE; Manuscript Preparation: AÜE and Critical Review: AÜE.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

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