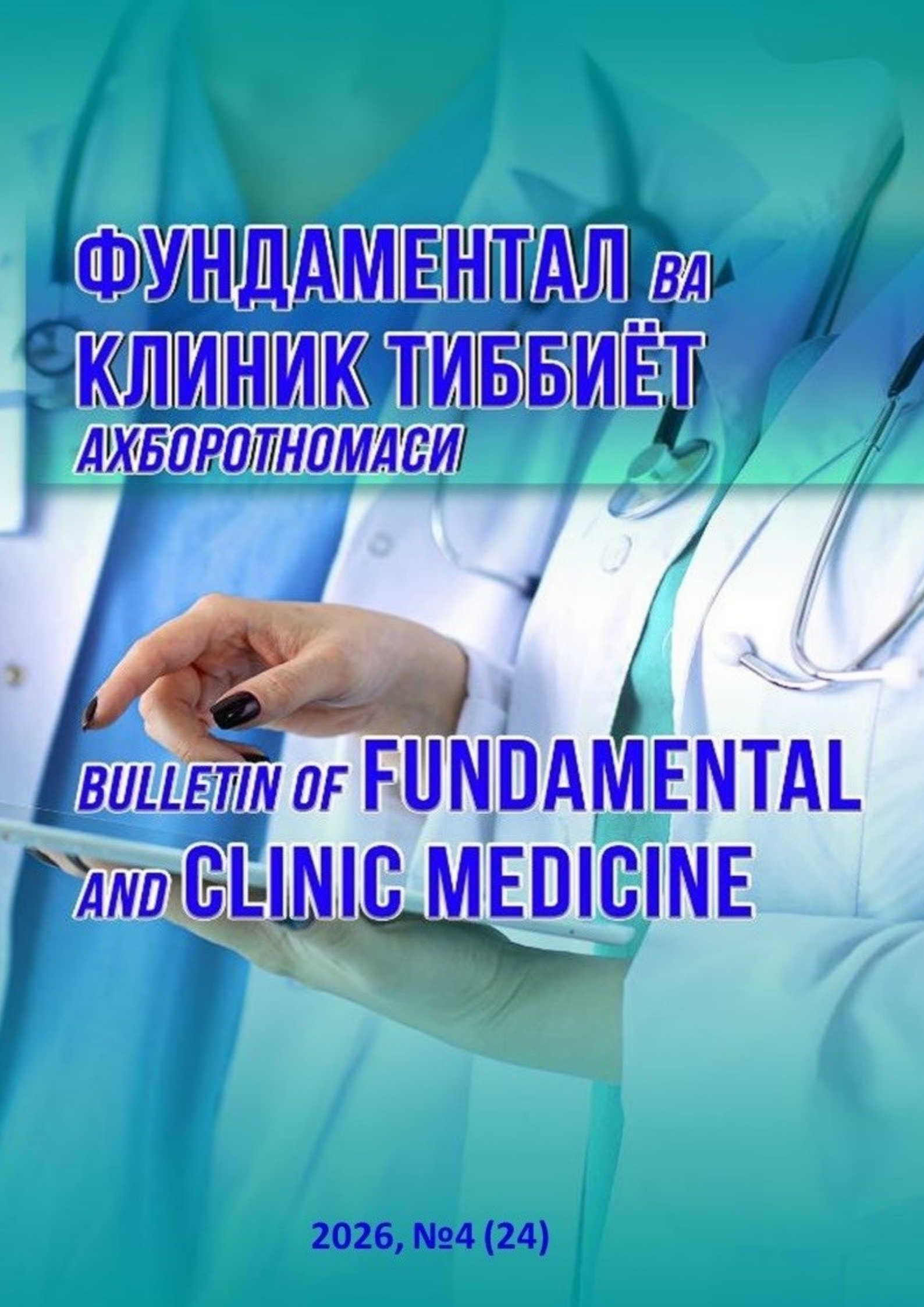

ФУНДАМЕНТАЛ ВА КЛИНИК ТИББИЁТ АХБОРОТНОМАСИ

BULLETIN OF FUNDAMENTAL AND CLINIC MEDICINE

2026, №4 (24)

МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ
РЕСПУБЛИКИ УЗБЕКИСТАН

BULLETIN OF FUNDAMENTAL AND CLINIC MEDICINE

ФУНДАМЕНТАЛ ВА КЛИНИК ТИББИЁТ АХБОРОТНОМАСИ

ВЕСТНИК ФУНДАМЕНТАЛЬНОЙ И КЛИНИЧЕСКОЙ МЕДИЦИНЫ

Научный журнал по фундаментальным и клиническим проблемам медицины
основан в 2022 году
Бухарским государственным медицинским институтом имени Абу Али ибн Сино
выходит один раз в 2 месяца

Учредитель Бухарский государственный медицинский институт имени Абу Али ибн Сино

2026, № 4 (24)

ISSN 2181-4198

Адрес редакции:

Республика Узбекистан, 200100, г. Бухара, ул. Гиждуванская, 23.

Телефон *(99865) 223-00-50*
Факс *(99866) 223-00-50*
Сайт *https://bsmi.uz/journals/fundamenial-va- klinik-tibbiyot-ahborotnomasi/*
e-mail *baymuradovravshan@gmail.com*

О журнале

Журнал зарегистрирован в Управлении печати и информации Бухарской области № 1640 от 28 мая 2022 года.

Журнал внесен в список утвержденный приказом № 370/6 от 8 мая 2025 года реестром ВАК в раздел медицинских наук.

Отпечатано в типографии ООО “Шарк-Бухоро”. г. Бухара, ул. Ўзбекистон Мустакиллиги, 70/2.

Редакционный совет:

UDC 616.98-002.28:616-092:616-07:615.33

DOI https://doi.org/10.5281/zenodo.19533552

THE IMPORTANCE OF INFLAMMATION MARKERS IN BRUCELLOSIS: DIAGNOSTIC, PROGNOSTIC, MONITORING, DIFFERENTIAL DIAGNOSIS, AND TREATMENT CONSIDERATIONS

Rashidova G.U.

Bukhara State Medical Institute named after Abu Ali ibn Sino, Bukhara, Uzbekistan

Resume. *Brucellosis is a widespread zoonotic infection caused by Brucella species, frequently complicated by osteoarticular involvement (10–85% of cases). Inflammation plays a central role in its pathogenesis due to intracellular persistence of the pathogen in macrophages. Traditional inflammatory markers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), white blood cell count, and derived ratios (neutrophil-to-lymphocyte ratio [NLR], platelet-to-lymphocyte ratio [PLR], systemic immune-inflammation index [SII]) serve as accessible, cost-effective tools for diagnosis, severity assessment, prediction of complications, differential diagnosis, and treatment monitoring, particularly in endemic regions. These markers help distinguish brucellosis from mimics like typhoid, tuberculosis, and viral fevers. They also guide prolonged antibiotic therapy (e.g., doxycycline + rifampin) and early detection of relapse. This review highlights the multifaceted value of inflammation markers in improving outcomes in resource-limited settings.*

Keywords: *Brucellosis; inflammation markers; C-reactive protein (CRP); erythrocyte sedimentation rate (ESR); neutrophil-to-lymphocyte ratio (NLR); osteoarticular involvement; differential diagnosis; treatment monitoring*

БРУЦЕЛЛЁЗДА ЯЛЛИҒЛАНИШ МАРКЕРЛАРИНИНГ АҲАМИЯТИ: ДИАГНОСТИКА, ПРОГНОЗ, МОНИТОРИНГ, ДИФФЕРЕНЦИАЛ ДИАГНОСТИКА ВА ДАВОЛАШ МАСАЛАЛАРИ

Рашидова Г.Ў.

Абу Али ибн Сино номидаги Бухоро давлат тиббиёт институти, Бухоро ш., Ўзбекистон

Резюме. *Бруцеллёз — Brucella туркумига мансуб бактериялар келтириб чиқарадиган кенг тарқалган зооноз инфекция бўлиб, кўпинча остеоартикуляр зарарланиш (10–85% ҳолларда) билан мураккаблашади. Яллиғланиш жараёни касаллик патогенезида марказий ўрин тутади, чунки патоген макрофагларда ҳужайра ичида сақланиб қолади. Анъанавий яллиғланиш маркерлари — С-реактив оқсил (CRP), эритроцитлар чўкиш тезлиги (ESR), оқ қон ҳужайралари сони ҳамда ҳосил қилинган нисбатлар (нейтрофил-лимфоцит нисбати [NLR], тромбоцит-лимфоцит нисбати [PLR], тизимли иммун-яллиғланиш индекси [SII]) — эндемик ҳудудларда диагностика, оғирлик даражасини баҳолаш, асоратлар башорати, дифференциал диагностика ва даволашни мониторинг қилиш учун қулай ва арзон воситалар ҳисобланади. Ушбу маркерлар бруцеллёзни тиф, сил ва вирусли иситмалардан фарқлашга ёрдам беради. Улар, шунингдек, узоқ муддатли антибиотик терапиясини (масалан, доксисиклин + рифампин) бошқариш ва релапсни эрта аниқлашда муҳимдир. Ушбу мақола ресурслари чекланган шароитларда яллиғланиш маркерларининг кўп қиррали аҳамияти-ни таъкидлайди.*

Калит сўзлар: *Бруцеллёз; яллиғланиш маркерлари; С-реактив оқсил (CRP); эритроцитлар чўкиш тезлиги (ESR); нейтрофил-лимфоцит нисбати (NLR); остеоартикуляр зарарланиш; дифференциал диагностика; даволаш мониторинги*

ЗНАЧЕНИЕ МАРКЁРОВ ВОСПАЛЕНИЯ ПРИ БРУЦЕЛЛЁЗЕ: ДИАГНОСТИКА, ПРОГНОЗ, МОНИТОРИНГ, ДИФФЕРЕНЦИАЛЬНАЯ ДИАГНОСТИКА И АСПЕКТЫ ЛЕЧЕНИЯ

Рашидова Г.У.

Бухарский государственный медицинский институт имени Абу Али ибн Сино, г. Бухара, Узбекистан

Резюме. *Бруцеллёз — широко распространённая зоонозная инфекция, вызываемая видами Brucella, часто осложняющаяся остеоартикулярным поражением (в 10–85% случаев). Воспаление играет центральную роль в патогенезе заболевания из-за внутриклеточного персистирования возбудителя в макрофагах. Традиционные маркёры воспаления, такие как С-реактивный белок (СРБ), скорость оседания эритроцитов (СОЭ), количество лейкоцитов и производные соотношения (нейтрофильно-лимфоцитарный индекс [НЛИ], тромбоцитарно-лимфоцитарный индекс [ТЛИ], системный иммуно-воспалительный индекс [SII]), служат доступными и недорогими инструментами для диагностики, оценки тяжести, прогнозирования осложнений, дифференциальной диагностики и*

мониторинга лечения, особенно в эндемичных регионах. Эти маркёры помогают отличить бруцеллёз от таких заболеваний, как брюшной тиф, туберкулёз и вирусные лихорадки. Они также помогают управлять длительной антибиотикотерапией (например, доксициклин + рифампицин) и раннему выявлению рецидивов. Новые биомаркёры, такие как ирисин и цитокины, ещё больше повышают клиническую ценность. Данный обзор подчёркивает многогранную значимость маркёров воспаления для улучшения исходов в условиях ограниченных ресурсов.

Ключевые слова: *Бруцеллёз; маркёры воспаления; С-реактивный белок (СРБ); скорость оседания эритроцитов (СОЭ); нейтрофильно-лимфоцитарный индекс (НЛИ); остеоартикулярное поражение; дифференциальная диагностика; мониторинг лечения*

e-mail: rashidovaguljahon99@gmail.com

Introduction. Brucellosis remains a significant zoonotic disease, with global annual incidence conservatively estimated at 2.1 million cases, predominantly in Asia and Africa, though underreporting is common due to diagnostic challenges. In endemic areas (e.g., parts of Central Asia, China, Iran), incidence rates can exceed 35–84/100,000 in high-burden regions like Ningxia (average 35.08/100,000 from 2010–2024) or certain Iranian provinces (>200/100,000 historically). The acute phase features systemic inflammation from bacterial dissemination and host response, often complicated by osteoarticular involvement (10–85%, most frequently 20–40%; sacroiliitis in ~48–62%, peripheral arthritis in children)[9]. Inflammation markers offer rapid, inexpensive insights for diagnosis (complementing serology/culture), severity grading, complication prediction (e.g., focal forms in 30–40% of cases)[5], differential diagnosis, and monitoring response to antibiotics (e.g., doxycycline + rifampin). Their importance is amplified in settings with delayed confirmation, where early marker assessment prevents progression to chronicity.

This review details the inflammatory basis of brucellosis and evaluates key markers' statistical performance in diagnosis, prognosis, differential diagnosis, and management.

Etiopathogenesis of inflammation in brucellosis. Brucella species enter and survive within macrophages primarily through their Type IV secretion system and a structurally atypical, low-endotoxin LPS that blunts early TLR4 signaling. This strategy effectively dampens initial innate immune activation, limiting neutrophil recruitment while simultaneously favoring a robust Th1-polarized adaptive response characterized by elevated production of IFN-γ, TNF-α, IL-6, and IL-12.

Ongoing intracellular replication of the pathogen perpetuates a sustained cytokine storm, driving persistent inflammation, granuloma formation in affected tissues, and progressive tissue injury. These processes account for the marked elevation of classical acute-phase reactants—most notably CRP (induced mainly by IL-6) and fibrinogen (which accelerates ESR)—even though peripheral white blood cell counts are frequently normal or reduced (leukopenia) as a result of effective immune evasion and bone marrow suppression.

Key intracellular signaling cascades, including NF-κB and MAPK pathways, become hyperactivated and amplify the inflammatory cascade, thereby contributing to the development of focal complications. Osteoarticular involvement is especially common (reported in 2–77% of cases depending on series and definition), while anemia occurs in 20–53% of pediatric acute brucellosis patients.

The observed heterogeneity in inflammatory biomarker profiles arises from the dual and opposing dynamics of the infection: strong suppression of certain innate immune arms contrasted with vigorous activation of adaptive (Th1) immunity.

Clinical importance of traditional inflammation markers. CRP and ESR serve as cornerstone acute-phase reactants in acute brucellosis. C-reactive protein (CRP) shows a rapid increase during active infection—commonly exceeding 10–50 mg/L—with reported diagnostic sensitivities of 65–80% and specificities around 72% (for example, one ROC analysis found 65% sensitivity and 72% specificity [1] , while other studies report up to 77.8% sensitivity and 95% specificity at an optimal cut-off of 3.33 mg/L). CRP levels closely track disease severity and typically return to normal following successful treatment.

Erythrocyte sedimentation rate (ESR) is elevated in the majority of cases (70–76%), often ranging from >20–50 mm/h (e.g., mean 35.6 mm/h in patients vs. 12.2 mm/h in controls, $p<0.001$). While valuable for longitudinal monitoring, ESR lacks the specificity of CRP.

White blood cell count (WBC) shows considerable variability: it is frequently normal or even reduced (leukopenia secondary to bone marrow suppression), though neutrophilia may occur in some patients; overall diagnostic performance is modest (sensitivity ~54%, specificity ~66%).

In complicated brucellosis (affecting 38–39% of cases overall), both ESR and CRP are markedly higher than in uncomplicated disease (e.g., ESR 48 vs. 38 mm/h, CRP 29 vs. 17 mg/L, $p<0.001$), underscoring their prognostic utility [2].

These traditional markers are particularly effective for treatment follow-up: failure of CRP and/or ESR to normalize, or their secondary rise, strongly suggests relapse, treatment failure, or the emergence of focal complications.[19]

Derived hematological ratios and systemic indices. Derived hematological ratios and systemic inflammatory indices provide valuable insights into immune responses during brucellosis. For instance, the neutrophil-to-lymphocyte ratio (NLR) is frequently lower in affected patients (e.g., median 1.69 vs. 2.07 in controls, p=0.013; AUC 0.644), while the platelet-to-lymphocyte ratio (PLR) shows variable findings, the lymphocyte-to-monocyte ratio (LMR) tends to be elevated (median 5.28 vs. 4.12, p=0.008), and the systemic immune-inflammation index (SII) may be reduced in certain pediatric cohorts. These shifts mirror altered immune dynamics in the infection.

Multivariate or combined models, such as one integrating mean platelet volume (MPV) with erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), demonstrate markedly improved diagnostic accuracy (AUC 0.891, with 84% sensitivity and 86% specificity) compared to single markers.[3][6]

In pediatric and focal/complicated presentations, elevated neutrophil-to-monocyte ratio (NMR) and CRP levels serve as predictors of osteoarticular involvement (OI, occurring in ~23.7% of cases in some series; e.g., CRP 30.2 vs. 9.8 mg/L, p=0.039; accompanied by lower white blood cell counts, p=0.015). Additionally, reduced MPV is linked to the presence of complications (p=0.038), highlighting its potential prognostic significance[4].

Special considerations: pediatric and complicated brucellosis. Osteoarticular involvement (OI) occurs in 10–85% of brucellosis cases, with peripheral joint involvement being more frequent in children, while sacroiliitis is more commonly seen in adults. Pediatric studies report significantly higher CRP levels, lower white blood cell counts, and elevated NMR values in patients with osteoarticular disease ($p < 0.05$)[4]. These laboratory markers can help stratify risk, guiding decisions about the need for targeted imaging and extended treatment duration.[6][8][9][20]

Differential diagnosis using inflammation markers. Acute brucellosis mimics numerous conditions due to nonspecific symptoms (fever, malaise, arthralgia), complicating diagnosis in endemic areas. Key differentials include infectious etiologies (malaria, typhoid fever, tuberculosis, leptospirosis, viral infections like influenza or dengue) and noninfectious ones (collagen-vascular diseases, lymphoma, histiocytosis, sarcoidosis). Inflammation markers aid differentiation: in brucellosis, CRP and ESR are often markedly elevated (CRP >20–50 mg/L in 70–90% of cases; ESR >50 mm/h in 70–76%), but WBC is normal or low (leukopenia in 20–40%, neutrophilia absent in most), contrasting with pyogenic bacterial infections (e.g., pneumonia, abscess) where leukocytosis (>10,000/μL) and neutrophilia predominate. For malaria or typhoid, similar low WBC may occur, but CRP is typically lower in viral fevers (e.g., <10 mg/L in uncomplicated influenza). Derived ratios like NLR are lower in brucellosis (median 1.69–2.5) vs. higher in acute bacterial infections (e.g., >5 in sepsis). In osteoarticular presentations, markers distinguish from rheumatoid arthritis (higher ESR/CRP with positive autoantibodies) or sacroiliitis from ankylosing spondylitis (normal WBC, variable CRP)[13]. Combined with serology (e.g., Rose Bengal test positive in 88–90%), markers achieve high diagnostic accuracy (e.g., ELISA + elevated CRP/ESR AUC >0.85 for sacroiliitis)[14]. Novel markers like endocan (elevated in brucellosis) may further refine differentials from healthy controls or subacute/chronic forms.[12]

Treatment considerations and role of inflammation markers in monitoring. Treatment of brucellosis requires prolonged combination antibiotics to prevent relapse (rates 4.8–10% with suboptimal regimens) and chronicity. World Health Organization guidelines recommend doxycycline (100 mg twice daily) + rifampin (600–900 mg/day) for 6 weeks (relapse risk ~8–10%), or doxycycline + streptomycin (1 g/day IM for 2–3 weeks; relapse ~4–5%, more effective for prevention)[15]. Recent meta-analyses favor doxycycline + gentamicin (1–2 weeks; SUCRA efficacy ranking 0.94, relapse <5%) or triple therapy (doxycycline + rifampin + aminoglycoside) for severe cases (e.g., endocarditis, meningitis; duration 4–6 months, case-fatality <1% with early intervention)[16]. For children <8 years, rifampin + trimethoprim-sulfamethoxazole (TMP-SMZ) for 6 weeks is preferred (avoid tetracyclines). In pregnancy, TMP-SMZ + rifampin is used (tetracyclines contraindicated). Inflammation markers guide therapy: baseline high CRP/ESR (>50 mg/L or >50 mm/h) predict need for prolonged courses; normalization (CRP <5 mg/L, ESR <20 mm/h) post-treatment indicates success (80–90% resolution in 2–3 weeks for uncomplicated cases). Persistent elevation (>2–4 weeks) signals relapse (10–15% risk) or complications, prompting extended therapy or adjunctive corticosteroids in severe inflammation. Cytokines (e.g., IL-6 decline) and ratios (NLR normalization) enhance monitoring, especially in resource-limited settings where culture (positive in 30–70%) is unavailable.[18]

Conclusion. Inflammatory biomarkers play a central role in the management of acute brucellosis, offering robust statistical support across multiple clinical domains. They aid in diagnosis (with CRP and ESR frequently achieving AUC values of 0.7–0.8 or higher), prognostication (elevated levels strongly associated with complicated disease, affecting 30–40% of cases), differential diagnosis (characteristic patterns, such as relatively low white blood cell counts, help distinguish brucellosis from bacterial mimics), and treatment monitoring—particularly relevant given the ongoing global burden of approximately 2.1 million new cases annually.

Both conventional markers (CRP, ESR) and derived hematological ratios (NLR, SII, among others) facilitate timely intervention in endemic regions, thereby helping to decrease long-term morbidity. When used in conjunction with established treatment protocols—most commonly doxycycline-based combination regimens—these tools contribute to improved patient outcomes.[19]

Future prospective studies validating combined biomarker models and establishing reliable diagnostic/prognostic cut-off values are expected to further refine and strengthen their clinical utility.

References:

1. Akya A, et al. Usefulness of Blood Parameters for Preliminary Diagnosis of Brucellosis. Int J Infect. 2020;7(1):e7125307.
2. Sen P, et al. Predictive Value of Inflammation Markers in Brucellosis. Arch Iran Med. 2019;22(12):710-716.
3. Çağlar Y, et al. Diagnostic Value of Hematological Inflammatory Ratios in Brucellosis. Preprints. 2025. doi:10.20944/preprints202510.1751.v1.
4. Böncüoğlu E, et al. Inflammatory marker comparison in childhood brucellosis: predicting osteoarticular involvement. Turk J Pediatr. 2025;67(2):1-10.
5. Xu N, et al. Improved Early Detection of Focal Brucellosis Complications with Anti-Brucella IgG. J Clin Microbiol. 2020;58(11):e00903-20.
6. Şahin AM, et al. The Role of Laboratory Parameters in Predicting Osteoarticular Involvement in Brucellosis. EJMI. 2025;9(1):47-53.
7. Erkan REC, et al. Investigation of new inflammatory biomarkers in patients with brucella. Bratisl Lek Listy. 2024;125(3):178-183.
8. Zhou L, et al. A novel diagnostic model for brucellosis spondylitis using serum PINP and inflammatory factors. BMC Infect Dis. 2025. doi:10.1186/s12879-025-12404-1.
9. Jin M, et al. Research progress on complications of Brucellosis. Front Cell Infect Microbiol. 2023;13:1136674.
10. Pappas G, et al. Brucellosis. Lancet. 2006;367(9523):1805-1815 (updated epidemiology references from 2023–2025 global estimates).
11. Demirdag K, et al. Serum cytokine levels in patients with acute brucellosis and their relation to the traditional inflammatory markers. Pathogens and Disease. 2003;39(2):149.
12. Brucellosis Differential Diagnoses. Medscape. Updated Sep 8, 2025.
13. Cift A, et al. Comparison of inflammatory markers between brucella and non-brucella epididymo-orchitis. Int Braz J Urol. 2018;44(4):771-778.
14. Barkay O, et al. Determining Diagnostic Sensitivity: A Comparison of Rose Bengal Test, Coombs Gel Test, ELISA and Bacterial Culture in Brucellosis Diagnosis. Diagnostics. 2024;14(14):1546.
15. Brucellosis Treatment & Management. Medscape. Updated Sep 8, 2025.
16. Huang S, et al. Updated therapeutic options for human brucellosis: A systematic review and network meta-analysis of randomized controlled trials. PLoS Negl Trop Dis. 2024;18(8):e0012402.
17. About Brucellosis. CDC. Updated May 2, 2024.
18. Alavi SM, et al. Treatment of brucellosis: a systematic review of studies in recent twenty years. Caspian J Intern Med. 2013;4(2):636-641.
19. Lavigne JP, et al. What's new in the diagnosis and treatment of human brucellosis? Infect Dis Now. 2025;55(3):104956.
20. Tekin R, et al. Comparison of Inflammatory Markers between Adult and Pediatric Brucellosis Patients. Jundishapur J Microbiol. 2020;13(8):e104058.

For citation: Rashidova G.U. The importance of inflammation markers in brucellosis: diagnostic, prognostic, monitoring, differential diagnosis, and treatment considerations // Bulletin of Fundamental and Clinic Medicine. – 2026. – № 4(24). – P. 332–335. doi: https://doi.org/10.5281/zenodo.19533552