

Background: Behçet's disease (BD) is a systemic variable vasculitis that is characterized by increased production of neutrophil extracellular traps (NETs). Citrullinated histone H3 (CitH3) is formed in the process of posttranslational modification of peptidylarginine into citrulline during NETosis. There is no data on the study of a specific marker of NETosis, CitH3, in peripheral blood in BD.

The aim of the work was to investigate the levels of CitH3 in serum in patients with BD.

Material and methods:

- This study included 74 patients with a reliable diagnosis of BD and 30 healthy controls.
- The median age was 32 [27; 39] years, and the median disease duration was 10 [5; 17] years.
- Disease activity was assessed using Behçet's Disease Current Activity Form (BDCAF), whose values were considered low (0–1 points), moderate (2–3 points), and high (4–12 points). CitH3 was measured in serum by enzyme-linked immunosorbent assay (ELISA) according to the manufacturer's protocol (BlueGene Biotech, China).

Results.

CitH3 levels were significantly higher in patients with BD compared to healthy controls (243.34 [124.38; 373.1] ng/mL vs. 106.09 [90.46; 192.09] ng/mL, $p < 0.0001$, Fig.1). Patients with moderate and high disease activity (BDCAF ≥ 2 points) had higher CitH3 levels than those with low activity (255.01 [174.85; 390.95] ng/mL vs. 98.55 [90.99; 339.75] ng/mL, $p = 0.024$). A significant association was found between high CitH3 levels and the presence of pustulosis (OR=2.67, $p = 0.048$). No clear association was found between CitH3 and other manifestations of BD. ROC analysis was performed to assess the diagnostic value of CitH3 in differentiating patients with BD from healthy controls (Fig. 2). The area under the ROC curve (AUC) was 0.762, 95% CI: 0.673-0.851, $p < 0.0001$. At a cut-off point of 238.79 ng/mL, CitH3 allows differentiation of BD patients from healthy donors with a sensitivity of 51.4% and specificity of 96.7%.

Fig.1. CitH3 in BD and healthy controls

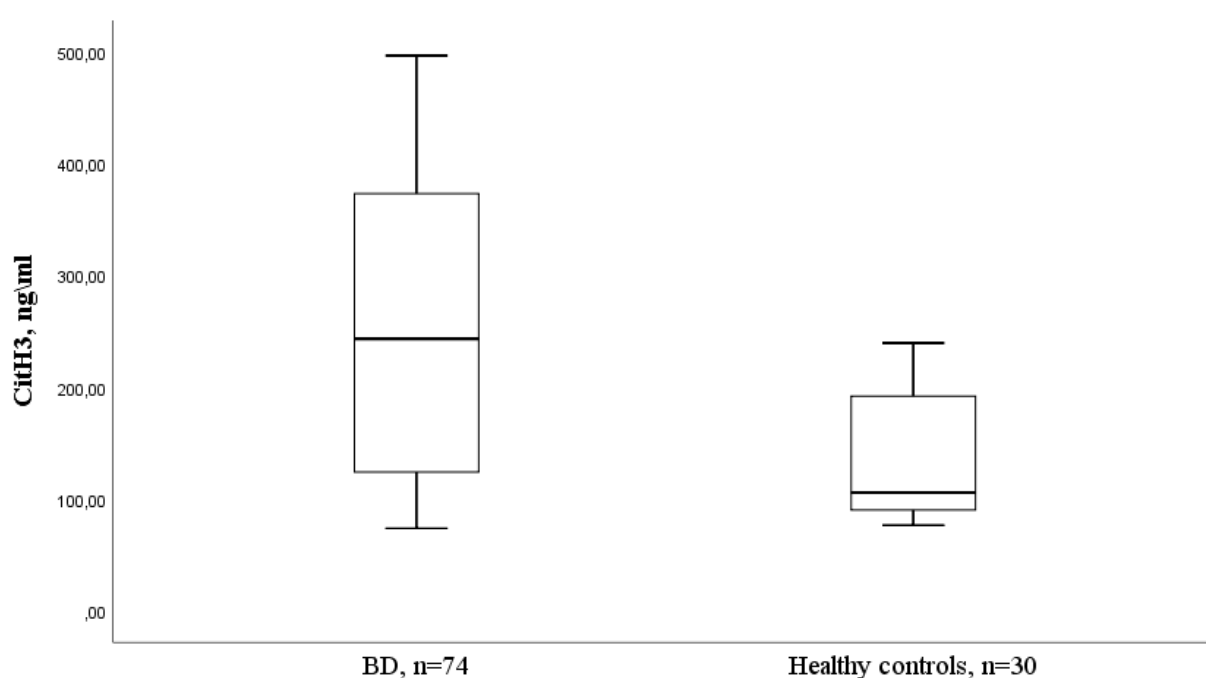
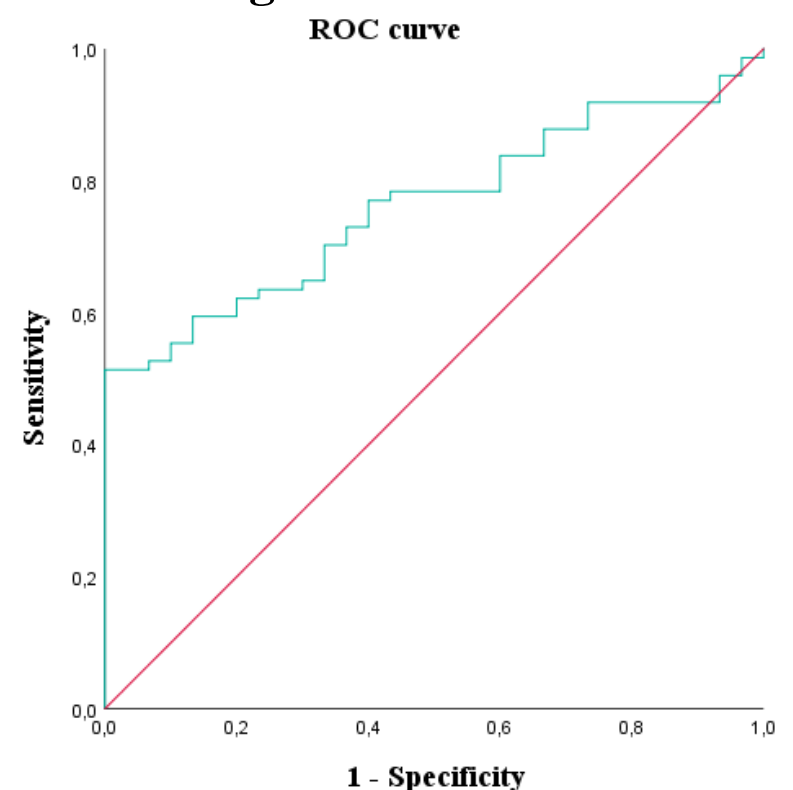


Fig.2. CitH3 in BD



Conclusion: An increase in the specific marker of NETosis, CitH3, was observed in BD patients, indicating activation of PAD4-mediated NETosis in BD.