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A REVIEW

Impact of brucellosis on health and economy

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Abstract : Brucellosis is one of the world's major zoonoses that still are of veterinarian, public health and economic concern in many parts of the world. It is an important zoonosis in humans in many parts of the world especially in the Mediterranean countries of Europe, north and east Africa, the Middle East, south and central Asia and Central and South America and yet it is often unrecognized and frequently goes unreported. Over half a million new cases occurs annually and prevalence rates in some countries exceeding ten cases per 100 000 population. Brucellosis has been constantly ranked among the most economically important zoonoses worldwide with multiple economic impacts attributable to human, livestock and wildlife disease. Human acquires *Brucella* infection directly or indirectly from animal sources. Brucellosis is a sub-acute or chronic disease which may affect many species of animals and cause placentitis followed by abortion in the pregnant female, usually during the last third of pregnancy, and epididymitis and orchitis in the male. The disease usually manifests itself as an acute febrile illness which may persist and progress to a chronic disease with severe complications. Animal brucellosis can be prevented, controlled and eradicated by farm hygiene and sanitation, restricted movement, prevention of contact, test and isolation/slaughter, mass vaccination, treatment and surveillance. Human brucellosis can be prevented and controlled by controlling and eliminating the diseases in animal reservoir and health education of the public working at high risk areas.

Key words : Brucellosis, Economic, Epidemiology, Health, Management

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INTRODUCTION

In case of humans, brucellosis is also known as "Undulant fever", "Mediterranean fever" or "Malta fever" (Dogany and Aygen, 2003). Brucellosis occurs worldwide in domestic and game animals (Seifert, 1996). It is essentially a disease of animals, especially domesticated livestock with human as an accidental host. It is an important zoonosis in humans in many parts of the world especially in the Mediterranean countries of Europe, north and east Africa, the Middle East, south and central Asia and Central and South America and yet it is often unrecognized and frequently

goes unreported (WHO, 2006). There are only a few countries in the world that are officially free of the disease although cases still occur in people returning from endemic countries.

Brucellosis is one of the world's major zoonoses that still is of problem in veterinarian, public health and economic concern in many parts of the world (Smits *et al*., 2005). Although brucellosis in livestock and transmission of infection to the human population has been significantly decreased following the instigation of effective vaccination-based control and prevention programmes in parts of the world, it remains an uncontrolled problem in regions of high endemicity such as the Mediterranean, Middle East, Africa, Latin America and parts of Asia (Corbel, 1997).

In livestock, brucellosis results in reduced productivity, abortions and weak offspring and is a major impediment for trade and export. A renewed scientific interest in human brucellosis has been fuelled by its recent re-emergence and enhanced surveillance in many areas of the world (Pappas *et al*., 2006). Furthermore, since brucellosis is an important cause of veterinary morbidity and mortality, the disease can also cause important economic losses in developing countries (Colmenero Castillo *et al.,* 1989).

Etiology :

Brucella is a facultative intracellular pathogen that can survive and multiply within phagocytic cells of the host. Different *Brucella* types infect different species preferentially. There are six important species of *Brucella*. *B. abortus* is normally associated with cattle, *B. melitensis* with sheep and goats, *B. suis* with swine, although biovars 4 and 5 are specifically associated with reindeer and rodents, respectively. *B. ovis* causes an infection specific for sheep and has not been conclusively implicated in human disease, and *B. canis* is usually associated with disease in dogs but occasionally causes human brucellosis. *B. neotomae* has been isolated on few occasions and has never been implicated in human disease. Most human cases are caused by *B. melitensis.*

Epidemiology :

Brucellosis remains the world's most common bacterial zoonosis, with over half a million new cases annually and prevalence rates in some countries exceeding ten cases per 100 000 population (Pappas *et al*., 2006). Despite being endemic in many developing countries (McDermott and Arimi, 2002), brucellosis remains underdiagnosed and under-reported (Godfroid *et al*., 2005). Brucellosis affects people of all age groups and of both sexes. Cattle, sheep, goats and pigs are the main reservoirs of *Brucella.* Susceptibility to brucellosis in humans depends on various factors, including the immune status, routes of infection, amount of the inoculum and, to some extent, the species of *Brucella.* In general, *B. melitensis* and *B. suis* are more virulent for humans than *B. abortus* and *B. canis,* although serious complications can occur with any species of *Brucella.*

Brucellosis is a zoonotic disease; hence the ultimate sources of infection are infected animals. The important species are the major food-producing animals such as cattle, sheep, goats and pigs. Other animal species including bison, buffalo, camels, dogs, horses, reindeer and yaks are less important, but they can be very significant local sources of infection in some regions. Recently, the infection has also been identified in marine mammals, including dolphins, porpoises and seals, and these may present an emerging hazard to persons occupationally exposed to infected tissues from them.

B. melitensis is the most frequently reported as a cause of human disease and the most frequently isolated from cases. It is the most virulent type and associated with severe acute disease. It is recorded as endemic in several countries and accounts for a disproportionate amount of human brucellosis. *B. abortus* is the most widespread cause of infection, but associated with much less human disease. Infection in human is often sub-clinical and, where disease does occur, it is usually less severe than that caused by *B. melitensis* or *B. suis*. *B. suis* has a much more restricted occurrence than *B. melitensis* and *B. abortus*. *B. canis* causes a widespread infection of dogs in many countries. It is infrequently associated with human disease and produce mild illness.

Laboratory workers handling *Brucella* cultures are at high risk of acquiring infection through accidents, aerosolization and/or inadequate laboratory procedures. In addition to this, abattoir workers, farmers and veterinarians are at high risk of acquiring the infection (Colibaliy and Yamego, 2000; Radostits *et al.,* 2006). Susceptibility of animal

to brucellosis depends on natural resistance, level of immunity, age, sex, breed, pregnancy status and environmental stress (Sukrija *et al.*, 2006). Sexually mature pregnant cattle are more susceptible to infection with the organism than sexually immature cattle of either sex. Susceptibility increases as stage of gestation increases (Radostits *et al*., 2006).

Economic impact of brucellosis :

Brucellosis has been constantly ranked among the most economically important zoonoses worldwide with multiple economic impacts attributable to human, livestock and wildlife disease (Zinsstag *et al*., 2007; Perry and Grace, 2009 and McDermott *et al.*, 2013). Although the public health importance of brucellosis is acknowledged throughout the world, the economic importance of animal brucellosis is felt most keenly by countries practicing intensive livestock farming, as the disease not only causes production losses (from abortion, stillbirth, sterility, a longer calving interval and lower milk yields), it also constitutes a barrier to trade (Akakpo *et al*., 2009).

Brucellosis has a considerable impact on animals and humans health, as well as wide socio-economic impacts especially in countries in which rural income relies largely on livestock breeding and dairy products (Gul and Khan, 2007). Costs include production loss associated with infection in animals, preventive programme, and in human disease cost of treatment and absenteeism from work brings many economical impacts. This is of greatest importance in beef herds where the calves represent the sole source of income. A high incidence of temporary and permanent infertility results in heavy culling of valuable and some deaths occur as the result of acute metritis following retention of the placenta. The effect of the disease on ram's fertility can influence the number of rams that are required in a flock; the required ram to ewe ratio is significantly reduced in *B. ovis*-free flocks (Gul and Khan, 2007).

In an attempt of eradication of brucellosis by culling of goats at fifteen goat farms in Malaysia caused a financial loss of at least 50,391.13 US Dollar (Bamaiyi *et al*., 2015). Available information indicates that brucellosis is one of the most serious diseases of cattle in Latin America and other developing areas. Official estimates put annual losses from bovine brucellosis in Latin America at approximately US$ 600 million (PAHO-WHO, 2001). In California, 30-40% of rams were thought to be affected and annual loss of US $ 2 million was estimated.

Transmission :

Brucella spp. can survive for long periods in dust, dung, water, slurry, aborted fetuses, soil, meat and dairy products. Human acquires *Brucella* infection directly or indirectly from animal sources, of which cattle, sheep, goats and pigs are by far the most important. In these natural hosts, the infection usually establishes itself in the reproductive tract, often resulting in abortion. Excretion in genital discharges and milk is common and is a major source of human infection. Direct inoculation through cuts and abrasions in the skin, inoculation via the conjunctival sac of the eyes, inhalation of infectious aerosols, and ingestion of infectious unpasteurized milk or other dairy products are also important source of infection. Person-to-person transmission of brucellosis is extremely rare; however, it may occur through blood transfusion, organ transplant and sexual transmission. Animal-to-animal transmission occurs as a result of the large number of organisms shed in the environment.

Certain occupations are associated with a high risk of infection with brucellosis. These include people who work with farm animals, especially cattle, sheep, goats and pigs. Farmers, farm labourers, animal attendants, stockmen, shepherds, sheep shearers, goatherds, pig keepers, veterinarians and inseminators are at risk through direct contact with infected animals or through exposure to a heavily contaminated environment. Food-borne transmission is usually the main source of brucellosis for urban populations. Ingestion of fresh milk or dairy products prepared from unheated milk is the main source of infection for most populations. Meat products are less frequently associated with infection, mainly because these are not usually eaten raw.

Disease in animals :

Brucellosis is a sub-acute or chronic disease which may affect many species of animals such as cattle, buffalo, sheep, goat, pig, horse, camel, buffalo, yak and reindeer. Five of the six currently recognized *Brucella* species cause infection and clinical signs in one or more animal hosts. In sexually mature animals the infection localizes in the

reproductive system and typically produces placentitis followed by abortion in the pregnant female, usually during the last third of pregnancy, and epididymitis and orchitis in the male. Abortion or premature births and retained placenta are the common characteristics of brucellosis in most animal hosts.

Brucellae are somewhat host-specific but cross-species infections occur, especially with *B. melitensis*. Infections in many wildlife species have been reported but those that obviously affect population fecundity and result in human infections are quite rare. *B. melitensis* infections in dairy herds, however, have severe economic and public health implications. Infections in sheep and goats are highly contagious because of the pathogenicity of *B. melitensis* and because of close contact due to high density of the flocks or herds, the commingling of those of different owners and heavy exposure in housing. The udder is often permanently infected, especially in the case of cows and goats. Shedding of organisms in milk is frequent. Localized infections in sheep result in orchitis or epididymitis in the case of *B. melitensis* and *B. ovis*. In goats, cattle, swine and dogs similar complications may follow infection with *B. melitensis, B. abortus, B. suis* and *B. canis*, respectively. Arthritis occurs rarely in *B. melitensis*-infected sheep and goats. Brucellosis in horses is often asymptomatic, however, local abscess formation in bursae may occur. Camels infected with *B. melitensis* shed the organisms in milk. Clinical signs of brucellosis in camels are very rare.

Disease in humans :

The incubation period is 2-3 weeks. The disease usually manifests itself as an acute febrile illness which may persist and progress to a chronic disease with severe complications. Human brucellosis has a wide spectrum of clinical manifestations. Although brucellosis in humans is rarely fatal, it can be severely debilitating and disabling. The disease is characterized by an intermittent or remittent fever accompanied by malaise, anorexia and prostration, sweats, fatigue, weight loss, headache, arthralgia and back pain. Untreated disease may persist for weeks or months. If untreated, the pattern of the fever waxes and wanes over several days ("undulant fever"). The acute phase may progress to a chronic one with relapse, development of persistent localized infection or a non-specific syndrome resembling the "chronic fatigue syndrome".

Bone and joint complications are the most frequent complications of brucellosis, occurring in upto 40% of cases. Gastrointestinal complications include nausea, vomiting, and abdominal discomfort. Rare cases of ileitis, colitis and spontaneous bacterial peritonitis have been reported. Hepatobiliary complications include epithelioid granulomas of liver and hepatic necrosis. Respiratory tract complications include hilar and paratracheal lymphadenopathy, interstitial pneumonitis, bronchopneumonia, lung nodules, pleural effusions, and empyema. Genitourinary complications include orchitis and epididymitis which are the most frequent genitourinary complications of brucellosis in men. In women, rare cases of pelvic abscesses and salpingitis have been reported. Cardiovascular complications include infective endocarditis which is most common cause of death from brucellosis. Neurological complications include neurobrucellosis which refers to a variety of neurological complications associated with brucellosis. Cutaneous complications include a variety of skin lesions like rashes, nodules, papules, erythema nodosum, petechiae, and purpura. Ophthalmic complications are uncommon, however, a variety of ocular lesions have been reported in patients with brucellosis. Childhood brucellosis once considered rare in children, it is now recognized that brucellosis can affect persons of all ages, especially in areas where *B. melitensis* is the predominant species.

Diagnosis in animals :

Intradermal test:

The test using a standardized antigen preparation such as Brucellin INRA or Brucellergene OCB, can be used for monitoring the status of herds in brucellosis-free areas. It is sensitive and specific but false positive reactions can occur in vaccinated animals.

Smear examination:

Diagnosis in animals can be made on the basis of smear examination using placental cotyledon, vaginal discharge or fetal stomach contents.

Cultural examination:

Brucella can be readily isolated in the period following an infected abortion or calving, but isolation can also be attempted post-mortem. *Brucella* is excreted in large numbers at parturition and can be cultured from a range of material including vaginal mucus, placenta, fetal stomach contents and milk using suitable selective media.

Serological examination:

Rose Bengal plate test (RBT) is a simple spot agglutination test where drops of stained antigen and serum are mixed on a plate and any resulting agglutination signifies a positive reaction. The test is an excellent screening test but may be oversensitive for diagnosis in individual animals, particularly vaccinated ones. The ELISA tests offer excellent sensitivity and specificity. Complement fixation test (CFT) is highly sensitive and specific but the method is complex to perform requiring good laboratory facilities and trained staff. The milk ring test (MRT) is a simple and effective method, but can only be used with cow's milk. The ELISA may be used to test bulk milk and is extremely sensitive and specific, enabling the detection of single infected animals in large herds in most circumstances.

Diagnosis in humans :

Culture:

In acute brucellosis, isolation of *Brucella* from blood or other tissues is definitive. Culture is often negative, especially in long-standing disease.

Serology:

It is the most commonly used diagnostic method. The important tests for serological diagnosis are RBT, tube agglutination and ELISA.

Disease management in animals :

Animal brucellosis is best prevented by careful herd management and hygiene. Bovine brucellosis has been eradicated from most industrialized countries such as in Finland, Norway, Sweden, Denmark, Germany, Australia, and Netherland (Acha and Szyfers, 2001). The following measures can be adopted for management of animal brucellosis-

Farm hygiene and sanitation:

The goal in the application of hygiene methods to the control of brucellosis is reduction of exposure of susceptible animals. Aborted fetuses, placenta and contaminated litter should be collected in leak-proof containers and disposed of preferably by incineration or deep burial using quicklime. Any area in which an abortion or infected parturition has occurred should be washed down with an approved disinfectant such as hypochlorite, iodophor or phenolic.

Restricted movement:

This may be regarded as an aspect of hygiene. However, it is essential in any programme to limit the spread of brucellosis. Unauthorized sale or movement of animals from an infected area to other areas should be forbidden.

Prevention of contact:

Replacement animals should be carefully selected. These, whether purchased or produced from existing stock, should originate from *Brucella*-free herds or flocks. Pre-purchase tests are necessary unless the replacements are from populations in geographically circumscribed areas that are known to be free of the disease. Purchased replacements should be isolated for at least 30 days. In addition a serological test prior to commingling is necessary.

Test and isolation/slaughter:

There are no pathognomonic signs of brucellosis in animals at individual level; the occurrence of abortion storms in naive herds/flocks is usually a strong indicator of infection. The immediate slaughter of test-positive animals is expensive and requires animal owner cooperation.

Mass vaccination:

B. abortus strains 19 and RB 51 are recommended for prevention of bovine brucellosis. *B. melitensis* Rev 1 is recommended for prevention of *B. melitensis* infections in sheep and goats.

Treatment:

Treatment has been used in animals of special breeding value, but because of the uncertain outcome it is not generally recommended.

Surveillance:

Human cases may be a useful indicator of the presence of disease in animal populations and may be the only source of information for surveillance. Herds and flocks should be included in surveillance measures such as periodic milk ring tests in cattle (at least four times per year), and testing of slaughtered animals with simple screening serological procedures such as the RBT.

Disease management in humans :

The most rational approach for preventing human brucellosis is the control and elimination of the diseases in animal reservoir and health education of the public working at high risk area (Dubie *et al*., 2014). Moreover, the prevention of human brucellosis is also based on occupational and food hygiene. The following measures can be adopted for management of human brucellosis-

Personal hygiene:

All persons carrying out high-risk procedures, which includes contact with animals suffering from or suspected of having brucellosis, should wear adequate protective clothing. This includes an overall or coat, rubber or plastic apron, rubber gloves and boots and eye protection.

Occupational hygiene:

It is important in preventing the disease in farmers, stockmen, shepherds, goatherds, abattoir workers, butchers, dairymen, artificial inseminators, veterinarians and those involved in the processing of viscera, hides, wool and skins. Farm workers and animal attendants in particular, should wear adequate protective clothing when contact with infected animals This is particularly important when dealing with animals that are aborting or giving birth, when the shedding of *Brucella* organisms will reach maximum levels.

Public health education:

It should emphasize food hygiene and occupational hygiene. Special precautions should be taken by laboratory workers. Physicians and health workers should be aware of the possibility of brucellosis.

Heat treatment of foods:

All dairy products should be prepared from heat-treated milk. Consumption of raw milk or products made from raw milk should be avoided. Meat should be adequately cooked.

Vaccination:

Two live attenuated vaccine strains have been employed extensively in heavily infected areas. *B. abortus* strain 19-BA was used from 1952 onwards in the former USSR. In China, the live attenuated strain *B. abortus* 104M has been used.

Treatment:

Lack of appropriate therapy during the acute phases may result in localization of Brucella in various tissues and organs and lead to sub acute or chronic disease which is very hard to treat (Mantur and Mangalgi, 2007). Antibiotic

treatment should be implemented at as early a stage as possible, even in patients who appear to be showing a spontaneous improvement. Tetracycline (500 mg every six hours, orally) should be administered for at least six weeks. Doxycycline is given in a dose of 100 mg twice daily orally for a period of six weeks.

Conclusion :

Brucellosis in humans is transmitted from animals and products derived from them. Therefore, the effort should be made for effective prevention, control or eradication of disease in animal populations. An effective surveillance system, based on the collaboration between the human and animal health services, is a prerequisite for brucellosis control or eradication programme. There is need of development of diagnostic tools having high sensitivity and specificity. There should be regular epidemiological surveillance of brucellosis in the animal populations. It is also needed to establish optimum treatment regimens and local and international control programmes of brucellosis.

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