CLINICAL AND LABORATORY FEATURES OF CHRONIC BRUCELLOSIS AT THE PRESENT STAGE: A REVIEW

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Abstract. Brucellosis remains one of the most significant zoonotic infections worldwide, especially in regions with developed livestock farming. The clinical presentation of chronic brucellosis is characterized by multisystem involvement, including musculoskeletal, nervous, cardiovascular, and reproductive systems. Laboratory diagnosis is often complicated by the persistence of immunological markers and nonspecific inflammatory changes. This review summarizes current data on the epidemiology, pathogenesis, clinical manifestations, laboratory characteristics, and modern diagnostic approaches to chronic brucellosis. **Keywords**: chronic brucellosis, zoonosis, clinical manifestations, laboratory diagnosis, epidemiology, serological tests, chronic infection, Brucella.

Introduction. Brucellosis is a widespread zoonotic infectious disease caused by Gram-negative intracellular bacteria of the genus Brucella. The disease remains a major public health concern in many countries of Central Asia, the Mediterranean region, the Middle East, Latin America, and Africa [1]. According to the World Health Organization, more than 500,000 new human cases are registered annually, while the actual incidence is believed to be significantly higher because of underdiagnosis and underreporting [2].

One of the major challenges associated with brucellosis is its ability to progress to a chronic form. Chronic brucellosis develops in approximately 10–30% of

patients and is characterized by persistent symptoms lasting more than 12 months after the onset of infection [3]. The disease often leads to reduced quality of life, long-term disability, and significant socioeconomic consequences.

Epidemiology of Chronic Brucellosis. Despite global control programs, brucellosis remains endemic in many developing countries. The highest prevalence rates are reported in regions where close contact between humans and livestock is common and veterinary control measures are insufficient [1]. In Central Asian countries, including Uzbekistan, brucellosis continues to be a significant public health problem due to traditional livestock breeding practices and occupational exposure among farmers, veterinarians, and slaughterhouse workers [4]. Recent studies indicate that chronic forms of brucellosis are becoming increasingly recognized because of improved diagnostic capabilities and longer survival of infected individuals [5].

The pathogenesis of chronic brucellosis is closely related to the unique biological characteristics of Brucella spp. These bacteria possess the ability to survive and replicate within macrophages, avoiding destruction by host immune mechanisms [3]. Intracellular persistence allows the pathogen to evade immune surveillance and establish long-term infection. Chronic stimulation of the immune system leads to continuous production of pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α), interleukin-1, and interleukin-6, which contribute to tissue damage and systemic manifestations [6]. Persistent antigenic stimulation may also induce autoimmune mechanisms, further complicating the clinical course of the disease [5].

Clinical Features of Chronic Brucellosis. The clinical manifestations of chronic brucellosis are highly variable and often nonspecific. Patients commonly present with prolonged fatigue, weakness, excessive sweating, low-grade fever, arthralgia, and myalgia [3].

Musculoskeletal manifestations. Musculoskeletal involvement is the most frequent manifestation of chronic brucellosis and occurs in up to 60% of patients [7]. Common clinical forms include: peripheral arthritis, sacroiliitis, spondylitis, osteomyelitis; chronic arthralgia.

Lumbar spine involvement is particularly common and may lead to significant disability if left untreated [8].

Neurological manifestations. Neurobrucellosis represents one of the most severe complications and may manifest as: chronic meningitis, encephalitis, peripheral neuropathy, radiculopathy, cognitive dysfunction [5]. Although relatively uncommon, neurological involvement significantly worsens prognosis.

Cardiovascular and other manifestations. Chronic brucellosis may affect the cardiovascular system, causing endocarditis, myocarditis, and vasculitis. Endocarditis remains the leading cause of brucellosis-related mortality [3].

Genitourinary involvement, hepatosplenomegaly, chronic lymphadenopathy, and dermatological manifestations have also been reported [6].

Laboratory features of chronic bucellosis. Laboratory diagnosis of chronic brucellosis remains challenging because bacteremia is often absent and clinical manifestations are nonspecific.

Hematological Changes. Common laboratory abnormalities include:mild anemia, leukopenia, relative lymphocytosis,eElevated erythrocyte sedimentation rate (ESR), Increased C-reactive protein (CRP) levels [4]. However, these findings are not specific and should be interpreted alongside clinical and epidemiological data.

Serological diagnosis. Serological methods remain the cornerstone of laboratory diagnosis. The most commonly used tests include: standard Agglutination Test (SAT), Rose Bengal Test, Coombs anti-Brucella test, Enzyme-linked

immunosorbent assay (ELISA) [2]. ELISA demonstrates high sensitivity and specificity and allows differentiation between IgM and IgG antibodies, facilitating assessment of disease activity [6].

Molecular diagnostic methods. Polymerase chain reaction (PCR) has emerged as a valuable tool for detecting Brucella DNA in blood and tissue samples [8]. PCR offers rapid diagnosis and may be particularly useful in chronic and complicated cases where traditional culture methods have limited sensitivity.

Modern challenges in diagnosis. Diagnosis of chronic brucellosis is complicated by the persistence of antibodies after successful treatment and the absence of pathognomonic clinical signs [7]. A comprehensive diagnostic approach should include: detailed epidemiological history, clinical examination, serological testing, molecular diagnostic techniques, Imaging studies when organ involvement is suspected. The combination of ELISA and PCR currently represents the most promising diagnostic strategy for chronic brucellosis [8].

Treatment and follow-Up. The World Health Organization recommends combination antibiotic therapy to prevent relapses and chronic complications [2].The most widely used regimen includes:Doxycycline (100 mg twice daily for 6 weeks); Rifampicin (600–900 mg daily for 6 weeks). Complicated cases may require additional aminoglycosides or fluoroquinolones [3]. Long-term follow-up is essential because relapses may occur months or even years after treatment completion [5].

Conclusion. Chronic brucellosis remains an important infectious disease characterized by diverse clinical manifestations and complex laboratory diagnosis. Advances in serological and molecular diagnostic techniques have improved the detection of chronic infection; however, challenges remain due to the persistence of antibodies and nonspecific symptoms. Musculoskeletal involvement continues to be the most common clinical manifestation, while

neurological and cardiovascular complications significantly affect prognosis. References:

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