



The Demographic Risk Factors for Brucellosis in Asia

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Author's contribution

The sole author designed, analyzed, interpreted and prepared the manuscript.

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ABSTRACT

Brucellosis is also known as Undulant fever, Malta fever, rock fever, intermittent fever, Gibraltar fever, contagious abortion, Maltese fever, Crimean fever, or even Mediterranean fever. Clinical manifestations commonly encountered are fever and arthralgia. It has veterinary importance making it the leading cause of abortion and infertility in animals. Countries in which mixed agriculture is still the leading occupation have reported this disease in high number. The disease is common in areas where the mixed type of farming is still practiced, it is a type of farming where owners cohabit with their animals in the shed during the nighttime. The incidence of the disease is reported more in humans who have direct contact with the animal's abortus fetus and reproductive secretions. A favorable environment is created for transmission when the healthy and infected animals are kept together free and are difficult to segregate. Diagnosis of the disease is done by isolation of the bacteria from the sample using the polymerase chain reaction (PCR) technique. The disease was claimed to be eradicated but now as the global trend of infectious diseases is constantly changing it now appears to be a re-emergent disease. The best way to prevent the spread of the infection is through the One Health approach. Although brucellosis has been widely reported in animals and humans only a few studies have addressed the true prevalence of the disease in the context of Asia which is quite a challenge. It is unable to provide the true context of the disease. The case burden is more prevalent in the developing countries where it is found to be endemic in animals as well as in humans. Thus, this paper highlights the risk factors commonly found in Asian countries that are associated with increased prevalence of infection in humans

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which has now been believed to be involved many generations across the globe. Countries in which mixed agriculture is still the leading occupation have reported this disease in high number. The disease is common in areas where the mixed type of farming is still practiced, it is a type of farming where owners cohabit with their animals in the shed during the nighttime. The incidence of the disease is reported more in humans who have direct contact with the animal's abortus fetus and reproductive secretions. A favorable environment is created for transmission when the healthy and infected animals are kept together free and are difficult to segregate. Diagnosis of the disease is done by isolation of the bacteria from the sample using the polymerase chain reaction (PCR) technique. The disease was claimed to be eradicated but now as the global trend of infectious diseases is constantly changing it appears to be a re-emergent disease. The best way to prevent the spread of the infection is through the One Health approach. Although brucellosis has been widely reported in animals and humans only a few studies have addressed the true prevalence of the disease in the context of Asia which is quite a challenge. It is unable to provide the true context of the disease. The case burden is more prevalent in the developing countries where it is found to be endemic in animals as well as in humans. Thus, this paper highlights the risk factors commonly found in Asian countries that are associated with increased prevalence of infection in humans which has now been believed to be involved many generations across the globe.

Keywords: Brucellosis; Risk factor association; Malta fever; agriculture.

ABBREVIATIONS

PCR : Polymerase Chain Reaction

1. INTRODUCTION

Brucellosis is also known as Undulant fever, Malta fever, rock fever, intermittent fever, Gibraltar fever, contagious abortion, Maltese fever, Crimean fever, or even Mediterranean fever [1]. Brucellosis has been known to be existing for more than 2500 years [2]. It is one of the most common zoonotic diseases with more than half-million reported cases every year in humans. The infection is acquired through the consumption of unpasteurized milk and its milk products from infected animals. Animals acquire infection through vertical transmission. The Asian region is growing rapidly with an average annual income increasing from 4% to 8%, population from 2% to 3%, urbanization to 6%, and meat consumption from 4% to 8%. To support this growth the region has estimated a rapid increase in population, but it is predicted to have a prevalence rate of 2.9% [3]. It also poses an occupational exposure hazard who work closely with infected animal's aborted fetuses and genital secretions [4].

Brucellosis is caused by small, non-motile, non-sporing, aerobic, gram-negative intracellular coccobacilli. They are catalase, oxidase, and urea-positive bacteria. Several species are known to cause this infection such as *Brucella melitensis*, *Brucella abortus*, *Brucella suis*,

Brucella canis, *Brucella microti*, *Brucella inopinata*, *Brucella ovis* *Brucella Ceti* and *Brucella pin-nipedialis* [5,6,7] *Brucella melitensis* is the most pathogenic of all the species found existing and is also the most common cause of serious infection. It is mainly found in cattle involved in mixed farming methods. It has been reported that in some cases the cattle can be affected by both *B. melitensis* and *B. abortus* and identification of the etiological factor can only be done when humans have been infected [8]. The clinical features include fever, sweats, chills, fatigue, headache, malaise, weight loss, nausea/vomiting [9]. Among which the most common clinical manifestations reported according to various publications were fever in 76.8%, joint pain/ swelling/ arthralgia in 74.7%, sweats in 73.3%, fatigue/asthenia/weakness in 50.3%, and back pain in 36.3%. Among the available obstetric outcome information 31.3% suffered preterm delivery, 37.5% had an abortion and 9.8% had intrauterine fetal death [8]. The gold standard method in diagnosing the disease is only by isolation of the bacteria from the sample by using polymerase chain reaction (PCR) but the cost-effective way of diagnosing commonly practiced in developing countries is by serological diagnosis [10]. Investigation arising from such case scenario where mixed farming is practiced may require more than just serology; isolation and PCR are very helpful in identifying the exact species causing infection in the human population [11,12,13].

2. METHODS

2.1 Literature Review

The main purpose of the literature review was to identify studies with brucellosis etiology data. All searches were conducted from the time frame of 1982 to 2021, they were identified using keywords such as brucellosis, etiology, risk factor, global scenarios, in Asia, or epidemiology. Titles and abstracts were screened to identify the potential studies related to risk factors associated with brucellosis in Asia. Eligible studies were abstracted for information with included risk factors associated with brucellosis in the context of Asia. The studies were grouped according to different countries; no statistical testing was undertaken during the formulation of the data.

The criteria for inclusion of the studies were:

- Study of brucellosis and its synonyms in the context of Asia
- Direct association of risk factor with the infection
- Various risk factors depending on the traditional practices in Asia
- Published data from 1982 to 2021 related
- Identification of the risk factor involved in the infection using One Health Approach

The study aimed to identify the risk factors that were associated with the infection. The study was designed with the most comprehensive risk factor association results. We have limited the results to risk factors associated with brucellosis in Asia.

3. RESULTS

Of the forty-three published articles, 16 articles were excluded because they did not meet the eligibility criteria. Forty-three articles were reviewed and studies that showed risk factor associated with brucellosis in the context of Asia. Studies from various countries in Asia like Malaysia, China, Israel, Iraq, India, Iran,

Bangladesh, Thailand, Nepal, Jordan, Tajikistan, and many more were identified. Multiple studies were conducted in 12 countries out of 48 countries in continent Asia.

4. DISCUSSION

4.1 Human Brucellosis in Asia

Most of the studies conducted in different countries in Asia showed that the introduction of new animals provided one of the highest risk factors for brucellosis in healthy livestock farms, and this is an important risk factor for farmers to guide against having brucellosis-free herds. Studies conducted in different Asian countries explain that the exposure to the risk factor that is the infected animals is by consumption of raw milk or by humans who directly in contact with these infected reservoir animals. The various publication demonstrates the association of the disease with the risk factor [1,2,5,6,7,8,15,16,17].

An interesting comparison between two groups of people living in Israel was demonstrated. It explained that the risk factor attributing to the prevalence of the infection was of the same nature. In southern Israel, the Bedouin tribes who live near their herds and consume lots of unpasteurized milk and dairy products reported a high number of endemic brucellosis, and some inhabitants of Israel, such as the Ethiopian Jews, do not raise animals or consume dairy products and yet are increasingly becoming infected with brucellosis. The cause was often overlooked. From the study, it was postulated that Brucellosis can also be transmitted by the traditional slaughtering of animals. Ethiopian Jews in Israel in which the animal is slaughtered, skinned, eviscerated and the meat is minced. Direct exposure to the pathogen can also cause the infection. Those who traditionally slaughter the animals are equally at risk with those who consume unpasteurized milk and milk products from the infected animals. Thereby exposing both the groups to the pathogen [18].

Table 1. Brucellosis species specific case reported in Asia [14]

Country	Man B. ab.	B. mel.	Country	Man B. ab.	B. mel.	Country	Man B. ab.	B. mel.
Syrian A.R.	+	+	Pakistan	?	++	Bangladesh	++	+
Lebanon	+	+	Saudi Arabia	?	...	Burma	+	...
Israel	++	++	Yemen	?	...	Thailand	++	+
Jordan	?	?	Kuwait	++	...	Laos	++++	+
Iraq	+		Sri Lanka	+	...	Qatar
Iran	++++	++++	India	+	+++	Bahrain	?	...
Afghanistan	+++	++	Nepal	++	+	UAE	?

A study recently conducted in Iran demonstrated that the most common source of infection with brucellosis was the consumption of unpasteurized fresh cheese. Occupational exposure was recorded in about 52.1% of patients [17].

In Malaysia, the risk factors demonstrated include mean age, occupation, and consumption of unpasteurized milk with farmers having 7.19 times the odds of developing brucellosis when compared to non-farmers with 90% confidence interval [CI]: 1.16-44.71; it also demonstrated that those who were 40 years and below had 7.16 times the odds of developing brucellosis than those above 40 years with 90% Confidence Interval: 1.16-44.41. Among those who consumed unpasteurized milk have 4.5 times the odds of having brucellosis than those who do not consume (90% CI: 1.03-19.15) [19]. The risk factors of brucellosis in Malaysian goats were found to be the introduction of new animals (OR: 5.25; 90% CI: 1.46-18.88), the younger age category of farms (OR: 5.53; 90% CI: 1.09-21.66), and farms with a single breed of goats (OR: 8.50; 90% CI: 1.27-41.97) [20,21].

In India, it has also been reported that there is a loss of 0.5 USD per goat due to brucellosis infection. [22]. A recently conducted study in rural India concluded that among 1,733 infected individuals, 998 had direct contact with animals, whereas 735 had no evidence of direct contact. Clinical symptoms resembling brucellosis were seen in 8.71% of the subjects. Animal contact especially during milking, parturition/abortion was the major risk factor, followed by raw milk ingestion. None of the participants knew about the disease brucellosis [23].

In Bangladesh, Brucellosis prevalence showed variation based on occupations of people and species of animals (3.7% in cattle, 4.0% in buffalo, 3.6% in goats, and 7.3% in sheep). The prevalence of brucellosis also varied in livestock farmers (2.6-21.6%), milkers (18.6%), butchers (2.5%), and veterinarians (5.3-11.1%) who have had direct contact with the animal and its products or who consume raw milk directly [24]. In Bangladesh the apparent prevalence of brucellosis in high-risk occupationally exposed and in pyretic patients is also low [25].

Thailand is still considered endemic for brucellosis and in recent years there have been concerted efforts beginning from 2009 to eradicate brucellosis in animals, but the high

volume of goat movements hampers the test and slaughter and compensation policy from achieving the needed objectives [26]. An outbreak of brucellosis in a goat farm in Thailand led to a fatal infection of a 79-year-old goat farmer with unprotected exposure to goat carcasses identified as the main risk factor. [27] Farmers and veterinary personnel must be careful while handling animals in endemic areas.

As recorded by various studies [28,29,30,31,32] the prevalence of brucellosis in the Nepalese gender specifically explains males 5.60% to 9.42%, and 2.90% to 60% in females. This higher incidence of brucellosis among slaughterhouse workers may have been due to occupational exposure and poor hygiene in slaughterhouses.

In Ningxiang, China, goats are referred to as the major source of Brucellosis for human infection. Most of the farmers and slaughter workers were involved with goats. The disease has caused a significant economic loss to local farmers. The consequences of infection were reported as abortion, stillbirths, and increased mortality in goats [33,34]. Another major cause identified was that improper disposal of the sick or dead goats adopted by local farmers in China is also a major cause of brucellosis in the human population. The most practical way of dealing with the dead goats identified was burying. However, local farmers often feed the contaminated carcasses of goats to the dogs or abandon them carelessly hence causing the bacteria to survive for months in the environment [35]. Thus, it was concluded that the indirect transmission may have occurred through the contacts between dogs and contaminated soil and water or vectors [35,36]. There was another risk factor also identified in this same study, it was the poor hygiene in lambing pen where it had a higher chance of contamination by abortions of goats. Introduction and poor hygiene in local goat farms were key risk factors for local farms having goats that were seropositive to Brucellosis [37]. The finding was similar to studies conducted in other countries [38,39,40] A goat farm having an introduction in the preceding year would have a dramatically increased risk of infection than a farm. This finding indicates that there might be risky trade practices adopted by local farms [37].

The study was conducted among 667 female sheep and goats >6 months of age from 21 villages surrounding the capital city, Dushanbe.

Fourteen villages had at least one seropositive sheep or goat, resulting in the apparent prevalence of 67 % at the village level. This indicates a high prevalence of Brucella infection among sheep and goats in the peri-urban area of the capital city in Tajikistan. Given the dense human population in such areas, this could constitute a threat to public health, besides causing significant production losses [39].

High herd prevalence of Brucellosis has also been reported in other Asia countries. A cross-sectional survey in Jordan reported 45.4% (95% CI: 30.3–61.6) in goat herds and 70.4% (95% CI: 55.5–84.9) in mixed sheep-goat flocks. [40].

Brucellosis in sheep and goats contributes to local human infection. The distribution of human cases was significantly more spatially correlated with the number of sheep and goats than with swine and cattle [41]. Control of Brucellosis in humans requires good control of Brucellosis in livestock. Unfortunately, there has been no reliable strategy of brucellosis control in many developing countries [42]. Understanding the epidemiology of brucellosis is the key to the development of an efficient control strategy for brucellosis control and risk factors identified.

4.2 One Health Approach of Identifying the Risk Factor and Controlling the Spread of Infection

A very fundamental way to control brucellosis was recently developed. It is gaining wide recognition around the developing countries where brucellosis remains an infection of concern. It is popularly known as the One Health approach. In the One Health framework healthcare professionals including from every field working to solve the infection spread that include veterinary, medical, environmental professionals, policymakers and experts involved all collaborate together with the one and only aim of identifying possible risk factors responsible for this infection and formulate a suitable approach in controlling and eradicating the infection [43]. To mitigate effective control and eradication of brucellosis, both the human and animal population, it is vital to understand that which species of Brucellae affect which animals and in return which of these animals can be a vital source of reservoirs, especially in developing countries where mixed farming is commonly practiced. [43]. Reservoir in these infected animals is responsible for the spread of infection and transmitting it to the human population

[20,43,44,45]. Unfortunately, in many underdeveloped and developing countries, this kind of collaboration is non-existent or weak which gives room for brucellosis to thrive unchecked especially in rural populations [43].

5. CONCLUSION

Brucellosis is a zoonotic infection most acquired to the human population from the infected animal reservoir. Consumption of raw milk and milk products poses the same amount of threat to those who handle the infected animals with close contact. Different studies available from Asian countries explain that mixed farming is commonly practiced in this region. Due to this, contact between the pathogen and host is inevitable. The pathogen survives in the host if a suitable environment is available to thrive in it. Brucellosis is likely to continue to be a global threat for years to come in Asian countries due to mixed farming, but concerted efforts and political willpower of various government agencies can facilitate the process of reducing the disease spread among animals and ultimately among the human population [45]. There is lack of data explaining the accurate incidence and prevalence of human brucellosis from many countries this causes underestimation of the actual burden of the disease. A very important key to controlling brucellosis in humans is controlling it in animals [46].

CONSENT

It's not applicable.

ETHICAL APPROVAL

It's not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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