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# EPIDEMIOLOGY AND EPIZOOTOLOGY OF BRUCELLOSIS: A REVIEW

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## INTRODUCTION

Brucellosis is one of the world's major zoonotic problems. Though it has been eradicated in many developed countries in Europe, Australia, Canada, Israel, Japan and New Zealand (Geering *et al*., 1995), yes it remains an uncontrolled problem in regions of high endemicity such as the Africa, Mediterranean, Middle East, parts of Asia and Latin America (Refai, 2002). Almost all domestic species can be affected with brucellosis except cats which are resistant to *Brucella* infection. Considering the damage done by the infection in animals in terms of decreased milk production, abortions, weak offsprings, weight loss, infertility and lameness, it is one of the most serious diseases of livestock. It is also a major impediment for the trade. Death may occur as a result of acute metritis, followed by retained fetal membranes (Radostits *et al.,* 2000).

Brucellosis is caused by members of genus *Brucella*. These are small, non-motile, aerobic, facultative intracellular, Gram-negative coccobacilli. The ability of *Brucella* to replicate and persist in host cells is directly associated with its capacity to cause persistent disease and to circumvent innate and adaptive immunity (Fichi, 2003). The species of *Brucella* and their major hosts are *Br. abortus* (cattle), *Br. melitensis* (goats), *Br. suis* (swine) and *Br. ovis* (sheep). *Br. abortus* also causes infection in horses and is commonly found in chronic bursal enlargements as a secondary invader rather than a primary pathogen (Radostits *et al.,* 2000). From public health view point, brucellosis is considered to be an occupational disease that mainly affects slaughter-house workers, butchers, and veterinarians. Transmission typically occurs through contact with infected animals or materials with skin abrasions. Symptoms in human brucellosis can be highly variable, ranging from non–specific, flu-like symptoms (acute form) to undulant fever, arthritis, orchitis and epididymitis (Plummet *et al.,* 1998).

The *Brucella* may enter the body through digestive tract, lungs or mucosal layers and intact skin. Then it may spread through blood and the lymphatic system to any other organ where it infects the tissues and causes localized infection (Lapaque *et al.,* 2005). The organism is able to escape phagocytic killing through inhibiting the phagosome-lysosome fusion and reproducing inside macrophages (Young, 2005). After a variable incubation period ranging from less than one week to several months, non-specific systemic symptoms such as fever, headache, malaise, night sweats and arthralgia follow, resembling a flu like disease. During the early stage of the disease, patients are frequently bacterimic that has a continuous pattern, making circulating *Brucella* easily detectable by blood culture. Once in the blood stream, the organism is seeded to multiple organs/systems, especially those rich in reticuloendothelial tissue, such as liver, spleen, skeletal and hematopoietic system (Greenfield *et al.*, 2002).

There are so many factors that can affect the prevalence of brucellosis in various species of livestock. Prevalence of brucellosis can vary according to climatic conditions, geography, species, sex, age and diagnostic tests applied.

### Geographic distribution

Several synonyms of brucellosis have been known like Malta fever, undulant fever, Rock of Gibraltar fever and Bang's disease. The disease has very old history, as organisms resembling *Brucella* had been detected in carbonized cheese from the Roman era. Brucellosis was first recognized as a disease affecting humans on the Island of Malta in the early 20$^{th}$ century. Though its distribution is worldwide; yet brucellosis is more common in countries with poorly standardized animal and public health programme (Capasso, 2002). The routes of infection are multiple i.e., food-borne, occupational or recreational, linked to travel and even to bioterrorism. New *Brucella* strains or species may emerge and existing *Brucella* species adapt to changing social, cultural, travel and agricultural environment (Godfroid *et al.,* 2005). The incidence of reactors in newly established cattle farms may be more than 30%, however, the highest rate (72.9%) of infection till now has been reported in the Palestinian Authority (Shuaibi, 1999). It is interesting to note that the second highest prevalence (71.42%) of brucellosis has been reported in mules from Egypt (Anonymous, 2007a).

Invariably, all domestic animals suffer from this disease. Brucellosis in buffaloes has been reported from Egypt (10.0%) and Pakistan (5.05%). Since cattle are found through out the world, prevalence of brucellosis (0.85 to 23.3%) in cattle has been reported from a wide range of countries (Table 1). In camels, brucellosis has been reported from Arabian and African countries (0.0-17.20%), where the disease also occurs in buffaloes, equines and swine. Variable prevalence of this disease has been reported in sheep and goats. Bio varieties of *Brucella* vary with respect to geographic region. *Br. melitensis* biovar 1 from Libya, Oman and Israel and *Br. melitensis* biovar 2 from Turkey and Saudi Arabia have been isolated (Table 1). *Br. melitensis* biovar 3 is

**Table 1: Prevalence of *brucellosis* in livestock in different countries**

| **Country** | **Species** | **Prevalence (%)** | ***Brucella* species** | **Reference** |
|---|---|---|---|---|
| Algeria | Sheep | 2.18 | _ | Refai (2000) |
| | Goat | 12.00 | _ | |
| Egypt | Buffalo | 10.00 | *Br. abortus* | Refai (1989) |
| | Cattle | 23.30 | *Br. melitensis biovar 3* | |
| | Donkey | 7.30 | _ | Hamoda and Montaser (1998) |
| | Horse | 5.88 | – | Montasser *et al.* (1999) |
| | Mule | 71.42 | – | |
| Eritria | Cattle | 8.20 | _ | Omer *et al.* (2000) |
| | Sheep | 1.40 | _ | |
| | Goat | 3.80 | _ | |
| | Camel | 3.10 | _ | |
| | Horse | 0.00 | _ | |
| India | Equine | 12.89 | _ | Sharma *et al.* (1979) |
| | Bovine | 6.37 | _ | |
| | Sheep | 3.42 | _ | |
| | Goat | 5.53 | _ | |
| Iran | Cattle | 0.85 | *Br. Abortus* | Zowghi *et al.* (1990) |
| | Goat | 10.18 | _ | |
| | Camel | 8.00 | _ | Zowghi and Ebadi (1988) |
| Iraq | Sheep | 15.00 | *Br. melitensis* | Al-Ani *et al.* (1998) |
| | Cattle | 3.00 | *Br. Abortus* | |
| | Camel | 17.20 | _ | |
| Libya | Camel | 4.10 | *Br. melitensis biovar 1*. | Gameel *et al.* (1993) |
| Nigeria | Cattle | 5.82 | _ | Cadmus *et al.* (2006) |
| | Goat | 0.86 | _ | |
| Oman | Camel | 8.00 | *Br. abortus* | Anonymous (1998) |
| | Cattle | 3.30 | _ | |
| | Sheep | 1.60 | _ | |
| | Goat | 6.40 | *Br. melitensis* | |
| Pakistan | Horse | 5.78 | _ | Ahmed and Munir (1995a & b) |
| | Dog | 9.33 | _ | |
| | Poultry | 4.00 | _ | |
| | Buffalo | 5.05 | _ | |
| | Cattle | 5.46 | _ | |
| | Camel | 2.00 | _ | Ajmal *et al.* (1989) |
| Saudi Arabia | Camel | 8.00 | *Br. melitensis biovar 2*. | Memish (2001) |
| | Cattle | 18.70 | _ | |
| | Sheep | 6.50 | _ | |
| | Goat | 9.70 | _ | |
| Sri Lanka | Cattle | 4.7 | *Br. abortus* | Silva *et al.* (2000) |
| | Buffalo | 4.2 | _ | |
| Sudan | Camel | 6.95 | *Br. abortus* | Yagoub *et al.* (1990) |
| | Camel | 0.00 | _ | El-Ansary *et al.* (2001) |
| | Cattle | 5.00 | _ | |
| | Sheep | 1.00 | _ | |
| | Goat | 4.00 | _ | |
| United Arab Emirates | Camel | 2.00 | *Br. abortus* | Afzal and Sakkir (1994) |
| | Cattle | 1.30 | _ | |
| | Sheep | 2.00 | _ | |
| | Goat | 3.40 | _ | |

the most commonly isolated species from animals in Egypt, Jordan, Israel, Tunisia and Turkey (Refai, 2002). *Br. abortus* biovar 1 in Egypt, biovar 2 in Iran, biovar 3 in Iran and Turkey and biovar 6 in Sudan have been reported (Halling and Boyle, 2002). The countries with the highest incidence of human brucellosis include, Saudi Arabia, Iran, Palestinian Authority, Syria, Jordan and Oman. Bahrain is reported to have no incidence (Refai, 2002). The percent prevalence of bovine brucellosis has been reported to decrease (Fig. 1) in Ireland and Italy during the year 1999-2000 but there had been a trend towards a significant increase in Azores (Jacques and Kasbohrer, 2002).

**Epidemic season**

In general, brucellosis can be found in any season of a year. The epidemic peak occurs from February to July (Fig. 2) and is closely related to the months associated with delivery and abortion in animals (Shang *et al.*, 2002). In humans, prevalence of the disease is high (39.5%) in summer season (Salari *et al.*, 2003). Notifications of human brucellosis, which are mandatory in Italy, reach a peak between April and June. However, considering the standard incubation period of 2-4 weeks, and the fact that lamb slaughter is traditionally at a peak during the Easter period, it might be expected that occupational exposure would result in a peak of human cases between March and May. The observed peak between April and June could be related to the production and consumption of fresh cheese, starting just after lamb slaughter (De-Massis *et al.*, 2005).

**Sex and age wise prevalence**

There are controversial reports regarding the prevalence of brucellosis in relation to sex of animals, as some of the research workers reported significantly higher prevalence in females than in males (Hussein *et al.*, 2005), whereas MacMillan *et al*. (1982) were of the view that *Br. abortus* causes intermittent bacterimea in the mares but not in the stallions. The relatively higher incidence reported among human females than males might be due to more involvement of females in handling of livestock. These females may be highly exposed to the risk of infection through direct contact with animals, consumption of raw milk and milk products. Moreover, risky practices in rural areas such as skinning of stillborn lambs and kids, as well as crushing the umbilical cord of newborn lambs and kids with teeth can also be contributing factors (Hussein *et al.*, 2005). However, some reports indicate that *Brucella* antibody titers are not associated with sex (Muma *et al.*, 2006).

The antibody titer against *Br. abortus* appears to be associated with age, as low prevalence in young stock has been reported than the adults (Ahmed and Munir, 1995b). Kazi *et al.* (2005) reported higher prevalence of infection in animals more than 4 years of age compared to younger animals. It appears that the high prevalence of brucellosis among older cows might be related to maturity with the advancing age. Thereby, the organism may have propagated to remain either as latent infection or it may cause clinical manifestation of the disease (Kazi *et al.*, 2005).

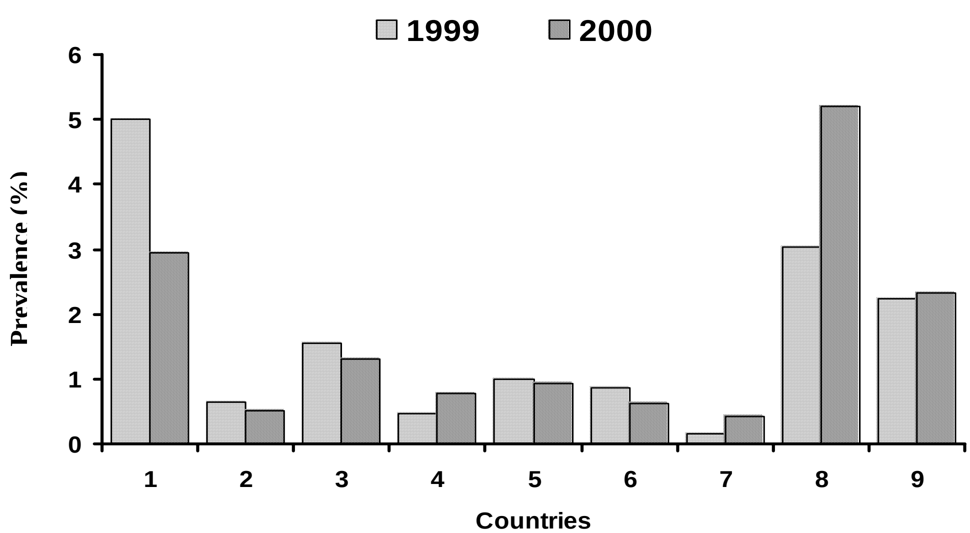


**Fig. 1: Prevalence (%) of bovine brucellosis in European Union (1 = Greece, 2 = Republic of Ireland, 3 = Italy, 4 = Northern Ireland, 5 = Portugal, 6 = Main Land, 7 = Madeira, 8 = Azores, 9 = Spain) during 1999 and 2000 (Jacques and Kasbohrer, 2002).**

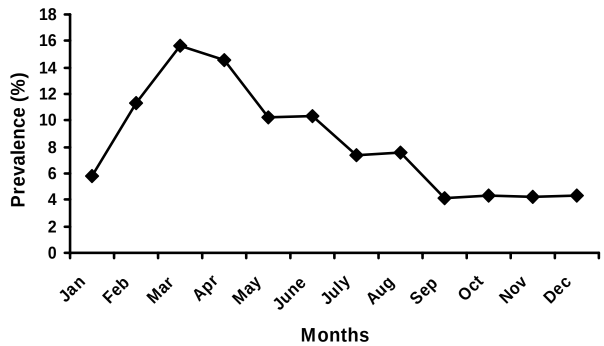


**Fig. 2: Monthwise prevalence of brucellosis in China from 1950 to 1999 (Shang *et al.*, 2002).**

Brucellosis is essentially a disease of the sexually mature animals, the predilection site being the reproductive tract, especially the gravid uterus. Allantoic factors including, erythritol, possibly steroid hormones and other substances stimulate the growth of most of the *Brucellae* (Radolf, 1994). The tropism of *Brucella* to the male or female reproductive tract was thought to be by erythritol, which stimulates the growth of the organism, but *Brucella* has also been found in the reproductive tract of animals with no detectable levels of erythritol (Anonymous, 2007b). Erythritol, a sugar alcohol synthesized in the ungulate placenta and stimulates the growth of virulent strains of *Br. abortus*, has been credited with the preferential localization of this bacterium within the placenta of ruminants (Smith *et al*., 1962).

**Test based prevalence**

The main serological test used for diagnosis of brucellosis is the Rose Bengal Plate Test (RBPT), which has very high (>99%) sensitivity but low specificity (Barroso *et al.,* 2002). As a result, the positive predictive value of this test is low and a positive result is required to be confirmed by some other more specific test like serum agglutination test (SAT) and ELISA. However, the negative predictive value of RBPT is high as it excludes active brucellosis with a high degree of certainty.

The SAT is recommended for collection of quantitative information on immune responses. It is the most frequently used confirmatory serological test and has become the standard method for the diagnosis of the brucellosis. The sensitivity and specificity of the SAT test are 95.6 and 100.0%, respectively, while that specificity of the ELISA is 45.6% (Memish *et al.*, 2002).

Prevalence of brucellosis on the basis of SAT and RBPT in various species of animals and humans varies very widely. Equine showed a wide variation of brucellosis occurrence (0.24-37.50%), followed by bovine (0.58-35.90%), caprine (0.40-33.3%), ovine (0.28-16.70%) and camelidae (1.8-7.48%) with humans had the least prevalence (0.89-4.10%, Table 2). *Brucella* has also been isolated from a variety of wildlife species such as bison, elk, African buffalo, reindeer, caribou, feral swine, wild boars, foxes and hares (Davis, 1990). Anti-*Brucella* spp. antibodies were detected by tube agglutination test, ELISA and immunoblotting in 53% serum samples of Pacific bottlenose dolphins (*Tursipa aduncus*) from the Solomon Islands (Tachibana *et al*., 2006).

Ribeiro *et al.* (2003) tested fistulus withers secretions from three horses by the plate agglutination test (PAT), SAT, buffered RBPT and 2-mercaptoethanol test (2-MET), and compared the results with standard agglutination test. Titers were higher in the PAT, SAT and 2-MET and positive

**Table 2: Prevalence (%) of brucellosis in various species based on SAT and RBPT**

| Species | | | | | | Test used | Reference |
|---|---|---|---|---|---|---|---|
| Equine | Bovine | Caprine | Ovine | Camelidae | Humans | | |
| 22.70 | - | - | - | 1.80 | - | SAT | Kulshrestha *et al.* (1977) |
| 12.89 | 6.37 | 5.53 | 3.42 | - | 0.89 | - | Sharma *et al.* (1979) |
| - | - | 3.00 | 1.69 | - | 0.95 | SAT | Masoumi *et al.* (1992) |
| - | - | - | - | - | 4.10 | SAT | Gameel *et al.* (1993) |
| - | - | - | - | 8.00 | - | RBPT | Radwan *et al.* (1995) |
| - | 17.00 | - | - | - | - | SAT | Isloor *et al.* (1998) |
| - | 3.65 | 3.35 | 0.28 | 7.48 | - | SAT | Montasser *et al.* (1999) |
| - | 35.90 | 33.3 | 16.70 | 3.10 | - | RBPT | Omer *et al.* (2000) |
| - | 18.70 | 9.70 | 6.50 | 8.00 | - | - | Memish (2001) |
| 37.50 | - | - | - | - | - | SAT | Welsh and Dirato (2004) |
| - | 0.58 | 7.24 | 6.26 | - | - | RBPT | Jackson *et al.* (2004) |
| - | 12.09 | - | - | - | - | - | Dhand *et al.* (2005) |
| 0.24 | - | - | - | - | - | RBPT | Acosta *et al.* (2006) |
| - | 5.82 | 0.86 | - | - | - | RBPT | Cadmus *et al.* (2006) |

reaction was observed in RBPT. *Br. abortus* was isolated from the secretion of fistulous withers, collected from one animal. These results suggest that the modified tests may be used as alternative test to diagnose brucellosis in horses with fistulous withers.

Ocholi *et al.* (2004a) isolated *Brucella* from aborted fetuses, hygroma fluid, milk and vaginal swabs obtained from aborting cattle, sheep, goats, pigs and horses. A total of 25 isolates, obtained mainly from cattle, sheep and horses, were biotyped. All strains belonged to one species, *Br. abortus* biovar 1. Ocholi *et al.* (2004b) isolated *Br. abortus* from a horse which had carpal bursitis. In a subsequent study, Ocholi *et al.* (2005) examined serum and milk samples from ewes for *Brucella*, a total of seven isolates of *Brucella* were obtained from milk samples and vaginal swabs collected from aborting ewes. All isolates were identified and bio-typed as *Br. abortus* biovar 1.

**Bioterrorism**

Brucellosis is not only a major zoonotic problem but is also linked with bioterrorism and belongs to category B (Anonymous, 2000). The severity of this disease, lack of vaccines suitable for use in man and frequent failure of clinical laboratories to correctly identify isolates led to the investigation of *Brucella* as an agent for bioterrorism. Before 1954, when Britain was focusing on anthrax, brucellosis was the first microorganism chosen by the United States to develop as a weapon. This microorganism could be effectively disseminated in four pound bombs (Yagupsky and Baron, 2005). Indeed, the American military weaponized *Br. suis* in 1954, however, changing global politics resulted in abandonment of these efforts following the biological and toxic weapons convention in 1972. *Brucellae* are not difficult to grow and disperse, and transmission to humans may result in prolonged illness and long-term sequelae (Yagupsky and Baron, 2005). Aerosol or food contamination could be the sources of dispersion. This microorganism has the advantage of being debilitating without being fatal. The infective dose for these organisms is very low, if acquired via the inhalation route. It has been estimated that 10-100 organisms are sufficient to constitute an infectious aerosol dose for humans. The economic impact of a brucellosis bioterrorist attack would cost $ 477.7 million per 100,000 persons exposed (Kaufmann *et al.,* 1997). Although *Brucella* has long been considered a potential microorganism for bioterrorism, no application in a bioterrorist attack has been reported so far (Shareef, 2006).

**Conclusions**

From the above discussion, it can be concluded that brucellosis is one of the world's major zoonotic problems. Nearly all animal species are susceptible. The disease caused by various *Brucella* species renders heavy economic losses. Various factors such as climatic conditions, geography, species, sex and age of the host have been reported to affect its prevalence. For serodiagnosis, RBPT and SAT are used commonly. Brucellosis prevalence varies very widely in equine (0.24-37.50%), bovine (0.58-35.90%), caprine (0.40-33.3%), ovine (0.28-16.70%) and camelidae (1.8-7.48%), while humans had the least prevalence (0.89-4.10%). Brucellosis is essentially a disease of the sexually mature animals, as organism resides in gravid uterus where erythritol is synthesized in placenta and stimulates the growth of virulent strains of *Br. abortus. Brucella* has been considered an organism for bioterrorism but no application has been reported so far.

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