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Brucellosis: Prevalence and Diagnosis

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Introduction

Brucellosis or Bang's disease was first described during Crimean War and Dr. David Bruce identified the causative bacterium for the first time in 1887. Several bacterial species such as *B.abortus*, *B.melitensis*, *B.suis*, *B.neotomae*, *B.ovis* and *B. canis* under the genus Brucella infect various animal species generically termed as brucellosis. Brucella species are Gram-negative, coccobacilli or short rods, aerobic, partially acid-fast, and facultative intracellular bacteria. It is zoonotic, *B.melitensis* is the most common species that infect humans. However, other Brucella species can also infect humans. This disease is also famous by name "Mediterranean fever" or "Malta fever" and "undulant fever" in humans.

Global and national prevalence of the brucellosis

The disease is prevalent in many countries around the world including India. In India, the disease is endemic in nature. In humans, from <0.01 to >200 per 100,000 population is affected with brucellosis. In India, the true prevalence of human brucellosis is not precisely known due to the lack of proper surveillance, but the disease is highly prevalent among people associated with animal and animal products. The reported prevalence rate varies between 0.8 and 26%. However, it reflects the only tip of the iceberg due to the lack of proper surveillance and diagnosis.

Susceptible animals

Different biovars of *B.abortus* are responsible for brucellosis in cattle. However, other species such as *B.melitensis* and *B. suis* can also infect cattle occasionally. Three biovars of *B.melitensis* are responsible for brucellosis in sheep and goats. Sheep and goats are rarely

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infected by *B.abortus* and *B.suis*. Moreover, most species of Brucella can infect other ruminants, equines, camels, dogs, wild animals, and marine mammals.

Transmission and spread of infection

Animal to animal contact with aborted fetus and placenta containing Brucella organism is a major route in transmission to susceptible animals. Animals also get infected by ingestion of organisms through the contaminated pasture, feed, and water. The infected animals excrete Brucella organisms in colostrum and milk, which act as a source of infection to young animals.In addition, skin contamination, inhalation, conjunctival inoculation, and udder inoculation from infected milking cups are other routes of disease transmission. With regard to sexual transmission, artificial insemination plays a major role, if semen from an infected bull is used in cattle. In swine and dogs, however, sexual transmission is a major route in disease spread.

Humans

The infection in humans is transmitted through direct or indirect contact with infected animals. Infected animals excrete Brucella organisms in the aborted fetus, placenta, milk, uterine/vaginal discharges, and semen, which act as sources of infection to humans. Consumption of raw milk and milk products from infected animals is also a major route in disease transmission. In addition, infected meat products also play an important role. Aerosol transmission through inhalation of Brucella contaminated dust particles has been reported in the literature. The infection is rarely transmitted sexually or through blood transfusion and tissue transplantation. Humans are considered to be the dead-end host for Brucella infection. In the laboratory, accidental ingestion, mucosal or skin contact, and inhalation while handling the Brucella cultures are possible ways of transmission of infection to laboratory workers.

Symptoms of brucellosis animals

Cattle: Abortions from 5 to 9 months of pregnancy, placentitis, retention of placenta, orchitis, epididymitis, infertility in both sexes, arthritis, with excretion of organisms in the milk, and uterine discharges are reported in cattle. The udder will remain infected permanently with Brucella organisms.

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Sheep and Goats: Abortion is reported in the last two months of gestation and is sporadic. Other symptoms are retention of the placenta, mastitis, and decreased milk production. Epididymitis, orchitis, and reduced fertility in males (common in sheep) are also reported.

Dogs: The disease is subacute to chronic. Abortion in mid to late gestation (45–59 days) and then brown-to-yellow vaginal discharge without any foul smell for 1–6 weeks, stillbirth, weak pups, infertility, diskospondylitis, neurological dysfunction, lameness, and muscle weakness are clinical manifestations in dogs. In males, symptoms are like brucellosis in other male animal species.

Pigs: Abortion between 50 and 110 days of gestation, infertility, arthritis, spondylitis, lameness, and posterior paralysis are some of the clinical symptoms exhibited by pigs. Both male and female may recover from the infection but remain carriers for rest of the life.

Horses: Swelling of the neck or back is a classical sign of brucellosis and is known as fistulous withers or poll evil. In pregnant mares, abortion or birth of weak foals is another symptom.

Humans: The disease has an incubation period varying from 2- 3 weeks to months. Symptoms include acute to subacute fever, which is intermittent or irregular, headache, general body pain, chills, arthralgia, prostration, central nervous system abnormalities, profuse sweating, testicular pain/epididymal-orchitis, weight loss, and weakness. Infection of organs leading to enlargement of liver, spleen, and lymph nodes may also occur.

Complications of brucellosis in humans

Osteoarticular: Up to 40% of human cases may have bone and joint involvement. Other complications include bursitis, sacroiliitis, osteomyelitis, peripheral arthritis, spondylitis, and tenosynovitis.

Gastrointestinal: It resembles typhoid fever and patients may show nausea, abdominal pain, and discomfort.

Hepatobiliary: Brucella species commonly infect the liver. However, liver function tests remain normal. Histologically it shows epithelioid granulomas and lesions like that of sarcoidosis.

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Respiratory: Bronchopneumonia, paratracheal lymphadenopathy, interstitial pneumonitis, nodules in the lungs, empyema, and pleural effusions have been reported due to aerosol infection by Brucella.Pregnancy and breastfeeding: In pregnant women, the infection may lead to abortion in the early trimester of intrauterine transmission of infection to the fetus. Infection transmission through breastfeeding is rarely reported.

Cardiovascular: Brucella infection causes infective endocarditis and is the most common cause of death in humans due to brucellosis. It mainly affects the aortic valve than the mitral valve.

Neurological: About 5% of B. melitensis infection causes acute or chronic CNS complications like meningoencephalitis or meningitis due to direct entry into the CNS system.

Samples to be collected for laboratory diagnosis

Animals

For bacterial isolation, aborted fetal stomach content, vaginal discharge, blood, milk (10-20 mL from each teat), hygroma fluids, and lymph nodes samples are collected from suspected animals. For serological diagnosis, serum and milk are preferred and shipped to the diagnostic laboratories under the cold chain.

Humans

Blood, wound, swabs, bone marrow aspirates, cerebrospinal fluid, and pus samples are preferred for bacterial isolation and serum samples for immunological diagnosis.

Diagnosis of brucella infection

Animals

Isolation and identification of organism: Different types of commercial dehydrated basal media such as tryptose (or trypticase) soy agar (TSA), blood agar, Columbia agar, serum dextrose, and glycerol dextrose agar can be used for isolation purposes.

Molecular identification: There are several PCR based assays described for identification and differentiation for Brucella species, however, most of these assays have not been validated appropriately.

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Serological tests: Serum agglutination test (SAT), Rose Bengal Plate Test (RBPT) and the buffered plate agglutination test (BPAT), enzyme-linked immunosorbent assays (Indirect & Competitive ELISA), and fluorescence polarization assay (FPA) are employed in the serological diagnosis.

Humans

In humans, due to a wide variety of symptoms, the disease is diagnosed by isolation of organisms and detection of antibodies by serological tests. Blood samples are most often used for isolation. To improve isolation from blood, concentration and lysis of leukocytes are preferred. The same culture media described above are suitable for bacterial isolation. Serologically, the disease can be diagnosed by serum (tube) agglutination test, RBPT, ELISA (to detect IgM or IgG), Coombs antiglobulin, and CFT.