# Brucellosis: A Global Challenge

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## ABSTRACT

Brucellosis (Malta fever, Mediterranean fever, or undulant fever) is a zoonotic infectious disease caused by bacteria of the genus Brucella. This disease affects both humans and animals, posing significant public health and economic concerns worldwide. Brucellosis remains a prevalent global issue, particularly in regions with inadequate veterinary control and surveillance systems. The transmission of brucellosis occurs primarily through direct contact with infected animals or consumption of contaminated products such as unpasteurized milk, cheese, and meat. The disease can spread through inhalation of infected aerosols or contaminated environmental sources. Human-to-human transmission is rare but possible, mainly through sexual intercourse, vertical transmission from mother to child, or laboratory. Clinically brucellosis in humans varies widely showing a flu-like illness, with symptoms including fever, chills, sweats, fatigue, myalgia, and joint pain. In some cases, brucellosis can become chronic and lead to more severe complications, such as arthritis, endocarditis, neurologic disorders, and reproductive. The management of brucellosis involves a multidisciplinary approach, i.e. accurate diagnosis, appropriate treatment, and comprehensive surveillance and control measures. Antibiotics are the mainstay of therapy, typically administered for several weeks or months, depending on the clinical presentation and severity of the disease. Preventive measures include the implementation of vaccination programs for livestock, strict hygiene practices in animal husbandry, pasteurization of dairy products, and public education regarding the risks associated with consuming unpasteurized animal products. Control of brucellosis requires collaboration between veterinary and human health sectors, as well as active participation from governments, international organizations, and communities. Improved diagnostic methods, surveillance systems, and public awareness are crucial to reducing the burden of brucellosis and preventing its spread.

**Keywords:** Brucellosis, Malta fever, global issue, public health, zoonosis.

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## 1. INTRODUCTION

Brucellosis (Malta fever, Mediterranean fever, or undulant fever) is a widespread zoonotic disease caused by the bacterial genus Brucella (B.) (Khurana et al. 2021). This infectious disease affects animal species, including livestock such as cattle, goats, pigs, and wildlife populations (Yagupsky et al. 2019). Brucellosis poses significant threats to both animal and human health, leading to substantial economic losses, public health concerns, and challenges in international trade (Bagheri Nejad et al. 2020). Brucella species, including *Brucella abortus*, *Brucella melitensis*, and *Brucella suis*, are responsible for the diverse outcomes of brucellosis in various host species (O'callaghan 2020). For instance, *B. abortus* primarily affects cattle, leading to reproductive disorders such as abortion and decreased fertility (Wang and Jiang 2020). *B. melitensis* is commonly associated with goats and sheep, causing significant economic losses in the form of reduced milk production and abortions (Alim et al. 2020). *B. suis*, affects pigs and can infect humans, leading to chronic debilitating symptoms (Di Bonaventura et al. 2021). *B. canis* mainly affects dogs, and rarely transmits to humans (Bosilkovski et al. 2021). Some least common species that can lead to brucellosis *B. neotomae* (infects desert wood rats) and *B. ovis* (affects sheep) (Zhou et al. 2020).

The significance of brucellosis extends beyond its impact on animal health (Bendrey et al. 2020). Economically, brucellosis can result in substantial losses in livestock production due to reduced productivity, culling of infected animals, and trade restrictions imposed by importing countries (Unuvar et al. 2019). Moreover, the disease's zoonotic potential is of great concern. Humans can contract acquire brucellosis through direct contact with infected animals, consumption of contaminated animal products, or occupational exposure, leading to a wide range of clinical symptoms (Lianou et al. 2022). The zoonotic transmission of brucellosis emphasizes the need for effective control measures to safeguard public health (Sibhat et al. 2022). An accurate diagnosis of brucellosis is crucial for effective disease management (Khan et al. 2021) Various laboratory methods, including serological tests, culture, and polymerase chain reaction (PCR) assays, are employed to detect Brucella species (Bakheet and Alnakhli 2019). However, diagnostic challenges persist due to the bacteria's slow growth rate, low bacteremia levels, and antigenic variability (Deka et al. 2020). The development of reliable and rapid diagnostic tools is essential to facilitate early detection and appropriate treatment, both in animals and humans (Barreto-Argilagos and Rodríguez-Torrens 2022). To combat the spread of brucellosis, comprehensive prevention and control strategies are necessary (Al-Sherida et al. 2020). Vaccination programs have proven effective in reducing the incidence of brucellosis in animal populations (Ghanbari et al. 2020). Vaccines, such as the *B. abortus* strain 19 vaccine for cattle and the *B. melitensis* Rev. 1 vaccine for small ruminants, have played a vital role in disease control (Berhanu and Pal 2020). Furthermore, a one health approach, which integrates human and animal health sectors, is crucial for addressing brucellosis comprehensively. Public health measures, such as education campaigns promoting proper hygiene practices and the promotion of safe food handling, are essential in reducing human exposure to Brucella species (Tialla 2022). By adopting a multidisciplinary and collaborative approach, we can effectively combat this disease and mitigate its impact on both animal and human populations (Zhang et al. 2019).

## 2. EPIDEMIOLOGICAL SURVEILLANCE, GLOBAL DISTRIBUTION AND PREVALENCE OF HUMAN BRUCELLOSIS

Conducting surveillance studies to monitor the prevalence, geographical distribution, and risk factors of brucellosis provides valuable data for targeted control interventions (Iqbal et al. 2020.) (Aragón-Aranda et al. 2020). Human brucellosis cases are distributed worldwide, with varying prevalence rates across regions of Asia and Africa (Siengsanan-Lamont et al. 2021). The disease is endemic in countries such as India and Pakistan, particularly in regions where livestock farming and close interactions with animals are common (Esmaeili et al. 2019). It affects both developed and developing countries but its occurrence is more pronounced in low- and middle-income countries, where livestock farming is less regulated (Sun et al. 2020). In Africa, human brucellosis is a significant public health concern, particularly in sub-Saharan countries. The disease is prevalent in regions with extensive livestock farming, such as Ethiopia, Nigeria, and Sudan (Recht et al. 2020). Lack of awareness, limited access to healthcare facilities, and poor veterinary control programs contribute to the high burden of brucellosis in these areas (Madut et al. 2019).
Moreover, nomadic lifestyles and the consumption of raw animal products perpetuate the spread of the disease (Dadar et al. 2022). Asia experiences a significant burden of human brucellosis. High disease prevalence in countries like India, China, and Pakistan is primarily due to large-scale livestock farming and consumption of unpasteurized dairy products (Hussain et al. 2021). Occupational exposure among farmers, veterinarians, and abattoir workers also contributes to the transmission of disease (Jadav and Raval 2019). Additionally, weak surveillance systems and inadequate diagnostic facilities hinder effective disease control and prevention strategies in many Asian countries (Ntivuguruzwa et al. 2021). Human brucellosis remains a concern in America Mexico, Peru, and Argentina reporting numbers of cases. In these regions, transmission occurs through the consumption of unpasteurized dairy products and contact with infected animals, such as goats, cattle, and pigs (Dadar et al. 2020). Inadequate veterinary control measures, limited access to healthcare, and challenges in diagnosis contribute to the persistence of brucellosis in these regions (Adel 2022). In Europe, human brucellosis is less common. However, some countries still face a considerable burden of the disease, including Greece, Italy, and Spain (Kefaloudi et al. 2022). Transmission occurs through the consumption of contaminated dairy products and contact with infected livestock. Control measures, such as vaccination campaigns and enhanced surveillance, have led to a decline in reported cases in recent years (Jamil et al. 2020).

## 3. BRUCELLOSIS-ASSOCIATED SOCIO-ECONOMIC BURDEN

The impact of brucellosis is not limited to the direct losses incurred by infected animals (production and reproduction losses) but also includes indirect costs associated with control measures, reduced productivity, trade restrictions, and human health implications (Mengele et al. 2023). Brucellosis requires prompt diagnosis and treatment, which adds to the economic burden on livestock producers (Machelart et al. 2020). Diagnostic tests, medication, and veterinary services contribute to the cost of managing infected animals. Additionally, implementing preventive measures and control strategies, such as vaccination campaigns and culling of infected animals, further increases the expenses for farmers and livestock producers (Baroncelli et al. 2022). The disease has significant public health implications, including debilitating symptoms such as fever, fatigue, joint pain, and prolonged illness (Uzunović et al. 2020). In some cases, it can lead to serious complications, affecting various organs, such as the heart, liver, and spleen. Infected individuals experience a loss of productivity due to the prolonged illness, leading to decreased work efficiency and absenteeism. The diagnosis, treatment, and follow-up care place a significant financial burden on individuals, families, and healthcare systems (Hussain et al. 2020). Brucellosis has a significant impact on international trade and food safety. The presence of brucellosis in animal population has great impact for international trade (Erkyihun et al. 2022). Countries such as

Australia, America and New Zealand, have strict regulations regarding the import and export of animals and animal products to prevent the spread of infectious diseases (About et al. 2023). The presence of brucellosis can result in trade restrictions on livestock and animal products (Troupin et al. 2022). Countries affected by brucellosis showed great economic loss, reduced market access, and decreased competitiveness in the international trade of livestock and animal-derived products (Bodenham et al. 2020). Food safety has great impact in brucellosis control. Consumption of unpasteurized dairy products, such as milk and cheese, derived from infected animals can lead to human brucellosis. Therefore, ensuring safe food production and implementing effective control measures, such as pasteurization and strict hygiene practices, is essential (Mol et al. 2020).

Meeting international standards for food safety is vital to prevent the transmission of brucellosis through contaminated animal products and maintain consumer confidence in global trade (Pinn-Woodcock et al. 2023). Brucellosis exerts a negative impact on wildlife populations, particularly in areas where domestic animals and wildlife come into close contact (Kucuk et al. 2021). Wildlife reservoirs, such as elk, bison, and feral swine, can perpetuate the infection cycle, leading the transmission to livestock and vice versa. The disease has detrimental effects on the population dynamics of wildlife species by reduced fertility and increased mortality (Grützke et al. 2021).

## 4. BRUCELLOSIS AND PUBLIC HEALTH

Brucellosis poses significant diagnostic challenges due to its nonspecific symptoms, leading to delayed diagnoses. This results in prolonged illness, increased morbidity, and the potential for secondary transmission (Zhang et al. 2021). Brucellosis requires prolonged antibiotic treatment, which can be expensive with side effects (Mortola et al. 2019). Inadequate access to healthcare facilities and medications exacerbates the burden on affected individuals (Jamil et al. 2021). Brucellosis can impact occupational health, particularly among farmers, veterinarians, and abattoir workers, who are at higher risk of exposure to infected animals (Lozano-López et al. 2022).

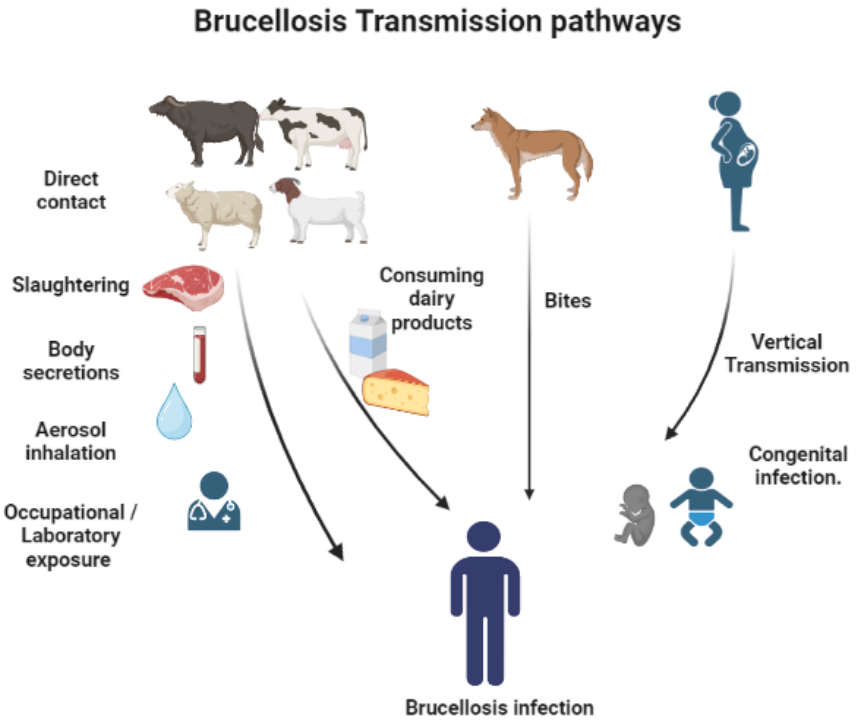


**Fig. 1:** Brucellosis transmission cycle from animals to humans

## 5. TRANSMISSION PATHWAY OF BRUCELLOSIS

Brucellosis is a zoonotic disease, and can be transmitted between animals and humans (Dafale et al. 2020). Domestic livestock, including cattle, sheep, goats, and pigs, are the primary sources of infection for humans (Santos et al. 2021). Other animals, such as dogs, camels, and wild ungulates, can carry and transmit the disease. The zoonotic potential of brucellosis have a significant impact on one health (Getahun et al. 2022).

## 6. BRUCELLOSIS CLINICAL SIGNS, DIAGNOSIS AND TREATMENT

Brucellosis causes a wide range of symptoms, often resembling a flu-like illness (Dadar et al. 2022). The incubation period of the disease varies from 5 days to several months. The most common symptoms include: Prolonged intermittent Fever with chills and sweating (Disease hallmark) lasting for weeks or months. Generalized body aches, joint pain, and muscle soreness, fatigue, night sweats, persistent headache, gastrointestinal symptoms (nausea, vomiting, abdominal pain, and diarrhea), respiratory Symptoms (cough, chest pain, and difficulty breathing) , and neurological complications (Avila-Granados et al. 2019). Diagnosis of brucellosis can be challenging due to its nonspecific symptoms (Bendrey and Fournié 2021). Healthcare providers should maintain a high “Index of Suspicion”, especially in individuals with a history of exposure to livestock or consumption of unpasteurized dairy products (Alhazmi et al. 2022). The following are the diagnostic tools for Brucellosis:
Treatment of brucellosis requires a combination of antibiotics for an extended period to ensure complete eradication of the bacteria and to prevent relapse (Waldrop and Sriranganathan 2019). The choice of antibiotics depends on the individual patient, disease severity, and drug susceptibility testing. Commonly used antibiotics include: Doxycycline (prescribed in combination with another antibiotic) (Tialla 2021) Rifampin (used with doxycycline to increase treatment efficacy) and Trimethoprim-Sulfamethoxazole (used as an alternative therapy) (Nthiwa et al. 2019). The treatment duration is usually 6 weeks and can extend up to several months, depending on the clinical response. Patients must complete the full course of antibiotics to ensure complete eradication of the bacteria (Kelly et al. 2021).

## 7. BRUCELLOSIS UNDER ONE HEALTH APPROACH

The one health approach emphasizes the importance of collaboration between sectors dealing with human, animal, and environmental health (Galarce et al. 2021). In the context of brucellosis prevention and control, the important measures are:
a) Effective collaboration between veterinary services, public health agencies, agriculture, and other relevant stakeholders. It includes Joint-efforts information sharing, mutual coordination, and the development of integrated strategies to tackle the disease (Mia et al. 2022).
b) Encouraging interdisciplinary research leads to a better understanding of the disease dynamics, transmission routes, and risk factors. This knowledge can guide the development of targeted interventions and policies for brucellosis prevention and control (Kauffman and Petersen 2019).
c) International cooperation and collaboration by sharing best practices, expertise, and resources to help countries with limited resources in enhancing their prevention and control efforts (Asante et al. 2019).
d) Launching public health measures and awareness campaigns by using strategies such as; Provision of health education and public awareness through different channels, ensuring the adoption of occupational safety practices by people with high-risk jobs (use of personal protective equipment, good hygiene practices, and regular health screenings) to minimize infection risk and implementing strict food safety regulations and standards (Milk pasteurization and proper handling of animal products), to reduces the risk of food-borne brucellosis transmission (Kim et al. 2019).

**Table 1:** Tests for diagnosis of brucellosis.

| Serial No. | Diagnostic test | Use | Limitation | References |
|---|---|---|---|---|
| 1 | Blood Culture | Gold standard for diagnosis<br>Cultured on specific media (Farrell's or Castañeda's medium) under enhanced safety conditions to avoid laboratory-acquired infections | ❖ Significant risk to laboratory personnel<br>❖ Time consuming (requires several weeks) | (Pascual et al. 2022) |
| 2 | Serological Tests | ❖ Rose Bengal test<br>❖ Standard Agglutination Test (SAT)<br>❖ Complement Fixation Test (CFT) and enzyme-linked immunosorbent assay (ELISA)<br>❖ Widely used due to their simplicity and high sensitivity<br>❖ Detect specific antibodies produced by the host in response to Brucella infection | ❖ False-positive results due to cross-reactivity (with Yersinia spp. and Francisella tularensis)<br>❖ False-negative results can occur during the acute phase of the disease. before antibody production or when immunosuppression<br>❖ Cannot distinguish between active and past infections | (Buhmann et al. 2019) |
| 3 | Polymerase Chain Reaction (PCR). | ❖ Can directly detect Brucella DNA in clinical samples<br>❖ Provides a rapid and specific diagnosis<br>❖ Various PCR formats (conventional PCR, real-time PCR, and multiplex PCR)<br>❖ Offer high specificity, even at low bacterial loads<br>❖ Can differentiate between different Brucella species and strains<br>❖ Significantly time-saving<br>❖ Facilitates timely treatment initiation | ❖ Requires well-equipped laboratories, skilled personnel, and expensive equipment<br>❖ False-negative results if the absence of the target DNA in the specimen or if the presence of inhibitors | (Saddique et al. 2019) |

e) Ensuring better surveillance and monitoring system for early detection, rapid response, and ongoing assessment of brucellosis prevalence and trends (Dhand et al. 2021). Essential strategies include: establishing a quick and effective disease-reporting system for veterinarians and farmers to prevent disease spread. Strengthening the laboratory infrastructure and diagnostic capabilities for accurate diagnosis of brucellosis (Khatibi et al. 2021).

## 8. PREVENTION AND CONTROL STRATEGIES: A COMPREHENSIVE APPROACH

Preventing brucellosis primarily focuses on reducing exposure to infected animals and their products (Shome et al. 2020). To alleviate the public health concerns and socio-economic burden of brucellosis, comprehensive prevention and control strategies are required. Following measures should be adopted to control Brucellosis:

1) Public education and awareness about brucellosis transmission, symptoms, and preventive measures to facilitate early detection and treatment of brucellosis (Ferreira et al. 2023).

2) Implementing vaccination programs for livestock to reduce the prevalence of brucellosis in animal populations, subsequently decreasing the risk of human infection.

3) Improving food safety practices by promoting pasteurization of dairy products, and ensuring proper meat-handling and cooking to minimize the risk of bacterial transmission (Al Jindan 2021).

4) Adapting personal protective measures by individuals at high risk of exposure, such as farmers, veterinarians, and slaughterhouse workers, through the use of protective clothing and gloves when handling animals or their tissues (Moreno 2022).
5) Vaccination programs for animals play a crucial role in preventing and controlling brucellosis in animals, primarily cattle, goats, and pigs, which are known reservoirs of the bacteria (Ma et al. 2022). The main aspects vital in effective vaccination programs are the use of live attenuated vaccines (RB51 strain for cattle and Rev 1 strain for small ruminants) which have been proven successful to control brucellosis. These vaccines provide long-lasting immunity and reduce the bacterial shedding of in animals, thus minimizing the risk of transmission to humans (Elrashedy et al. 2022). Early vaccination of animals is essential to prevent the infection within flocks. Timely vaccination of young animals, preferably prior to sexual maturity, is important for reducing the risk of brucellosis transmission (Nyerere et al. 2020). Implementing comprehensive herd vaccination programs help achieve higher vaccination coverage and enhance overall disease control. Regular monitoring of vaccination status, coverage rates, and revaccination are critical for the success of these programs (Bahmani and Bahmani 2022). Strong surveillance and reporting should be done to ensure effective control (Tao et al. 2021).

## 9. BRUCELLOSIS CONTROL

Control of brucellosis plays an important role in minimizing the disease spread and the economic loses. Switzerland successfully eradicated bovine brucellosis through a comprehensive control program involving strict movement controls, test-and-slaughter strategies, and vaccination. The country achieved disease-free status in 1999, highlighting the effectiveness of integrated control measures (Pal et al. 2020). Spain implemented a nationwide control program that included systematic surveillance, test-and-slaughter strategies, and vaccination campaigns (Tian et al. 2020; Almashhadany 2021). Similarly, Mongolia successfully reduced the incidence of brucellosis in both humans and animals through a one health approach (Machavarapu et al. 2019). Collaborative efforts involving veterinary services, public health agencies, and communities led to increased awareness, improved diagnostics, and enhanced surveillance and control measures (Rahman et al. 2019).

## 10. CONCLUSION

Brucellosis prevention and control requires a comprehensive approach that combines vaccination programs for animals, the One Health approach, public health measures, and surveillance systems. By implementing these strategies, we can reduce the incidence of brucellosis in animals, minimize the risk of transmission to humans, and mitigate the socio-economic impacts associated with this significant public health threat. To effectively combat brucellosis globally, collaborative efforts and continuous implementation of prevention and control measures are required.

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