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## Complications and Sequelae of Brucellosis in Animals and Humans (A Brief Review)

### Article Info.

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#### Abstract

Abstract

Brucellosis is a bacterial disease caused by *Brucella* species. These bacteria are small, non-motile, facultative intracellular, obligate aerobes, coccobacilli. Their ability to replicate and survive within host cells is closely connected to their capacity to cause long-term illness and evade both innate and adaptive immune responses. It is a worldwide zoonotic disease that leads to significant economic losses in ruminant farming systems. Notable rise in intra- and interspecific infection rates documented in recent years, mainly due to poor management and limited resources, especially in developing countries. Humans can become infected by consuming contaminated milk or through direct contact with infected animals. Clinically, it manifests as undulant fever and chronic debilitating disease, along with various other symptoms. This review article examines the complications and consequences of brucellosis in both animals and humans. It also emphasizes the severity of these pathological outcomes of infection and aims to identify preventative strategies to reduce the incidence of both acute and chronic complications, minimize economic losses, and lower treatment costs.

**Keywords:** Brucellosis, complications and sequelae, Animals, Humans.

## Introduction

Domestic and wild animals are mainly affected by brucellosis, but human health is also considerably impacted. Brucellosis represents a chronic public health and economic problem, especially in developing countries where livestock farming is a primary livelihood. (1-3).

Brucellosis is a serious zoonotic disease leading to long-lasting, debilitating conditions in both animals and humans. While it mainly affects the reproductive systems of livestock, causing significant economic losses, in humans, it manifests as a multisystem illness with potential for chronic complications, especially if not treated (4,5).

Brucellosis, in animals known as Bang's disease, is a significant international zoonotic disease that poses a significant threat to human health. Further, Studies on knowledge, attitudes, and practices have revealed that a lack of awareness of the potential risk of contracting brucellosis in humans is the main cause of human cases. (6,7).

Several *Brucella* species have been considered causative agents in both animals and humans, including *B. abortus*, *B. ovis*, *B. melitensis*, *B. suis*, and *B. canis*. (4)

It was documented that *Brucella melitensis* primarily affects goats and sheep. It is the most common and virulent cause of human brucellosis worldwide. Additionally, *Brucella abortus* mainly affects cattle, buffalo, and camels. It is a major cause of human infection, often resulting in milder symptoms than those caused by *B. melitensis*. Furthermore, *Brucella suis* primarily impacts pigs. It causes severe, chronic infections in humans. Lastly, *Brucella canis* mainly affects dogs and other canines. It is a less common cause of human brucellosis compared to the others, but cases are increasing. (8-10)

On the other hand, other *Brucella* species have also been linked to rare infections; for example, *Brucella ovis* causes infections in sheep but has very limited or no zoonotic potential. Additionally, *Brucella neotomae* infects desert wood rats, with no reported human cases. However, Marine Mammal Strains (*B. ceti* and *B. pinnipedialis*), found in dolphins, whales, and seals, can occasionally cause human infection, often resulting in neuro- type of brucellosis. (1,2,11).

It was also noted that brucellosis is common across many countries, particularly in sub-Saharan Africa, the Middle East, and South Asia. In wealthier nations, occasional outbreaks also occur.

(12) A characteristic of brucellosis is its ability to cross species barriers (4,5). The zoonotic nature of the disease underscores its importance within the One Health strategy, affecting all three sectors. (4,13)

It has been shown that humans are generally infected by consuming unpasteurized dairy products (e.g., milk and cheese). Additionally, occupational exposure affects veterinarians, slaughterhouse workers, and farmers who come into contact with tissues, blood, or placenta. Furthermore, geographical risk varies, with the highest prevalence observed in the Mediterranean, the Middle East, Asia, and Latin America (14,15).

This article highlights the significance of brucellosis in animals and humans as a disease endemic in many countries worldwide, and explains some of the complications and health consequences (sequelae) resulting from it.

### **Brief background**

The disease, known since ancient Antiquity, was previously described by Hippocrates as a febrile condition similar to brucellosis (16). *Brucella melitensis* was isolated by Sir David Bruce from British soldiers who had contracted "Malta fever" in Malta (10,17). Other *Brucella* species, for instance, *B. abortus* in cattle, *B. suis* in pigs, and *B. canis* in canines, were found, further explaining data on the host range and epidemiology of the disease (18,19).

It was proposed that, given the interconnectedness of environmental, animal, and human health, the One Health approach, which encourages international and interdisciplinary collaboration, is particularly effective for controlling brucellosis (20). Although brucellosis has been around for centuries, the disease remains underrepresented in global health discussions. This is partly because it has been classified as one of the neglected zoonotic diseases that primarily impact vulnerable communities in resource-limited settings (21).

On the other hand, it has been shown that, due to their durability, *Brucella* species can persist under certain environmental conditions. Specifically, in cold, moist environments, these bacteria can persist for weeks to months on soil, water, and feedstuffs. This endurance plays a crucial role in the disease's epidemiology, facilitating indirect transmission and hindering eradication (22).

For the sake of accurate scientific knowledge, Intracellular Survival: *Brucella* infects and replicates in host macrophages, which it uses to inhibit phagosome-lysosome fusion to avoid immune killing (23). Further, Lipopolysaccharide (LPS): The smooth LPS of *Brucella* evades host immune detection and is less immunogenic than the LPS of most Gram-negative bacteria (4,5,7). Also, the Type IV Secretion System (T4SS) delivers effector proteins into host cells, enabling intracellular replication and immune evasion (23). Furthermore, granuloma formation: chronic infections result in granulomas, in which bacteria exist in a latent state, thereby inducing chronicity and susceptibility to relapse (7,17).

### **Complications and Sequelae in Humans**

Untreated or inadequately treated human brucellosis can transition from an acute "undulant fever" phase to chronic, focal infections, which can last for years. Therefore, the most important consequences and complications of the disease in humans can be summarized as follows: as mentioned by (1,3,5,10)

1-Osteoarticular Complications (Most Common, 2–77%): Includes sacroiliitis (inflammation of the sacroiliac joint), spondylitis (arthritis of the spine), peripheral arthritis (knees, hips, ankles), and osteomyelitis.

2-Cardiovascular complications (most serious, <2%): Endocarditis, which is inflammation of the heart lining, is the leading cause of death and often requires surgery. Other concerns include myocarditis, pericarditis, and mycotic aneurysms.

3-Genitourinary Complications (2–20%): Unilateral epididymo-orchitis (swelling of the testicles or epididymis) is common in men and may lead to abscesses or, rarely, atrophy. In women, it can cause miscarriage or rare tubo-ovarian abscesses.

4-Neurological (Neuro-brucellosis) (0.5–25%): Meningitis, encephalitis, radiculitis, stroke, and brain abscesses.

5-Hepatosplenomegaly (Approx. 50%): Enlargement of the liver and spleen.

6-Hematologic: Anemia (20-53% in children), leukopenia (8-38%), thrombocytopenia, and pancytopenia.

7-Other: Chronic fatigue syndrome, uveitis (eye inflammation), and skin rash.

8-Relapse: Occurs in 5% to 15% of cases within 12 months, usually caused by inadequate treatment.

It is important to note that the complications from this disease are numerous, severe, and greatly affect human health both directly and indirectly. This requires ongoing and systematic monitoring and follow-up to reduce human infections. (12,13).

On the other hand, the most significant complications and sequelae of the disease in animals are as follows. Which mentioned by(4,7,12,17)

### **Complications and Sequelae in Animals**

Brucellosis causes widespread reproductive failure and chronic infection in livestock, primarily cattle, sheep, goats, and pigs.

1-Reproductive Failures: Miscarriage (abortion), usually in the last trimester, is the main sign. It also leads to stillbirths, birth of weak offspring, and retention of the placenta.

2-Infertility: Permanent or temporary infertility affecting both females and males.

3-Male Reproductive Issues: Epididymitis, orchitis (testicular inflammation), and testicular abscesses that can cause lifelong infertility.

4-Reduced Productivity: Notable decrease in milk production.

5-Localized Infections: Inflammation, edema, and necrosis of reproductive tissues (placenta).

6-Other: Hygromas (fluid-filled swellings, especially in cattle), arthritis, and, in pigs, spondylitis.

It was also documented by(2,13-14,22) that both humans and animals can experience long-term effects, potentially suffering from chronic sequelae even after the acute phase of the infection has been treated. Those include:

1-Chronic Fatigue Syndrome: Ongoing tiredness, depression, and muscle pain can persist for years after infection.

2-Disability: Skeletal deformities and chronic joint damage from untreated spondylitis or arthritis can result in permanent physical disability.

3-Relapse: About 5–15% of cases experience symptom recurrence, typically within 6–12 months after finishing treatment.

4-Infertility: In animals, chronic infection often causes permanent reproductive failure and culling.

Generally, the risk of developing these complications in both animals and humans rises significantly when diagnosis is delayed by more than 30 days. Other signs include underlying conditions, severe joint pain, and notably elevated inflammatory markers, such as C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR).

### **Conclusion**

It has been concluded that although brucellosis is dangerous and negatively impacts infected animals and humans, the complications and pathological consequences are often even more detrimental to health. These result in chronic illnesses, more severe outcomes, and significant health and economic losses.

### Conflicts of interest

The authors declare no conflict of interest in this article.

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## مضاعفات وعواقب داء البروسيلات في الحيوانات والبشر (مراجعة بحثية موجزة)

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### الخلاصة

داء البروسيلات مرض جرثومي تسببه أنواع من جراثيم البروسيلات. وتعد هذه الجراثيم صغيرة الحجم، غير متحركة، اختيارية التطفل داخل الخلايا، هوائية، وعصيات مكورة سالبة الغرام. ترتبط قدرتها على التكاثر والبقاء داخل خلايا العائل ارتباطاً وثيقاً بقدرتها على التسبب في أمراض مزمنة والتهرب من الاستجابات المناعية والتكيفية. وهو مرض حيواني المنشأ منتشر عالمياً، ويؤدي إلى خسائر اقتصادية كبيرة في أنظمة تربية المجترات. وقد شهدت معدلات العدوى داخل النوع الواحد وبين الأنواع المختلفة ارتفاعاً ملحوظاً في السنوات الأخيرة، ويعود ذلك أساساً إلى سوء الإدارة ومحدودية الموارد، لا سيما في البلدان النامية. يمكن أن يُصاب الإنسان بالعدوى عن طريق تناول الحليب الملوث أو من خلال الاتصال المباشر بالحيوانات المصابة. سريريًا، تتجلى العدوى في صورة حمى متموجة، غالباً ما تترافق مع مرض مزمن مُنهك، إلى جانب أعراض أخرى متنوعة. تتناول هذه المقالة البحثية مضاعفات وآثار داء البروسيلات في كل من الحيوانات والبشر. كما تُسلط الضوء على خطورة هذه النتائج المرضية للعدوى، وتهدف إلى تحديد استراتيجيات وقائية للحد من حدوث المضاعفات الحادة والمزمنة، وتقليل الخسائر الاقتصادية، وخفض تكاليف العلاج.

**الكلمات المفتاحية:** داء البروسيلات، المضاعفات والعواقب، الحيوانات، الإنسان.