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Brucellosis: A Highly Infectious Foodborne Zoonotic disease of Public health concern

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Foodborne zoonosis is defined as an infectious disease, which is caused by the ingestion of contaminated food from animal sources. The impact of foodborne zoonoses on human health is not well studied in many nations. Currently, over 32,0000 cases of foodborne zoonoses are reported every year from European Union. In India, about 70% of foodborne diseases are resulted due to consumption of livestock products. There are many foodborne bacterial zoonoses, such as aeromoniais, brucellosis, campylobacteriosis, *Escherichia coli* 0157:H7 infection, listeriosis, *Mycobacterium bovis* infection, salmonellosis, *Vibrio parahaemolyticus* infection, and yersiniosis, which are reported from developing as well as developed countries of the world. Among this, brucellosis (Cyprus fever, Gibraltar fever, Malta fever, Mediterranean fever) is a highly infectious re-emerging bacterial zoonosis, which remains an important economic and public health problem in many regions of the world. The disease affects both humans as well as many species of animals. Globally, over 50,0000 human cases of brucellosis are reported annually. Disease is endemic in bovine population causing a financial loss of US Dollar 344 billion to the livestock industry. It is estimated that annual losses from bovine brucellosis in Latin America is approximately US$ 600 million. Many countries such as, Australia, Austria, Belgium, Bulgaria, Canada, Denmark, Finland, France, Germany, Great Britain, Hungary, New Zealand, Norway, Rumania, Sweden, Switzerland, and United States are considered free of bovine brucellosis. Disease still remains an uncontrolled problem in many regions, such as Africa, Central Asia, Mediterranean, Caribbean, Middle East, and Latin America. Brucellosis in humans occurs in sporadic and epidemic form, both sexes, in all age groups, and rural and urban settings. Earlier studies have indicated that *Brucella* infection is commonly encountered in males aged between 20 to 50 years from rural areas. Disease is reported from more than 100 countries of the world including India. The seasonal character of brucellosis in Mediterranean region revealed maximum cases in May-June and minimum in winter months with consumption of untreated milk products as the chief mode of transmission. The epidemiology of disease is complex as many animals act as reservoir of infections. Hence, emphasis is given to undertake systematic and comprehensive studies on the epidemiology of brucellosis. Human brucellosis can be prevented by controlling the infection in animals. Adequate pasteurization of milk and dairy products and wearing of protective clothing are important safety measures where the disease is endemic.

Brucellosis in humans in mainly caused by *Brucella abortus, Brucella melitensis* and *B. suis*. However, most human cases worldwide are caused by *B. melitensis*. The genus *Brucella* was named in honour of Sir David Bruce who isolated the organism from the spleen of a patient during an investigation of a fatal disease outbreak affecting British soldiers on the island of Malta. The organism is Gram negative, pleomorphic,

coccobacillary, intracellular, non-motile, and non-spore forming. It is sensitive to many disinfectants, such as hypochlorite, iodophores, 70 % ethanol, formaldehyde and phenol; and also destroyed with moist heat at 121˚C for 15 minutes. The organisms are killed by heat under pasteurization conditions. It is pertinent to record that nearly all strains of *Brucella* are susceptible to broad spectrum antibiotics like gentamicin, tetracycline and rifampicin. In addition, many strains are also susceptible to ampicillin, chloramphenicol, erythromycin, kanamycin, streptomycin, and trimethoprim. However, the sensitivity to various antibiotics may differ among species, biovars, and even strains. Recent molecular studies based on 16s-rRNA gene sequence indicated that species *B. melitensis* includes 5 biovars namely, *abortus, canis, neotomae, ovis*, *and suis*.

Brucellosis in humans is transmitted through direct contact with diseased animals and their discharges, ingestion of raw milk, unpasteurized dairy products, like soft cheeses, yoghurts and ice cream prepared from unpasteurized milk and uncooked meat, raw animal products (bone marrow from reindeer, liver from goat) from infected animals and inhalation. Rarely, infection can also occur via blood transfusion, tissue transplantation and sexual contact. Consumption of unpasteurized milk was attributed in 67 % of the cases. Persons travelling to disease endemic areas, and ingesting raw milk, non-pasteurized dairy products and undercooked infected meat are at major risk of acquiring *Brucella* infections. Brucellosis is recognized as an occupational hazard to animal handlers, butchers, abattoir workers, veterinarians, shepherds, dairy farmers, reindeer herders, food processing plant employees, hunters, and laboratory personnel. It is important to mention that *Brucella* organisms are responsible for up to 2 % of all laboratory acquired infections. Most cases of brucellosis in Mexico are attributed to the consumption of infected raw milk and unpasteurized cheese from goat and cows. The author diagnosed a small epidemic of brucellosis where four persons from a poor family of the Indian village were affected. All the four patients were male young adults who drunk infected raw goat milk. One investigation from Germany described high incidence of brucellosis among Turkish Migrants who acquired infection by eating unpasteurized cheese. In Saudi Arabia, ingestion of raw milk from goat, sheep, and camel resulted many cases of brucellosis in humans. An outbreak of human brucellosis during 2012 to 2013 was reported on Jeju Island of South Korea due to consumption of raw materials of fetal calf. Based on several studies, brucellosis may be recognized as travel associated foodborne zoonosis.

Brucellosis is a multi-systemic disease in human as it can affect almost all organs and systems. Disease may present with a broad spectrum of clinical manifestations, such as fever, fatigue, malaise, chills, sweats, headache, anorexia, weakness, myalgia, arthalgia, weight loss, abdominal pain, nausea, vomiting, diarrhea, constipation, insomnia, colitis, ileitis, cough, bronchitis, pneumonia, epistaxis, jaundice, hepatomegaly, splenomegaly, lymphadenopathy and orchitis. In some cases, only joint pain, low back ache, involuntary movements of limbs, burning feet or ischemic heart attacks are observed. Certain complications like spondylitis, osteomyelitis, endocarditis and meningoencephalalitis are also recorded. Earlier studies reported weakness and fever in over 90 % of the cases; and more than 70 % of cases showed chills, sweating and anorexia.

The symptoms in human brucellosis are not specific and therefore, laboratory help is mandatory to make an unequivocal diagnosis of disease. The isolation of bacterium from clinical specimens of patient is the gold standard of diagnosis. Cultural isolation of *Brucella* is tedious, hazardous and hence requires high security laboratory with level 3 bio-safety facility. A battery of tests, such as Rose Bengal plate test (RBPT), standard tube agglutination test (STAT), complement fixation test (CFT), enzyme linked immunosorbant assay (ELISA), polymerase chain reaction (PCR) and fluorescence polarization assay (FPA) are used for diagnosis of disease. RBPT was originally employed for screening of animals for *Brucella* infections; however, it is now used for the diagnosis of human brucellosis. Brucellosis should be differentiated from other diseases, such as typhoid fever, influenza, malaria, Kala azar, rheumatic fever, leptospirosis, tuberculosis and tularaemia. It is important to mention that all cases of pyrexia of unknown origin (PUO) should be investigated for *Brucella* infections.

The standard treatment for adult acute brucellosis requires a combination therapy of doxycycline (200 mg/day orally) and rifampicin (600 - 900 mg/day orally) for 6 weeks, or the combination of doxycycline (100 mg twice/day orally for 6 weeks) with streptomycin (1 g/day intramuscularly for 2-3 weeks) or a combination of doxycycline (100 mg twice/day orally for 6 weeks) plus parenteral administration of gentamicin (5 mg/kg body weight for 7 days). In mild case, tetracycline at the dosage rate of 500 mg/12 hourly orally for two weeks showed satisfactory results. The patients with complications, such as spondylitis, osteomyelitis, endocarditis and meninigoencephalitis may require prolonged therapy for at least 8 weeks. Acute phase may progress to chronic one with relapse. In order to prevent relapse, it is imperative that the patient must take complete course of medication. Prognosis of disease is good if an early treatment is taken. In untreated patients, fatality may reach 1 to 5 %. There is need to undertake further clinical trial to establish the optimal therapy for brucellosis during pregnancy.

Certain measures, such as ingestion of boiled milk, pasteurized dairy products and cooked meat, use of protective clothing by high risk groups, active surveillance of *Brucella* infection, control of disease in animals and educational programme of public to increase awareness about zoonotic importance of brucellosis are suggested to mitigate the incidence of this widely prevalent bacterial disease. Although a number of vaccines are employed for immunization of animals, hitherto, no suitable vaccine against human brucellosis is available. Therefore, sincere attempts should be made to develop safe, potent and low cost vaccine, which can be afforded by poor resource nations to immunize the high risk groups against brucellosis.

It is advised that persons travelling to endemic areas should not consume raw milk, unpasteurized dairy products, uncooked meat, raw liver and raw sea foods. Currently, no vaccine is commercially available to immunize humans and therefore, sincere efforts are required to control and eradicate brucellosis in animals, which are the major source of human infections. There is a need to strength interventional polices to diminish the socioeconomic impact of human brucellosis, especially in developing nations of the world. It is recommended that Rose Bengal plate test should be widely used as rapid screening tool for diagnosing *Brucella* infection in humans at primary health centers of rural areas where good laboratory facilities due to financial constraints are not available. As zoonoses are primarily animal diseases, it is therefore, very pertinent that medical students must be taught about zoonoses in syllabus so that they become more aware about the impact of animal diseases on human health.