TREATMENT OF CHRONIC BRUCELLOSIS IN WOMEN OF FERTILE AGE AT THE CURRENT STAGE

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Abstract. Chronic brucellosis poses significant therapeutic challenges, particularly in women of fertile age, due to the risk of relapse, drug toxicity, and concerns regarding reproductive health. This review explores modern strategies in the treatment of chronic brucellosis, highlighting the importance of tailored antimicrobial therapy, safety considerations during pregnancy, and approaches to fertility preservation. Evidence-based recommendations are presented based on international guidelines and recent clinical studies.

Keywords. Chronic brucellosis; women of reproductive age; combination therapy; antimicrobial resistance; fertility; doxycycline; rifampicin; relapse prevention.

Introduction. Brucellosis is a widespread zoonosis caused by *Brucella* spp., with over 500,000 new cases reported annually worldwide. Chronic forms may persist for months or years, especially in inadequately treated individuals. Women of reproductive age represent a special population due to concerns related to pregnancy, lactation, and long-term fertility [1, 2].

Pathogenesis and Clinical Features in Fertile Women.

The pathogenesis of chronic brucellosis in women of fertile age is a complex interplay between the persistence of *Brucella* spp. in the host tissues,

immune evasion mechanisms, and the specific involvement of reproductive organs. After initial hematogenous dissemination, *Brucella melitensis*, the most virulent species for humans, can localize in the uterus, ovaries, and other pelvic structures, resulting in chronic inflammation, tissue granulomas, and even necrosis [1].

Women in the reproductive age group frequently present with non-specific clinical manifestations. These include low-grade fever, night sweats, polyarthritis, chronic fatigue syndrome, and depression-like symptoms, which are often mistaken for autoimmune or psychosomatic disorders [4]. Reproductive symptoms may include irregular menstruation, chronic pelvic pain, infertility, and adverse pregnancy outcomes such as spontaneous abortion and preterm birth [3].

Franco et al. noted that *Brucella* organisms possess the ability to persist intracellularly within macrophages, escaping the host immune system and contributing to chronic infection [2]. The chronic inflammatory response leads to the release of cytokines such as IL-1β, TNF-α, and IL-6, which are involved in both systemic symptoms and localized organ damage [8].

In female patients, involvement of the genital tract is not uncommon. Colmenero et al. described cases of *Brucella*-induced endometritis, salpingitis, and tubo-ovarian abscesses, which may mimic pelvic inflammatory disease (PID) or endometriosis in their clinical presentation [9]. Furthermore, brucellosis has been associated with hormonal imbalances that may disrupt ovulatory cycles, which in turn leads to decreased fertility potential [7].

Pregnancy further complicates the clinical course of brucellosis. Khan et al. emphasized that during pregnancy, immune tolerance is increased, potentially reducing the host's ability to clear the pathogen and leading to transplacental transmission [3]. This poses a significant risk for intrauterine fetal infection, miscarriage, and fetal growth restriction.

In chronic forms of the disease, diagnosis is often delayed. The slow progression of clinical signs, combined with low sensitivity of blood cultures and serologic tests during latency, often leads to underdiagnosis or misdiagnosis [10]. As a result, many women undergo unnecessary investigations for rheumatologic, gynecologic, or even psychiatric conditions before the correct diagnosis of brucellosis is established.

In summary, chronic brucellosis in women of fertile age is characterized by immune evasion, reproductive organ tropism, and clinical heterogeneity. Understanding its pathogenetic basis is crucial for timely diagnosis and prevention of long-term reproductive complications.

Therapeutic Approaches and Antimicrobial Strategies.

The WHO recommends a combination of doxycycline (100 mg BID for 6 weeks) and rifampicin (600–900 mg daily), which remains the standard regimen [5]. For chronic cases, especially with osteoarticular involvement or relapsing forms, triple therapy including streptomycin or gentamicin may be used [6]. However, concerns arise regarding the teratogenicity of doxycycline and ototoxicity of aminoglycosides in pregnant patients [7].

In non-pregnant women of childbearing age, doxycycline remains effective, but clinicians must ensure contraception during treatment to prevent fetal risk. In case of pregnancy, alternative regimens like rifampicin with cotrimoxazole are suggested, albeit with caution due to hematologic side effects [8].

Reproductive Considerations and Fertility Impact. Brucellosis may negatively impact fertility through chronic inflammation of pelvic organs or hormonal disturbances. Early diagnosis and eradication of infection are crucial to minimize reproductive sequelae. Assisted reproductive techniques (ART) may be considered in select cases post-treatment, but infection must be fully resolved before attempting conception [9].

Relapse Prevention and Monitoring. Chronic brucellosis is notorious for relapse, occurring in up to 15–20% of cases. Factors contributing include incomplete therapy, immunosuppression, and persistent foci in reproductive organs [10]. Serologic monitoring (e.g., SAT, ELISA) and periodic PCR testing post-treatment help detect subclinical reactivation. Long-term follow-up and patient education regarding symptom recurrence are essential.

Conclusion. Treatment of chronic brucellosis in women of fertile age requires a delicate balance between efficacy and safety. Personalized therapeutic strategies, consideration of reproductive status, and long-term monitoring can reduce complications and preserve fertility. Future research should focus on optimizing regimens for pregnant and lactating women and improving early detection techniques.

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