CLINICAL AND LABORATORY SIGNIFICANCE OF SYSTEMIC INFLAMMATORY MARKERS IN VARIOUS FORMS OF BRUCELLOSIS AND OPTIMIZATION OF TREATMENT

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Abstract

Brucellosis remains a significant zoonotic infection worldwide, characterized by a wide spectrum of clinical manifestations and a tendency toward chronicity. Systemic inflammatory response plays a key role in the pathogenesis and clinical course of the disease. This article analyzes the clinical and laboratory significance of systemic inflammatory markers in different clinical forms of brucellosis and discusses approaches to optimizing treatment strategies based on these markers. Assessment of inflammatory biomarkers allows for improved early diagnosis, evaluation of disease severity, monitoring of therapeutic effectiveness, and prevention of complications.

Keywords: *brucellosis, systemic inflammation, biomarkers, C-reactive protein, cytokines, diagnosis, treatment.*

Introduction

Brucellosis remains one of the most common zoonotic infectious diseases worldwide and continues to represent a serious medical, social, and economic problem, particularly in endemic regions. According to the World Health Organization, more than 500,000 new cases of human brucellosis are reported annually, although the true incidence is believed to be significantly higher due to underdiagnosis and misreporting. The disease is especially prevalent in countries with developed livestock farming, where close contact with infected animals and consumption of unpasteurized dairy products remain the main routes of transmission.

Brucellosis is characterized by a polymorphic clinical course and a wide spectrum of manifestations, ranging from acute febrile illness to chronic debilitating forms with multisystem involvement. The causative agents, bacteria of the genus Brucella, are facultative intracellular pathogens capable of long-term persistence within macrophages and other cells of the reticuloendothelial system. This intracellular localization allows the pathogen to evade immune surveillance and contributes to chronic inflammation, relapses, and resistance to therapy.

One of the key pathogenetic mechanisms of brucellosis is the development of a systemic inflammatory response. Activation of innate and adaptive immunity leads to excessive production of pro-inflammatory cytokines, acute-phase proteins, and other inflammatory mediators. These processes play a dual role: on the one hand, they are

necessary for controlling infection, while on the other hand, their persistence contributes to tissue damage, clinical severity, and chronicity of the disease.

Systemic inflammatory markers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), procalcitonin, and cytokines including tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β) have gained increasing attention in recent years. These markers reflect the activity of the inflammatory process and may serve as valuable tools for early diagnosis, assessment of disease severity, differentiation of clinical forms, monitoring of treatment response, and prediction of outcomes in brucellosis.

Clinical forms of brucellosis—acute, subacute, chronic, and focal (localized)—differ significantly in their immunopathological features. However, standardized criteria for evaluating inflammatory activity and guiding individualized treatment strategies remain insufficiently developed. Improving therapeutic approaches based on the assessment of systemic inflammatory markers may help optimize antibacterial therapy, reduce the duration of treatment, prevent complications, and improve long-term prognosis.

In this context, the present article aims to analyze the clinical and laboratory significance of systemic inflammatory markers in various forms of brucellosis and to explore possibilities for improving treatment strategies through a more personalized, pathogenetically justified approach.

Identification and interpretation of systemic inflammatory markers are essential for understanding disease activity and guiding therapeutic decisions. Therefore, studying their clinical and laboratory significance is of high relevance.

Material and methods

Study Design and Setting

This study was conducted as a prospective observational clinical and laboratory investigation aimed at evaluating the clinical and laboratory significance of systemic inflammatory markers in patients with various forms of brucellosis. The research was carried out at a specialized infectious diseases hospital and outpatient departments over the period from 2022 to 2024.

Study Population. The study included 120 patients with confirmed brucellosis aged between 18 and 65 years. The diagnosis of brucellosis was established based on clinical presentation, epidemiological history, and laboratory confirmation. Patients were classified into clinical forms of brucellosis according to disease duration and manifestations: acute, subacute, chronic, and focal (localized) forms.

A control group consisted of 30 apparently healthy individuals matched by age and sex, with no history of acute or chronic inflammatory diseases.

Laboratory Investigations

All patients underwent comprehensive clinical and laboratory assessment at admission and during follow-up. Laboratory investigations included:

complete blood count (CBC) with differential;

erythrocyte sedimentation rate (ESR);

C-reactive protein (CRP);

serum procalcitonin levels;

cytokine profile assessment, including tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β), measured by enzyme-linked immunosorbent assay (ELISA);

serological tests for brucellosis (Rose Bengal test, Wright agglutination test);

blood culture in selected cases.

Treatment and Monitoring

All patients received standard antibacterial therapy in accordance with national and international clinical guidelines, including combinations of doxycycline, rifampicin, and, when indicated, aminoglycosides. Treatment duration and regimen adjustments were individualized based on clinical form, severity of disease, and laboratory indicators of inflammatory activity.

Systemic inflammatory markers were assessed before treatment initiation and dynamically during therapy to evaluate treatment response and guide therapeutic optimization.

Statistical Analysis. Statistical analysis was performed using standard statistical software packages. Quantitative variables were expressed as mean ± standard deviation (SD) or median with interquartile range, as appropriate. Comparisons between groups were conducted using Student's t-test or Mann–Whitney U test. Correlations between inflammatory markers and clinical severity were assessed using Pearson or Spearman correlation coefficients. A p-value <0.05 was considered statistically significant.

General Clinical Characteristics

A total of 120 patients with confirmed brucellosis were included in the analysis. According to clinical presentation and disease duration, 38 patients (31.7%) were diagnosed with acute brucellosis, 34 patients (28.3%) with subacute brucellosis, 32 patients (26.7%) with chronic brucellosis, and 16 patients (13.3%) with focal (localized) forms. The majority of patients presented with fever, sweating, fatigue, arthralgia, and myalgia, while focal forms were characterized by osteoarticular, genitourinary, or neurological involvement.

Laboratory evaluation revealed significant differences in systemic inflammatory markers between patients with brucellosis and the control group. Patients with acute and subacute forms demonstrated pronounced inflammatory responses, including leukocytosis or relative leukopenia with lymphomonocytosis, elevated ESR, and increased CRP levels.

Mean ESR values were significantly higher in acute (38.6 ± 9.4 mm/h) and subacute forms (31.2 ± 7.8 mm/h) compared to chronic brucellosis (18.5 ± 6.1 mm/h) and the control group (8.4 ± 2.6 mm/h) ($p < 0.05$). Serum CRP concentrations were markedly elevated in acute and subacute brucellosis and showed a gradual decline in chronic and focal forms.

Assessment of pro-inflammatory cytokines revealed significantly increased serum levels of TNF-α, IL-6, and IL-1β in patients with brucellosis compared to healthy controls ($p < 0.01$). The highest cytokine concentrations were observed in acute brucellosis, followed by subacute forms. In chronic brucellosis, cytokine levels remained moderately elevated, indicating persistent low-grade inflammation.

A strong positive correlation was identified between IL-6 levels and CRP values ($r = 0.68$, $p < 0.01$), as well as between TNF-α concentrations and clinical severity scores ($r = 0.61$, $p < 0.05$).

Serum procalcitonin levels were moderately increased in acute brucellosis but remained within normal or slightly elevated ranges in chronic and focal forms. This finding suggests limited diagnostic value of procalcitonin for chronic brucellosis, while it may be useful in differentiating acute bacterial infections with systemic involvement.

Following initiation of antibacterial therapy, a significant reduction in CRP, ESR, and cytokine levels was observed by the end of the second week of treatment in patients with acute and subacute brucellosis ($p < 0.05$). In chronic forms, normalization of inflammatory markers occurred more slowly and was incomplete in some cases, correlating with persistent clinical symptoms.

Patients with focal brucellosis demonstrated prolonged elevation of inflammatory markers, necessitating extended or modified treatment regimens.

Conclusion

Systemic inflammatory markers play a crucial role in the clinical and laboratory assessment of brucellosis. Their evaluation provides valuable information on disease activity, severity, and response to therapy. Incorporation of inflammatory biomarker monitoring into clinical practice contributes to optimization of treatment strategies, reduction of complications, and prevention of chronic disease forms. Further studies are needed to establish standardized biomarker-based algorithms for the management of brucellosis patients.

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