

# Brucellosis in Saudi Arabia: Review of Literature and Epidemiology

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## Abstract

Brucellosis is a zoonotic disease, which is endemic in Saudi Arabia. It's an infectious systematic disease that can affect any organ, with no specific symptom to this disease. The diagnosis of Brucellosis depends mainly on the investigations. Treatment of Brucellosis requires an extensive course of antibiotics used for at least 6 weeks to avoid relapse or recurrence. This disease is caused by *Brucella spp.* It's considered to be a major problem in endemic countries, due to poor hygiene, and unprotected contact with animals. Brucellosis is a challenging disease diagnose since there are no special symptoms for this disease. The incidence of Brucellosis globally is up to 500,000 people infected annually therefore, it's the most widespread zoonotic disease. There are some rare cases of Brucellosis in the Kingdom of Saudi Arabia. Several laboratory tests are used to confirm the diagnosis, and the most common laboratory test used in Saudi Arabia is the SAT. Preventing brucellosis depends on contact isolation from infected beings, safety cautions in labs, Pasteurization of milk, and controlling of vectors.

**Keywords:** Brucellosis; *Brucella*; Zoonotic; Saudi Arabia; Epidemiology

**List of Abbreviations** ELISA: Enzyme-Linked Immunosorbent Assay; LPS: Lipopolysaccharide; PCR: Polymerase Chain Reaction; RBAT: Rose Bengal Agglutination Test; SAT: Standard Agglutination Test; SMX: Sulfamethoxazole; TMP: Trimethoprim

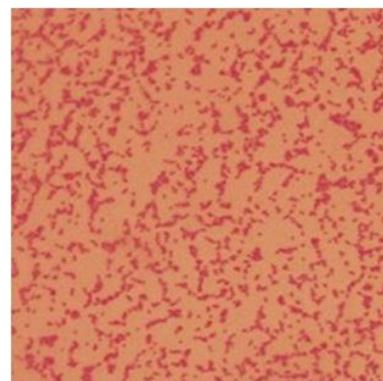
## Introduction

In 1886, Brucellosis was named Bruce by means of the causative agent of the Malta dog. Where he was named the cause of *Brucella melitensis*, which was isolated from goat's milk. In 1993, the *Brucella abortus* was resistant in the UK, and also in animals, the *Brucella melitensis* was not isolated in the UK. Brucellosis [1] is caused by approximately 12 species of *Brucella* bacteria. This group is preceded by *Brucella melitensis*, followed by *Brucella abortus* and the third is *Brucella Canis*. *Brucella spp.* is a Gram-negative, coccobacillus bacteria. Since it is a systemic disease, it can affect any organ and with vague symptoms. Clinically, it is known that Brucellosis cause systemic symptoms such as a headache, night sweats, and fever. Diagnosis of Brucellosis is confirmed by several tests, the most important one is the Standard Agglutination Test (SAT). An annual global incidence of more than 500,000 [2,3]. Treatment of Brucellosis is done by giving intensive antibiotics at a prolonged time. Managing is different in dose, duration, and type of antibiotic depends on the case and the condition of the patient.

## Microbiology

Brucellosis is a zoonotic disease caused by a Gram-negative, coccobacillus bacterium, called *Brucella* bacteria (Figure 1) [4,5]. *Brucella* has nearly about 12 species [4,6-8]. The most common species causing Brucellosis worldwide are *Brucella melitensis* (from sheep and goats), *Brucella abortus* (from cows), and *Brucella Canis* (from dogs) respectively, also there are *Brucella suis* (from pigs), *Brucella ovis*,

*Brucella neotomae*, *Brucella pinnipedialis*, *Brucella microti*, *Brucella ceti*, *Brucella cetaceae*, *Brucella binnipediae*, and *Brucella inopinata* [9,10]. *Brucella* bacteria infect animals first, then after contact with infected animals, the pathogen is transmitted to human. Infection can be transmitted by consuming raw dairy, uncooked meat, contact with infected animals or their secretions, Exposure to bacteria in the laboratory, and by Breastfeeding on mother to the child [4,11,12] *Brucella* bacteria lives and multiply within the cells of the monocyte pagans, the dandruff cells, and placenta cells. It also can live and reproduce within animal cells, such as Microglia, fibroblast, epithelium, and endothelium. There are three stages for *Brucella* bacteria in the body, which are incubation, acute, and chronic; to simplify these three stages, the incubation stage is mere without any clinical symptoms. Second, the acute phase is characterized by the spread of the pathogen and the invasion of the tissues of the body; the last stage is chronic which in the organ damage occur and can lead to the death of the infected person [7].



**Figure 1:** Gram staining of isolated *Brucella* bacteria. Positive blood agar for bacteria separation [6].

## Immunology and Pathogens

*Brucella spp.* has a special wall that makes them stealthy and difficult for the immune system to respond and eliminates it completely [7]. Its wall contains the lipopolysaccharide (LPS) that stimulate the toll-like receptor 4 (TLR4), which induces the release of inflammatory cytokines and the beginning of the elimination of pathogen. The longer the LPS in the wall of the bacteria, the weaker the stimulation of TLR4 becomes, also becomes less toxicity due to a longer chain of LPS [7]. There are also some *Brucella* bacteria that don't have OPS in the LPS, and this makes them more toxic, and some of *Brucella abortus* and *melitensis* toxins are libd-carbohydrate-protein-2, keto-3-dexyctulosonic acid. The immune response against *Brucella* is initiated by releasing of cytokines IL12, TNF-alpha, and IFN-gamma, to destroy and accelerate the death of bacteria [7,9,13]. This is not the only way of defense, it varies depending on the type of *Brucella* bacteria and its mutation and resistance for example, in *Brucella abortus* a dose of 10-1000 is enough to cause the disease [14-16]. The immune response is different depending on the antibodies IgM, IgG, IgA, and stage of the disease [9].

## Symptoms and Signs

Symptoms of Brucellosis include irregular fever, night sweats, headache, tremors, loss of appetite, abdominal pain, joints pain, and muscle aches [2,11,17]. Signs include endocarditis, hepatomegaly, splenomegaly, and obvious loss of weight [3,4,18]. The lymph nodes involvement in Brucellosis is rare [19]. Multiple rare cases of Brucellosis were reported with vague signs and symptoms in Saudi Arabia. First case, a 54 years old male known case of diabetes was diagnosed with an abscess in the prostate. The case was confirmed by a pus test and was found to contain *Brucella* bacteria. Second case, a 67 years old male known case of diabetes, hypothyroidism, benign prostatic hypertrophy, vitiligo, and a previous history of Brucellosis, presented with a mass in the spinal vertebrae from C5-C7, the patient said he drank unpasteurized milk a month ago.

## Diagnosis

The diagnosis of Brucellosis is divided into two steps. The first step, identifying the clinical picture of the patient including the history of contact with animal or its products, new symptoms and signs, such as

arthralgia, fever, sweating, headache, fatigue, and muscle pain. The second step, in which confirmation of the disease is made by laboratory investigations [3,4].

## Laboratory Investigations

Polymerase Chain Reaction (PCR) shows a high specificity (100%) and a high sensitivity of 80% (1.25 GE/μl), and more reliability [8,20]. Enzyme-Linked Immunosorbent Assay (ELISA) sensitivity 94.1% and specificity 97.1% can determine between IgG, IgM, IgA also it's more beneficial and sensitive in acute *Brucella* [21]. Rose Bengal Agglutination Test (RBAT) is a quick test but with poor sensitivity and specificity [22]. Standard Agglutination Test (SAT) sensitivity 95.6% and specificity 100.0%, which makes it the most accurate and preferable in diagnosis [4,12,21].

## Epidemiology

### In Saudi Arabia

Brucellosis is an endemic disease in several countries such as the Mediterranean basin and the Arabian Peninsula. Saudi Arabia has an infection rate of about 70 per 100,000 people (Figures 2 and 3) [9]. An annual global incidence of more than 500,000 and more than 10/100,000 of the population in some affected countries [2,4,5,10,23,24].

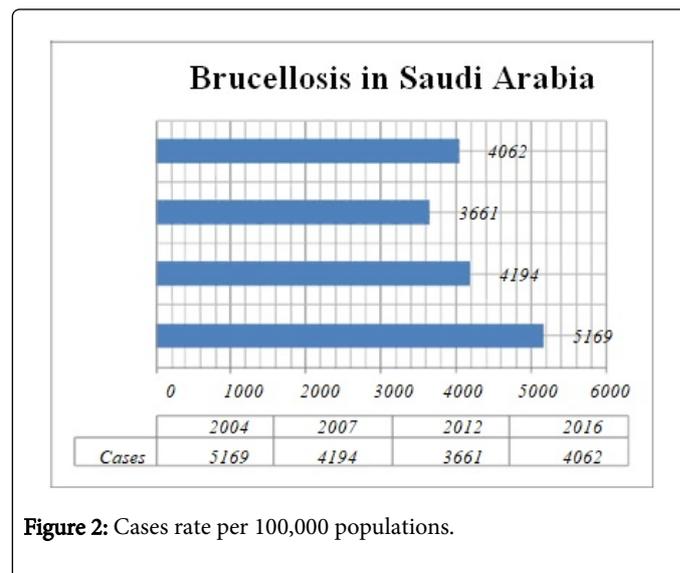


Figure 2: Cases rate per 100,000 populations.

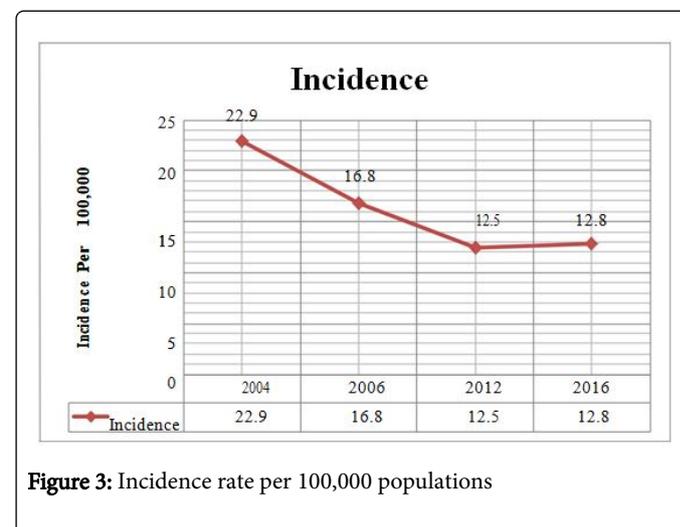


Figure 3: Incidence rate per 100,000 populations

### In worldwide

Brucellosis is known to be the commonest zoonotic infection worldwide, due to traveling internationally, and socioeconomic reasons. Many endemic countries have controlled the disease over years. Here are some infection rates in countries. The average incidence in Greece between 2007-2012 was estimated to be

1.43/100,000 [25,26] In Iran, the reported average incidence between 1991 to 2008 is 43.24/100,00 [27]. The annual incidence in 2009 was 2.7/100 000 population of human brucellosis in the People's Republic of China [28]. The incidence of brucellosis in Germany has an average rate of 0.03/100,000 population during 1998-2001 [29]. However, in Saudi Arabia even after decreasing the infection rate over years, it still considered high compared to other countries, making it endemic to the disease.

## Treatment

Management of Brucellosis needs intensive and careful using of antibiotics at extensive intervals. Many studies showed the necessity to use antibiotics for at least six weeks or more to avoid relapse or developing resistance [12]. Researchers found that double and triple antimicrobial regimen with aminoglycoside either streptomycin or gentamicin for the first 2-3 weeks was effective. It should be noted that the choice and duration of antibiotics depends on the characteristics and current health of the patient. Treatment commonly used for children is age specific. If the patient is older than eight years, the treatment used is Complex treatment systems including, oral doxycycline (4 mg/kg/day), rifampicin (20 mg/Kg/day). Children under 8 years of age are routinely treated with Trimethoprim (TMP) (6-8 mg/kg/ day), Sulfamethoxazole (SMX) (30-40 mg/kg/day), rifampicin (20 mg/kg/Day). Doxycycline is not used for children at this age to avoid its side effects, including discoloration of teeth [4]. Antibiotics are usually described from six to eight weeks for adults. Treatment of *Brucella* depends on the site of infection and progression of the disease. Two rare cases of cervical abscess and prostatitis were treated and managed in Saudi Arabia. Prostate abscess due to *Brucella* bacterial infection, which was managed by intravenous fluids, antibiotics including sulfamethoxazole-trimethoprim, gentamicin, and ciprofloxacin [5]. Cervical abscess between the fifth and the seventh cervical spines due to *Brucella* bacteria, which was treated using doxycycline, aminoglycoside, and rifampicin [10].

## Prevention and Control

As known, prevention is much easier, safer, fewer side effects, and less costing, unlike the treatment. Therefore, prevention is an essential part in the controlling of diseases, and when facing a zoonotic disease such as Brucellosis, controlling the vectors is very important for preventing. Methods used in preventing brucellosis infection include eating processed meat, pasteurizing milk, regular checkup of animals, and their vaccinations, also taking care of health safety when dealing with infected animals, and during work in laboratories dealing with *Brucella spp.* [12,23-25].

## Conclusion

Brucellosis is a zoonotic infectious disease, also it is considered as one of the neglected diseases that does not have enough awareness like other infectious diseases. This review is focused on Brucellosis in Saudi society since it is an endemic disease in Saudi Arabia. The incidence of the disease in Saudi society is higher in 2016 than in 2014. The disease incidence in Saudi Arabia when compared with a developed country such as Greece, shows a significant difference between the two countries in terms of infection rate. The disease rate could be higher due to misdiagnosis and unreported cases of brucellosis. The *Brucella spp.* is a gram-negative bacterium that has about 12 species, four of them are the most common causative organisms for Brucellosis, which are *B. melitensis*, *B. abortus*, *B. canis*, and *B. suis*. It has a special wall

that makes it stealthy and difficult to eliminate from the body. The treatment of brucellosis is mainly depending on multiple complex antibiotics therapy including aminoglycosides, TMP-SMX, tetracyclines, and rifampicin. Brucellosis symptoms are vague and systematic symptoms such as fever, night sweat, muscle ache, and abdominal pain. Signs of brucellosis can include hepatomegaly and splenomegaly. This obvious difference in incidence put Saudi Arabia in the classification of endemic countries for brucellosis. The awareness of transmission methods of *Brucella* can guide the community, and prevent further infections. Controlling of animals that might carry the pathogen is essential, especially in countries which have culture, and daily contact with these animals. However, animal's dealers and raw milk consumers should be careful when contacting with animals, and make sure to boil milk or pasteurized milk to avoid brucellosis. A rapid field test on animals for early detection is necessary. Regular checkups and vaccination should be mandatory to prevent the spread of Brucellosis; all this can help in the fight against the disease, and put it outside the scope of endemic diseases in Saudi Arabia.

## Competing Interests

The authors declare that they have no competing interests.

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We would like to point out that this research is unfunded, a personal work by the authors.

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