
Article review: Global Burden of Brucellosis in Animals and Human

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ABSTRACT

Brucellosis is one of the most neglected zoonotic diseases, which caused by different species belong to the genus of *Brucella* resulting in a significant threats to both animals and human, impacting agricultural economies and public health systems worldwide. In animals, the disease can cause severe reproductive losses (in particular abortion), decreasing in meat and milk productivity, and long-term health complications (arthritis, lameness, and mastitis) in addition to expensive treatment costs and trade-restriction schemes to prevent the transmission of infection to human as well as other animals. In human, brucellosis (also known Malta fever or undulant fever) can be transmitted due to direct contact with infected animals or their unpasteurized dairy products causing diverse and non-specific debilitating symptoms that making the diagnosis is challenging such as fever, chills, sweats, fatigue, headache, muscle and joint pain, and weight loss. In chronic phase, human brucellosis leads to arthritis, spondylitis, endocarditis, and neurological manifestations that require prolonged therapy. Despite advancements in control and prevention, several challenges remain due to the lack of safe and effective human vaccines, resource constraints, limited infrastructure, and inadequate surveillance systems. In conclusion, extensive knowledge and awareness are the cornerstones of prevention. Educating the public especially those at high risk of exposure about the routes of transmission and clinical manifestations of the disease is essential. Additionally, effective communication and collaboration among public health agencies, veterinary services, research institution and community stakeholders are paramount for successful prevention of brucellosis. Removing barriers to communication among human and veterinary medicine, agronomy, and ecological and environmental science encourages multidisciplinary strategies.

1. History

Brucellosis as one of the ancient and most widespread zoonotic diseases affects humans as well as the animals, a bacterial disease resulted by a Gram-negative, facultative intracellular bacterium of the genus *Brucella* (Berhanu and Pal, 2020). The brucellosis causative agent named firstly as *Micrococcus melitensis* in 1887; and then, it found that the organisms have the capability to transmit by diseases animals particularly goat for human by the milk contaminates with the organism (Pradeepkiran *et al.*, 2021). Post that, *Brucella abortus* was reported in cattle and their abortive fetus with identifying other organisms in aborted pig known later as a *Brucella suis* (Xavier *et al.*, 2009; Olsen and Tatum, 2016). During these periods, *Brucella* was studied additionally and according to obtained results, it found that the method of milk pasteurization is best technique for controlling the infection (Islam *et al.*, 2023).

2. Bacteriology and taxonomy

Various species of *Brucella* were known as facultative grown inside the cells as coccobacilli, and each one has a number of biovars are existed (Corbel, 2020). Currently, the scientifically communities referred to six separately species that characterized by their non-zoonotic effect which infect small ruminant; *B. ovis* and *B. neotomae*, which infecting rodents, in addition to high zoonotic species that infect small ruminants, bovine, porcine, and canine animals involving *B. melitensis* and *B. abortus*, *B. suis*, and *B. canis* respectively (Hinić *et al.*, 2008; Rossetti *et al.*, 2022). As well as, infections of mammal have resulting by proposition newly species as *B. maris*, *B. pinnipediae* and *B. cetaceae* (Gonzalez-Barrientos and Hernandez-Mora, 2023). However, many

morphological variations were reported among and through the types of *Brucella* genus. *B. abortus*, *B. melitensis*, and *B. suis* considered as the most great importance due to their virulence which attributed to presence of S-LPS covering the outer membranes of cells (Głowacka *et al.*, 2018; Manafe, 2020). *Brucella ovis* and *B. canis* demonstrated to loss O-polysaccharide (OPS), lipopolysaccharide (LPS) and rough LPS (RLPS) on their membranes except smooth LPS (SLPS). This loss in OPS made RLPS is great immunogenically within the hosts. The evasion of innate immunity and the capacity to induce the inflammation by activation of the cytokines were considered by many researchers as the ability of the SLPS. The move safeguards the organism against firstly the immunity responding as well as the boosting of their survival capabilities within the hosts (Cardoso *et al.*, 2006; Conde-Alvarez *et al.*, 2012). In macrophages and monocytes, the SLPS species had the capacity of averting the presentation of antigen (Ag) by T-helpers against MHC II enabled in the ill cells. SLPS allow the pathogen to block apoptosis by the sick cells. This strategy of evasion provided the SLPSs with virulence when compared with the RLPS disease that cannot block the immune responses of the host as well as having an enormous influence to the innate immune host and hence, being incapable of existent high harmful consequences on the hosts (Skendros, 2011; Sytnikova *et al.*, 2020). The other difference is the way the DNAs are cleaved by the use of a phage of a certain species specifically the *Brucella* since about 40 phages might result in a complete lysing of the genome of one or more species (Farlow *et al.*, 2014; Li *et al.*, 2019). Further, the species of the *Brucella* do not show variations, but among other variations of *Brucella* that contain many different biovars. this biovar-variation in biochemically and growing feature such as variation in capability of growing in the presence of CO₂, to produce H₂S, to agglutinate the A and M antisera, and to grow in presence of urea produced this difference of biovar. Opposed to these biochemical attributes, laboratory uses it as a contrast between their biovars (Pérez-Etayo *et al.*, 2018; García Lobo *et al.*, 2019).

3. Epidemiology

3.1. Distribution

3.1.1. Asia

In some of the developed nations, wether eradication of brucellosis has been achieved through test and slaughter, vaccination and limitation of movement of animals (Blasco and Molina-Flores, 2011). Human and animal brucellosis is rife in other regions of the world including the Mediterranean region, Middle East, Western Asia, parts of Africa and Latin American (Corbel, 2020). But countries that record the highest rates of the disease, in the world, are found in Asia though the biggest gaps are in the prevalence rates. Worldwide, major endemic areas include countries of the Mediterranean basin, Middle East, including Iraq, the Indian subcontinent, and parts of Mexico and Central and South America. New foci that have emerged include the Balkan Peninsula and many of the former Soviet Union Asian Republics, such as Kazakhstan, Kyrgyzstan, and Tajikistan (Suresh *et al.*, 2020). Whereas, the decreasing trend *Brucella* was reported in Russia and increasing in South Korea and China. Based upon previously information recorded online, Syria appeared for having a higher level of infection occurrence amongst the world (Yang *et al.*, 2020). This event obtained a subnational report which prevalent in areas of Iraq could greater than 268 per 100,000 inhabitants infected. In Iran, several studies revealed that about more one hundred of cases were occur for every 100,000 humans and is apparently associated with the infection among human and consuming the dairy derivatives from large and small ruminants (Alshwany, 2019). Among Middle Eastern countries, cases of human infections were resulted due to *B. melitensis* infections (Musallam *et al.*, 2016). There uncertainly information if bovine animals in Iran are diseased by *B. abortus* or *B. melitensis* (Akbarmehr and Ghiyami, 2011). Several countries were successfully isolated *B. melitensis* from bovine, camelide and equine as well as from the small. In Jordan, it found that 8.5% of equines were positives to *Brucella* spp. (Abo-Shehada, 2009). In Palestine, outbreaks of *B. melitensis* were reported usually in cows that lectured or habit near sheep and goats (Awwad, 2010). In other countries of Asia, *Brucella* found to be endemic in India with increasing the incidence rate of *B. canis*, *B. suis*, *B. ovis*, *B. abortus*, and *B. melitensis*. However, information detected in India about the prevalence of brucellosis is rare (Namdev *et al.*, 2024; Ullah *et al.*, 2024). Kumar (2010) reported that there a large herds and flocks of animals amongst the world have no controlling measures are applies resulting in millions of positive infections among the animals. Also, incidence of *B. melitensis* is high as 29% resulting in increasing the chance of disease transmission to humans as well as to other animals (Zhang *et al.*, 2018).

3.1.2. Africa

Brucellosis considers endemic in North Africa based on many reports written on infection incidence in human as well as animals (Ekiri *et al.*, 2020). The dominance of *B. melitensis* circulates in Egypt throughout ovine and caprine, bovine, and camelidae which diseased by this type of organism (Menshawy *et al.*, 2025). Few of data are studied regarding the incidence of *Brucella* in Africa though many researchers thought that their countries are endemic (Dean *et al.*, 2012). In North Africa, *B. abortus* predominate each of bovine and camelidae; whereas in South and West and Africa, *B. melitensis* disease seem to be dominate (Dadar *et al.*, 2022). However, resource of infection controlling is largely limit, and other infections presented in Africa might with great mortalities than expected; therefore, infection prevention priority in animals and human should consider with careful throughout these areas (Simpson *et al.*, 2021).

3.1.3. America

In Canada, brucellosis has eradicated, and transmission event wasn't recorded until now; while in USA, the controlling of infections and effort started since 1934, during this period, the prevalence of infection in bovine was 10% (Yang and Stanford, 2025). Infections caused by *B. melitensis* have never been endemic in USA; however, *B. ovis* infection is likely endemic in Colorado, Utah, and Wyoming (Pinn-Woodcock *et al.*, 2023). However, a recently published epidemiologically study showed that there a lack of data related to *B. melitensis* that naturally the initial type of *Brucella* incriminated in induction of infection in humans (Laine *et al.*, 2022). In goats, surveillance data indicate that the actual disease incidence appeared to considerably higher than expected, and that disease prevalence in goats remains high though the caprine brucellosis control program has been established since 1971 (Pei *et al.*, 2025). In last years, cross-section prevalence studies in goat exist individually or as flocks that the levels of incidence are approximately 21-82% (Edao, 2021). In cattle and pigs, the prevalence of infection is wider than expected particularly in some border areas to Mexico. No information can be detected about the incidence rate of infection in goat, and information related to humans was few (Pinn-Woodcock *et al.*, 2023). In South America, the disease still represents a great zoonotic problem in particular in Ecuador, Brazil, and Argentina; while in Uruguay and Chile, brucellosis is nearly achieved disease-free status (Rodrigues *et al.*, 2023; Garrido-Haro *et al.*, 2025).

3.1.4. Europe

The disease is declined in European countries since 2011; however, Greece, Italy, Portugal, Spain, Balkan Peninsula, and Turkey remain at high endemicity due to *B. melitensis* that of great concerns in many areas. As well as, numbers of official reports are greatly underestimated with absence the proper source of organism (Higgins, 2015; Zange and Scholz, 2023).

3.2. Transmission

Infection by *Brucella* in animals can be sustained through inhalation of aerosols containing the bacterium especially in crowd and dry circumstances and through ingestion of food and grass that are contaminated by the organism. Direct contact with the mucous membrane and skin wounds in the polluted environments with *Brucella* excreted and transmits the organism through the venereal contacts or by the intercourse of the neonate infections (Jawad, 2024). Infections that occurred in naively pregnant adults were, in most cases, leading to aborted babies or had weak births. The problem of incapability to carry the babies to the end of their pregnancy and fetus weight, fetal fluid and placentas are a burden to the organism that pollutes the surroundings. The infected livestock can shed (transmit through the discharge and in milk) the organism and further contaminate the environments and an infection risk to the suckling livestock and other animals are presented (Udainiya *et al.*, 2025). Male could be infected through semen that was contaminated (Okeleji *et al.*, 2024). Finally, ewes may give births of latent infect lambs whose showed no positive results for brucellosis by serology; however, the latent infective lambs could spread the organism post the 1st gestation (Al-Hamada, 2021).

4. Pathogenesis

The pathogenesis of *Brucella* is identically same observed in many animals and human. Firstly, the organism invaded the mucosal barriers throughout skin abrasions or injuries, particularly during ingestion that considers as the initial route for horizontally spreading of infection (Qureshi *et al.*, 2023). In submucosa, phagocytes ingest *Brucella* organisms during the inflammatory responses. Post ingestion, organism being capable for evading and hindering the phagolysosom activity for neutrophil or macrophage through redirect of traffic of phagolysosom activity. The organisms survived being capable for replication in phagocytes without disruption of cell-metabolism or resulting in destruction of cells. Intracellular bacteria having the ability to inhibit the host cell apoptosis, also especially in SLPS strain (Su *et al.*, 2022). At final stage, affected neutrophil or macrophage localized within the regional lymph nodes, mostly those adjacent for sites of infection to enlarge because infiltrating the inflammatory cells and hyperplasia (González-Espinoza *et al.*, 2021). The technique for escaping organism by phagocytosis has not discovered; however, the total end is cellular destruction. The existence of *Brucella* in macrophages and neutrophils can allow bacterium to replication within it, resulting in liberation of organism from these cells and development of the bacteremia that allow the bacteria to colonize in multiple organs. In animas, *Brucella* is mostly colonized in the lymphatic tissue, udders as well as in reproductive system (González-Espinoza *et al.*, 2021). In humans, bacteremic phase could affect many organs to result in clinical symptoms that being expressive for the affected organs (Shi *et al.*, 2021).

In pregnant livestock, *Brucella* localizes mainly within reproductive system leading for colonizing the chorionic trophoblasts existed in the placental tissues. The affinity of *Brucella* spp. for these tissues might be due to existence the steroidal hormone

that known as “erythritol”, which stimulate the organism to replicate (Xiao *et al.*, 2022). *Brucella* uses erythritol as a source of energies as well as for carbonic ions, yet glucose found. Cause to this preferred condition for using erythritol may because the easy for up-taking it by *Brucella*, in comparison to sugars. These make erythritol is greatly existed for growth of the organism to consumptive of sugar (Lázaro-Antón *et al.*, 2024). Replication of *Brucella* spp. resulting in inflammation of placenta, ulcers in chorionic and allantoic membranes, as well as for separation of endometriums from uterine membranes leading for later abortion of fetus (Zavattieri *et al.*, 2023). Erythritol existence in testis of males can lead for a localizing the organism in reproductive system which result in inflammation of epididymis and testis (Okeleji *et al.*, 2024).

5. Clinical signs

5.1. Humans

The infections in human, mostly originate due to animals’ reservoirs (Godfrod, 2009). It can cause a dangerous, weaken and chronically illness affects different tissues (Dean *et al.*, 2012). *Brucella* species have great importance as they causes an infection in humans globally which take the form of acutely phase; but sometimes, disease appeared as sub-clinically or chronically phases (Kyebambe, 2005; Lucero *et al.*, 2008). Incubation period is usually 1-3 weeks, but may extend to several months. The almost commonly symptoms observed during *B. melitensis* infections include undulant fever, sweating, abnormal odor, chill and debilitating, anorexia, headache, nervous behavior and depression (Kong, 2018). Depending on the site of infection, complication and affecting of different bodily tissues could be variable (Ulu Kilic *et al.*, 2013). In human, unusual spontaneously abortion observed among gestation can occur during the 1st stage, endocarditis due to *B. melitensis* is responsible on the almost (80%) deaths caused by brucellosis (Seleem *et al.*, 2010). Splenomegaly, hepatomegaly, hepatosplenomegaly meningitis, meningomyeloencephalo-spondylosis, encephalitis, ischemic attack, facial palsy, chorea, brain abscess, and meningoencephalitis were detected as rare cases (Megid *et al.*, 2010).

5.2. Animals

Brucella infections in animals are resulted usually by *B. melitensis*; however, many countries showed that goats could infect by *B. abortus* (Rossetti *et al.*, 2022). *Brucella* spp. located mostly within reproductive system in addition to lymphatic system in both genders (González-Espinoza *et al.*, 2021). In female, the mainly observed clinical symptoms of *Brucella* infections include abortions at the last trimester of pregnancy, retention of placenta, and weak births dead usually during peripartum (Baumgartner *et al.*, 2021). Animals generally abort only once; however, aborted females shedding huge number of organism to their environments resulting in contamination of pasture, soils, and water by their vaginal fluids. This secretion of organism might be extended for 8 or 12 weeks post parturition or the abortions (Dubey *et al.*, 2022). Khurana *et al.* (2021) reported that despite giving normally birth, infected cows continues shed *Brucella* throughout their milk, vaginal fluid and placenta. Mammary glands usually affected and mastitis seen commonly as a characteristic of infection, and excretion of bacteria for long periods through the milk could detect in animals (Islam *et al.*, 2023). In males, infections could produce inflammatory processes in genital tissues, in ampulla of deferent ducts, seminal vesicle, epididymis, and testis. In acute phase, infection can detect as inflammations in scrotal sac, tunica vaginalis, and orchitis which might be distended through either fibrino-purulent exudates or hemorrhagic. In chronically stages, hygromas and joints’ inflammation can observe in male goat (Otaravaeva *et al.*, 2022). Additionally, males might be affected and produced a bad quality of semen which consequently causes a decreased fertility (Stewart and Shipley, 2021). Rarely in both female and male, *Brucella* spp. may colonize in synovial membrane, cortex of kidney, bone marrow and CNS to produce focal granulomatous lesion (Enright, 1990).

6. Diagnosis

The clinical diagnosis of brucellosis has never been straightforward in either animals or humans, and must be complemented by serology, culture, and molecular techniques (Di Bonaventura *et al.*, 2021). Diagnostic assays were used to confirm of detection, surveillance for avoiding the re-introduction of infections to regions in which the disease is controlled, and to certificate and screening / prevalence studies (Khurana *et al.*, 2021). Also, these assays are divided to directly testing of organism that isolated or diagnosis through using the DNAs using the molecular techniques, and indirectly testing of blood or milk. *Brucella* can be isolated or detected molecularly by PCR assays that consider the only available technique for confirming of infection (Kurmanov *et al.*, 2022).

7. Treatment

Limited numbers of antibiotics are available traditionally for treating the cases of brucellosis due to intracellular localization of *Brucella*. Long terms using multiple drugs are required for preventing the therapy traits and latterly relapsing of the patient.

However, the applied regiment frequently changed throughout the last century (Bosilkovski *et al.*, 2021). In most patients, combination of antibiotics is used for effectively controlling the organism; however, infection remains of high importance (Dadar *et al.*, 2021). In clinics, many types of antibiotics were used such as streptomycin, doxycycline, chloramphenicol, quinolones, rifampicin, aminoglycosides, trimethoprim-sulfamethoxazole, and tetracycline (Munang'andu, 2024). Clinical trials recommended combination of streptomycin and doxycycline for treatment the cases of uncomplicated brucellosis (Majzoobi *et al.*, 2022). Rifampin and doxycycline combination commonly prescribed, though the combination related with higher rates of relapsing rates. In complicated cases of infections, several months are required for treating with using of triple antibiotics (Maduranga *et al.*, 2024). Extended-spectrum cephalosporin-ceftriaxone in combination with rifampin and doxycycline demonstrated to be the preferred choice of therapy (Salas *et al.*, 2022). Although, therapeutic protocols were not changed dramatically in recently decades, the definition of successful therapeutic outcomes has questioned. Advancing in PCR assays allows the successful measurement of microbial load and providing a definitive assessment of treatment success (Huang *et al.*, 2023). Detection of DNAs specific to *Brucella* in diseased humans and animals after several years of successful therapeutic regimens have suggested that this bacterium can exist in some patient in a latent phase as in tuberculosis (Melenotte *et al.*, 2019). In animals, treatment with antibiotics shown to successfully eliminate the disease according the stopping the shedding of organism in milk and lack of *Brucella* in cultured tissues (Moreno *et al.*, 2022).

8. Control and prevention

Controlling and preventing of zoonotic infections in humans depend usually on the extensive controlling measures of disease in animals. Consequently, decreasing of brucellosis needs to reduce the time of exposures between the human the pathogenic agents (Bosilkovski *et al.*, 2021). Primarily, two exposure patterns are exist, which have an importance during intervention include occupational-associated exposure, in which, individual contracted infection directly from the diseased animal that shed the organism, or indirectly by inhalation of aerosols containing bacteria in environments contaminated from the infected animals (Blacksell *et al.*, 2023). The second source of exposure occurs by contaminated ingested diets such as raw milk and other dairy products made from raw milk with high water content, and fresh and soft cheese made from raw milk. Ingestion of the organism throughout such products can be resulted in illness (Grützke *et al.*, 2021). Vaccination and culling of infected domestic animals were applied for controlling of human brucellosis in the last century. Many studies have suggested that vaccination effort alone is insufficient for effective controlling of the infection (Darbandi *et al.*, 2022). Additionally, the efficacy of vaccination strategies depending largely on the quality of employed vaccine (Li *et al.*, 2019b). Although, no vaccine is available to directly protect human, effective *B. melitensis* vaccine for ovine and caprine in addition to *B. abortus* vaccine for bovine is available traditionally. The combining of test and slaughter system is usually implemented for eradication of disease (Heidary *et al.*, 2022). Vaccination can initially prevent the clinical effect of brucellosis which leading for transmission of infection to human (Elbehiry *et al.*, 2023). Rev1 is the only available vaccine against *B. melitensis* infections, which proved as an effective vaccine for controlling and preventing of infection in ovine and caprine (Heidary *et al.*, 2022). Individual doses of subcutaneous injection can induce a long-lasting serologic response that makes an eradication program following the combined testing and slaughter impractical. However, Rev1 vaccine can induce abortions in pregnant animals (Pellegrini *et al.*, 2022). As well as, the potential public health risk with the Rev1 vaccine is that the served strain can result in infections in human (Vives-Soto *et al.*, 2024).

9. Conclusion

Extensive knowledge and awareness are the cornerstones of prevention. Educating the public especially those at high risk of exposure about the routes of transmission and clinical manifestations of the disease is essential. Additionally, effective communication and collaboration among public health agencies, veterinary services, research institution and community stakeholders are paramount for successful prevention of brucellosis. Removing barriers to communication among human and veterinary medicine, agronomy, and ecological and environmental science encourages multidisciplinary strategies.

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