

Journal of the Hellenic Veterinary Medical Society

Vol 74, No 1 (2023)



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doi: [10.12681/jhvms.24522](https://doi.org/10.12681/jhvms.24522)

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To cite this article:

Ahmad, M., Akhtar, R., Altaf, I., Bhutta, Z., & Farhab, M. (2023). Prevalence of brucellosis in Pakistan with reference to South Asia and Middle East: A comparative review. *Journal of the Hellenic Veterinary Medical Society*, 74(1), 5111–5118. <https://doi.org/10.12681/jhvms.24522> (Original work published April 11, 2023)

Prevalence of brucellosis in Pakistan with reference to South Asia and Middle East: A comparative review

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ABSTRACT: After rabies, brucellosis is the second most important disease that also have zoonotic concern. On one hand, prevalence of this disease has been increased significantly in developing and under-developed countries for the last few decades, but on the other hand, many developed countries have eradicated this disease by implementing the proper disease control strategies such as vaccination or test and slaughter policy. Because of high zoonotic potential, *Brucella* species pose a significant threat to the human population involved in handling, rearing, and consumption of contaminated dairy products. The economy of many countries in the world mostly depends upon the rearing of the healthy and high-yielding livestock population. This disease causes notable economic losses in terms of low production, abortion, followed by low fertility and repeat breeding. In this review we have compared the prevalence of brucellosis in Pakistan with the selective South Asian and the Middle East countries, along with the generalizing information regarding economic losses and public health issues.

Keywords: Farm animals, Public health, Pakistan, worldwide, brucellosis, Dairy products, Economy, Zoonotic

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Date of initial submission: 28-01-2021

Date of acceptance: 19-09-2022

INTRODUCTION

One of the most ancient diseases that can be detected back to the 5th Egyptian Plaque in 1600 BC is brucellosis (Seleem Boyle and Sriranganathan, 2010). It was discovered from the spleen of a British soldier by a Scottish pathologist David Bruce in Malta. It remained a mystery until 1905. In late 1905, Themistocles Zammit found its zoonotic potential by recognizing the *B. melitensis* in goat's milk. It proved a breakthrough in the epidemiology of this disease (Seleem Boyle and Sriranganathan, 2010). Except the cats being resistant, almost all domesticated species are prone to it. It is caused by *Brucella* species which are aerobic, non-motile, facultative intracellular and gram-negative coccobacilli that lacks endospore, flagella, and capsule. Its replication inside the host cell, may cause persistent infection and activates the adaptive and innate immunity of the host (Gwida Al Dahouk Melzer Rösler Neubauer and Tomaso, 2010).

Nine different species of *Brucella* are currently known, each of which has different host ranges. *B. melitensis* (sheep and goat), *B. abortus* (cattle), *B. suis* (pigs), *B. ovis* (sheep), *B. canis* (dogs), *B. neotomae*, *B. microti* (rodents), *B. ceti* (Whales and dolphin), and *B. pinnipedalis* (seals and sea-lions). In humans, the first three species are the main causative agents of brucellosis (D'anastasio Staniscia Milia Manzoli and Capasso, 2011). In livestock, brucellosis is associated with the abortion in their 3rd trimester of pregnancy. The shedding of bacteria by infected animals occurs through vaginal secretions, uterine discharge and milk (England Kelly Jones MacMillan and Wooldridge, 2004). The different ways of transmission of *Brucella* to the healthy animals include intact skin or wound, mucous membrane and ingestion of infected material such as contaminated milk, and placenta from infected animals (Dean Crump Greter Hattendorf Schelling and Zinsstag, 2012). Breed, age, parity, and gender are the possible associated risk factors of bovine brucellosis at individual level whereas farm management, herd size and abortion history are the possible associated risk factors of bovine brucellosis at herd level (Makita Fèvre Waiswa Eisler Thrusfield and Welburn, 2011; Anka Hassan Khairani-Bejo Zainal bin Mohamad Salleh and Adzhar, 2014; Lindahl Sattorov Boqvist Sattori and Magnusson, 2014). The survival of *Brucella* for a longer period in cold and humid environments is also a very important factor in its transmission among humans and animals (Aune Rhyen Russell Roffe and Corso, 2012). However, brucellosis has been eliminated in northern and

western Europe, Japan, Australia, Canada, and New Zealand but it is still considered an endemic disease in the Middle East, Africa, Mediterranean, Latin America and certain countries of Asia (Refai, 2002). According to the World Animal Health Information System (WAHIS), no sufficient data regarding clinical cases is available in Pakistan. People from rural areas of Pakistan rely majorly on the dairy industry which shares a major portion of the country's economy. Ninety percent (90%) of the country's dairy industry comprises of small-holder farms having less than 10 animals on the farm (Afzal, 2009). The estimated population of water buffalo and cattle is 40 and 48 million respectively. Additionally, their annual milk production consists of 36,180 and 21,691 million tons, respectively. Water buffalo contributes to the 75% of total milk production. Hence, water buffalo is considered as the chief milk-producing animal in Pakistan. About 30 million people, the majority of them living in rural areas, are employed in the livestock sector. The prime restrictions regarding dairy sector in Pakistan include low-quality feed, elevated environmental stress, small herd, poor genetic potential, reproductive failure, lack of skilled manpower, inappropriate marketing system, substandard extension services as well as traditional management practices. The economic losses due to brucellosis have been discussed in a previous study (Sarwar Khan and Iqbal, 2002).

Human Zoonosis:

Zoonosis is referred to as the disease transferable between humans and animals. It is stated that around 61 percent of all diseases in humans and 73 percent of newly emerged infectious diseases are zoonotic (Jones Patel Levy Storeygard Balk Gittleman and Daszak, 2008). Brucellosis is the most common bacterial infection in humans throughout the world. Although controlled in domestic animal population, it is still present as endemic issue in human population of several parts of the world (Yagupsky Morata and Colmenero, 2019). As a result of domestication of sheep, goats, bovines and camels, it was appeared as "Human Disease". This claim was proved around 79 A. D when it observed as "Brucellar Spondylitis" in 17% skeleton uncovered in the city of Herculaneum (D'anastasio Staniscia Milia Manzoli and Capasso, 2011). It is highly communicable disease to humans because of its multiple routes of transmission such as gastrointestinal and respiratory tracts, abraded skin, conjunctivae and venereal route as well. Transplacental route during bacteremic maternal course, gen-

ital secretions during delivery and breast feeding are also reported as an important mode of transmission among neonates (Yagupsky, 2010). People of all ages are vulnerable to human brucellosis. In children, brucellosis accounts for 20 to 30 percent of all known cases (Bukhari, 2018). According to a research finding conducted in Babol and Northeast Iran mostly the children above 5 years of age are more affected due to their high involvement in animal care, whereas 82 children were found positive with a peak season (45.9% cases) in summer (Sasan Nateghi Bonyadi and Aelami, 2012; RH Roushan and JS Amiri, 2013) (Sasan Nateghi Bonyadi and Aelami, 2012). Since the first discovery of brucellosis, it is now considered as the most neglected zoonotic disease with extended public health issues worldwide. It is now estimated that there are more than 500,000 cases being reported annually in disease endemic areas (Pappas Papadimitriou Akritidis Christou and Tsianos, 2006). The global incidence of human brucellosis since 2000 in Europe, Africa, North America, Central and South America and Asia clearly depicts that its prevalence is exceeding beyond 10 cases per 100,000 people (Pappas Papadimitriou Akritidis Christou and Tsianos, 2006; Franco Mulder Gilman and Smits, 2007). Most of the *Brucella* species can infect humans such as *B. melitensis* having the highest zoonotic prospective succeeded by *B. suis* and *B. abortus* (Young, 1995). Along with relapsing fever, back pain, and arthralgia,

it may cause life-threatening issues like endocarditis, hepatomegaly, splenomegaly, and neuropathies (Dadar Shahali and Whatmore, 2019). Spondylitis, depression and chronic fatigue are some typical symptoms of chronic infection that persists for several years (Castaño and Solera, 2009). *Brucella* can easily be spread via aerosol to humans (Tuon Gondolfo and Cerchiari, 2017). It can be used as a potent biological weapon. The infective dose is as low as 10 bacteria which can lead to the development of clinical signs in 50 to 80% exposed individuals. The first organism used in 1954 by the USA as a biological weapon was *B. suis* (Guihot Bossi and Bricaire, 2004). According to an expert committee of the World Health Organization, it is believed that if 50 kg *B. melitensis* is disposed of in the form of aerosol droplets to a city of 100,000 populations, it would cause 5,000 casualties with 125,000 diseased persons and an economic loss of 477.7 million of US dollars (Neubauer, 2010).

A most common route of transmission of brucellosis is by ingestion of contaminated dairy products. Subsequently, direct contact with the infected animal or aborted fetus as well as by inhalation of bacteria during working in the lab are some of the other common ways of its transmission. Human to human transmission via sexual contact is too low hence considered non-significant (Figure 1) (Godfroid et al, 2005).

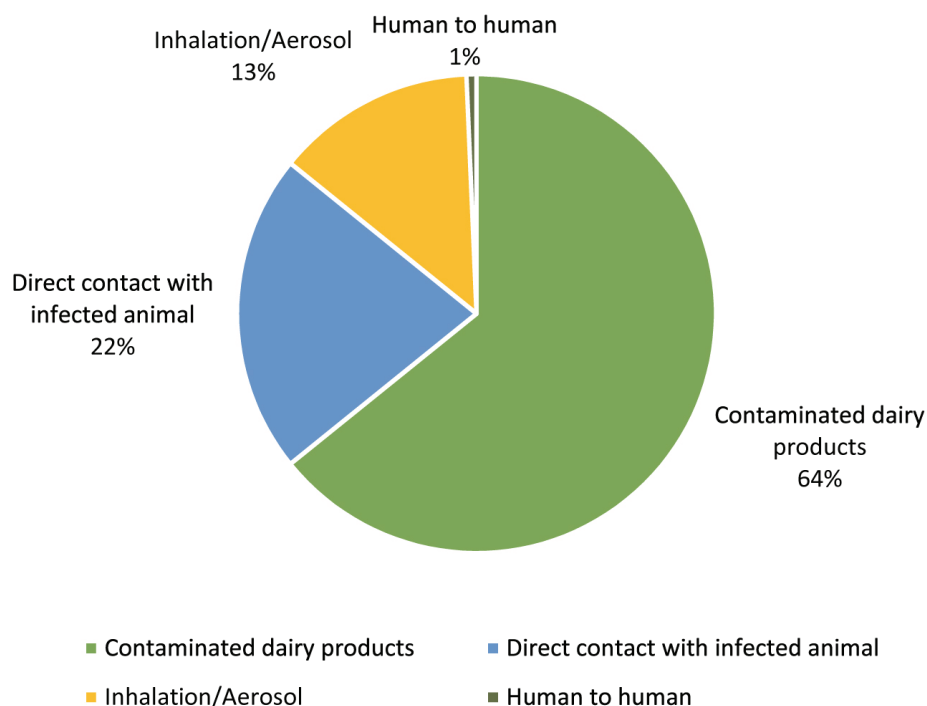


Figure 1. Different routes of transmission of human brucellosis (Godfroid et al, 2005)

The prevalence of human brucellosis in Swat, Pakistan was evaluated as 2% and 3.66% prevalence by Standard tube agglutination test (STAT) and Standard plate agglutination test (SPAT) respectively. The final results were confirmed by polymerase chain reaction being 2.66%. The highest cases of human brucellosis has been observed in humans above 30 years of age. The disease was found to be more frequently affected male than female population, having the male to female ratio of 1.7:1 (Ahmad et al, 2017).

In pregnant women, the complications include abortion, vaginal bleeding, intrauterine fetal death as well as an intrauterine infection. It was also revealed that pregnant women in rural areas of Pakistan are more seropositive (6.5%) than those who live in urban areas (4.7 %). Because of the poor economic situation, women in rural areas have no access to medical healthcare. Hence it is indicated that in Pakistan, brucellosis has become a chronic infection in women. Infecundity due to chronic infection in women is also reported. It puts huge mental pressure on childless women. It is also documented that pregnant women consuming raw milk are at higher risk (76.5%) than those who never consumed raw milk (2.9%) (Ali et al., 2016).

Pregnancy associated problems in pregnant women are uncommon. However, in Saudi Arabia most of the cases occurred were reported in the 1st and 2nd trimester with the prevalence of 43% and only 2% in the third trimester (Khan Mah and Memish, 2001). It has been observed that the low incidence of abortion in the human pregnant female is due to the absence of erythritol in the placenta and fetus (Poole et al., 1972). Table 1 provides summary of the incidence of human brucellosis in some countries of the South Asia and Middle Eastern countries.

Among other countries like Syria (1609/million per year), Kuwait (500/million for the last 20 years) and Turkey (15000 cases in 2004) has been registered (Pappas et al., 2006). In Turkey prevalence of brucellosis has been reported to be between 1% to 26.7 % (as high as 27.2%). Brucellosis is more prevalent in males due to occupational hazards. Cases of brucellosis reported are less than existing because of deficient diagnosis and reporting (Köse et al., 2014). In Tanzania, the prevalence of human brucellosis among the livestock handlers was found to be 46% (Shirima et al., 2010). Although a notifiable disease, still no surveillance program has initiated to diagnose human brucellosis in South Africa (Frean et al., 2018). It is

Table 1. Incidence of human brucellosis in different countries of South Asia and Middle East (Pappas et al., 2006)

Country	Incidence (annual cases permillion of population)
Pakistan	No data available, possibly endemic
Afghanistan	3. 8
India	No data available, possibly endemic
China	8
Bangladesh	No data available, possibly endemic
Sri Lanka	No data available, possibly endemic
United Arab Emirates	41
Saudi Arabia	214. 4
Iraq	278. 4
Iran	238. 6
Oman	35. 6
Syria	1603. 4
Turkey	262. 2
Kuwait	33. 9

under-diagnosed and under-reported disease because of its pernicious and non-specific nature. Most of the human practitioners have very little or no experience at all to diagnose and treat their affected patients. In 2016, two cases of human brucellosis were reported in Western Cape (Wojno et al., 2016), and Mpumalanga provinces respectively (Frean et al., 2018). Hence it is also an occupational hazard to veterinarians, para-veterinary staff, abattoir workers, butchers, shepherds, livestock farmers, milkers and laboratory workers (Khan and Zahoor, 2018; Mujuni et al., 2018).

Animal brucellosis:

In animals, it causes serious reproductive and clinicopathological consequences. Orchitis, hygro-ma, vesiculitis, and infertility due to epididymitis are the possible outcomes of brucellosis in bulls. In cows, it may result in reduced milk production, retention of placenta, recurrent breeding failure, metritis, stillbirth, abortion and the birth of debilitated calves (Shareef, 2006). It is also revealed that brucellosis can also spread through unrestricted trade among *Brucella* endemic countries. Bulls are kept for a shorter time hence spread of infection is less likely to occur. Cows are three times more susceptible to brucellosis because of calving stress and their less slaughtering policy (Ayoola et al., 2017). In cattle, the main cause of brucellosis is *B. abortus*. It has a considerable affinity for the uterus of pregnant animals. Confinement of *B. abortus* in male and female reproductive tract leads to infertility and abortion respectively. Fibrosis of parenchyma of testes and chronic orchitis may cause

temporary or indefinite infertility in bulls. Venereal transmission of infection is not common, rather artificial insemination is considered as the possible cause of brucellosis.

Prevalence:

Brucellosis may occur in any part of the world being endemic in Mediterranean countries like Southern France, Italy, Greece, Portugal, Spain, Turkey, and North Africa. Among these countries, the highest incidence of brucellosis has been observed in countries of South Asia followed by Sub-Saharan African countries. Around 1 billion poor people (66 percent from rural while 33 percent from urban areas) depend on livestock for their sustenance providing 6 to 36 percent fulfilling protein requirement. Approximately 12 percent of the animals are infected with brucellosis having an 8 percent decreasing production trend as a whole (Grace et al., 2012).

USA invested 3.5 billion US Dollars to decrease the incidence of bovine brucellosis from 11.5% to 0.0001% (Franc et al., 2018). In 2008, although all states of the United States are considered free from *B. abortus* in cattle (Higgins et al., 2012), it is still present in wildlife and can cause occasional spread. The primary source of infection for cattle is elk (Rhyen et

al., 2013). Except for Texas, all states in the USA are considered free from porcine brucellosis. The most virulent species of the *Brucella* genus is *B. melitensis*. Goats and sheep are the natural and favourable hosts of *B. melitensis*, respectively (Wareth et al., 2015). In developed countries, the nomadic and marginal farming system is practiced by landless farmers. Many countries are suffering from the re-emergence of the disease in sheep and goats. Brucellosis is considered endemic in Middle East countries. The consumption of unpasteurized dairy products is a significant risk factor for seropositivity in the Middle East. In Jordan seroprevalence in awassi sheep is 2.2% and 45% at individual and farm level respectively (Franc et al., 2018). Figure 2 depicts the data of animal brucellosis in different South Asia and Middle Eastern countries.

The prevalence of brucellosis in Pakistan is increasing at private farms in comparison with government farms, hence it may pose a serious threat to the human population consuming milk of these farms (Gul et al., 2015). In Pakistan, at government livestock farms, the prevalence of brucellosis in cattle and buffalo was found to be 14.70% and 15.38%, respectively. While in private farms the incidence was found to be 18.53% for cattle and 35.40% for buffaloes (Nasir et al., 2004). Another study conducted in

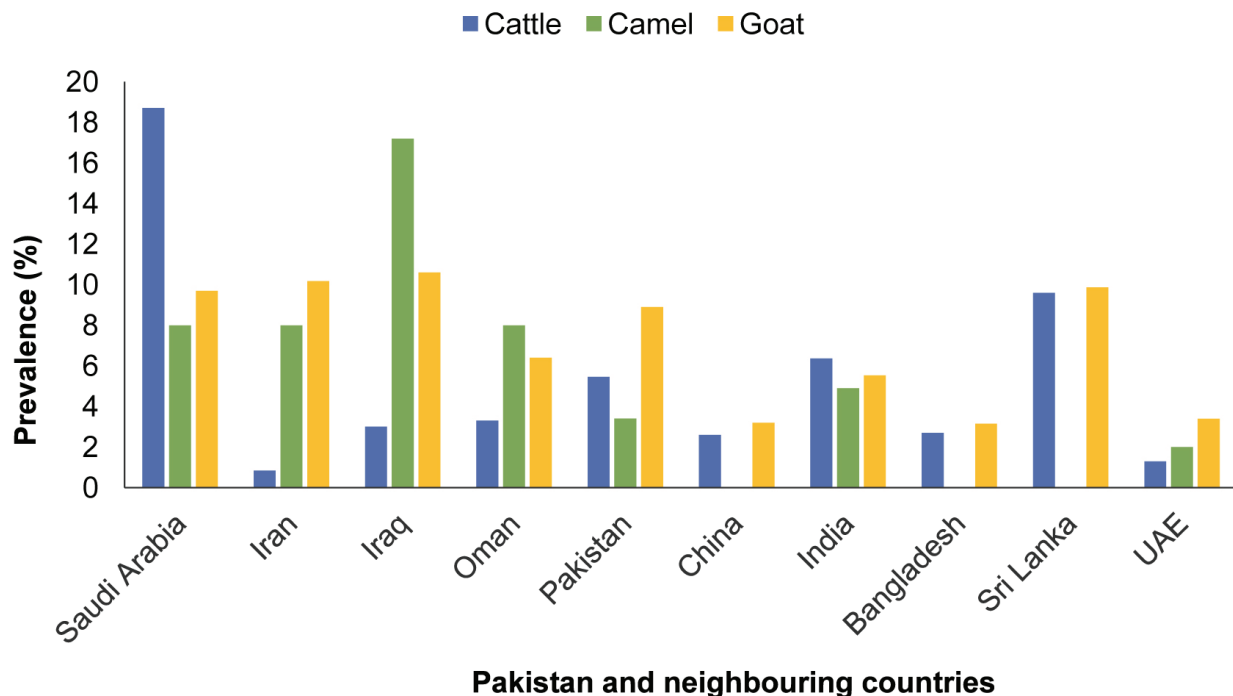


Figure 2. Prevalence of brucellosis in South Asia and Middle-Eastern Countries [adopted from (Shome et al., 2013; Gul et al., 2015; Shahzad et al., 2017; Jamil et al., 2021; Khurana et al., 2021)]

districts of Rawalpindi and Islamabad revealed that the incidence of brucellosis is 1.6% in buffaloes and 6.6% in cattle (Ahmad et al., 2017).

In China, brucellosis is endemic and even highly prevalent especially in Inner-Mongolia and its incidence is increasing day by day due to the increase in public demand for dairy products as well as increased dairy cattle transport. A current study revealed that from 2008-2018 the prevalence of bovine brucellosis in dairy cattle increased from 1.6% to 2.6% (Ran et al., 2019).

In 23 states of India, a fairly large study revealed the overall prevalence of 2% while 17% was found in organized farms with a history of retained placenta and abortion (Deka et al., 2018). This study lacked the possibility of selection. Overall prevalence from the studies conducted in different states was found to be 12% or lower due to under-reporting. Some factors effectively contribute to the prevalence of brucellosis in endemic countries of the world such as under-reporting, lack of financial resources, insufficient data recording and lack of cooperation between veterinary and medical officials. In India, the cultural, historical and religious importance of cows and their banned slaughtering have played a pivotal role in increasing public health risk as well as added a layer of complexity to control the disease (Deka et al., 2018).

Economic Importance:

Brucellosis is considered one of the leading diseases in the world which causes huge economic losses to the dairy industry including both direct (high mortality and decrease milk yield) and indirect losses (culling and vaccination cost). Visible (repeat breeding and abortion), invisible (low fertility) and other additional costs (treatment and vaccination) related to economy are also important to discuss (Montiel et al.,

2015). In India, a recent study reviewed an average loss of 3.4 billion USD to the livestock industry of which 96 percent was attributed to the dairy sector (Singh et al., 2015).

According to another study in India, brucellosis results in a total average loss of 3425.3 million USD. While the individual economic losses are estimated to be USD 7.1, 48.9, 71.6, 1357.1, 918.3 million for pig, sheep, goat, buffaloes, and cattle respectively (Singh et al., 2015). For active surveillance 58.8 million USD is spent per year for bovine brucellosis (Kollannur et al., 2007).

CONCLUSION

Brucellosis is now considered as not merely a risk to livestock but also a human health issue especially in under-developed and developing countries of the world. This is because of the unfortunate fact that these countries lack the required facilities regarding accurate disease diagnosis and proper treatment. Lack of awareness among people especially from rural areas of endemic countries regarding the zoonotic potential of brucellosis is one of the major contributing risk factors for human health. Due to huge economic losses in terms of production, reproduction, diagnosis, treatment, and control in livestock, brucellosis can be considered as one of the most economically important diseases in developing and underdeveloped countries of the world. The best ways to control the spread of disease are mass vaccination, early diagnosis, and culling of seropositive animals. For an early diagnosis, further research is required to develop a reliable, easy to handle, field base diagnostic test applicable for humans and livestock populations equally. For the complete elimination of brucellosis, we also need extensive research to develop an effective and broad-spectrum vaccine.

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