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Bovine Tuberculosis: A public health concern

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Abstract

Bovine tuberculosis is a chronic bacterial zoonotic infection caused by *Mycobacterium tuberculosis* complex, primarily by *Mycobacterium bovis.* It is listed in the WHAO Terrestrial Animal Health Code. The disease is contagious in nature and can be transmitted by direct contact with the infected animal or by indirect contact with the contaminated materials. Bovine milk is the main source of infection for man. The disease progress slowly and takes months/ years to become fatal. Infected animal sheds the organism before the appearance of the clinical signs. The disease takes a more severe form in children and immunocompromised patients. Though cattle are considered as the major host for bovine tuberculosis, the disease has been reported from other animals as well. The common clinical signs of the disease include weakness, loss of appetite, fever, dyspnoea and intermittent hacking cough, enlarged lymph node, diarrhoea, subcutaneous nodule etc. The disease can be diagnosed by tuberculin test, meat inspection, IFN- Gamma Release Assay, ELISA, Mycobacterial culture, histopathology and molecular diagnosis. Controlling bovine T.B is a tedious job and requires contribution from all stakeholders.

Introduction

Tuberculosis is one of the world's most brutal infectious diseases listed in the World Organization for Animal Health (OIE) Terrestrial Animal Health Code. Tuberculosis is known as one of the major causes of morbidity and mortality throughout the globe. It is being neglected in both developed and third world countries (Kochi 1991). Albeit, global actions have dwindled the number of T.B. cases and saved many lives. Yet, it still remains a subject of concern in Africa, Asia, the Middle East and Latin American including Mexico. Despite the fact that the disease pose serious threats in developing countries, regional foci can also be traced in USA, Australia and several European countries (Murai *et al.*, 2019).

Robert Koch made the remarkable discovery of tubercle bacillus *Mycobacterium tuberculosis*, the causative agent of human T.B. in 1882 (Koch., 1882). The name 'tuberculosis' comes from a Latin word for 'nodule' or 'tubercle' which occurs in the lymph node and other organs of the affected individual. In 1898, Smith came up with discovery of *Mycobacterium bovis*, a bacillus responsible for

causing T.B. in various species (Smith, 1898). *Mycobacterium bovis* can cause the disease tuberculosis in human beings, this having zoonotic potential. The majority of cases in human can be attributed to Mycobacterium tuberculosis; however, few cases are caused by Mycobacterium bovis (Brahma *et al.*, 2019). 5-10% or more of human cases in various countries and less than 2% cases in developed nations are caused by *Mycobacterium bovis*.

Mycobacterium species

Mycobacterium bovis forms Mycobacterium tuberculosis complex (MBTC) along with *Mycobacterium tuberculosis, Mycobacterium caprae, Mycobacterium microti, Mycobacterium africanum, Mycobacterium canetti, Mycobacterium pinnipedii, Mycobacterium bovis* BCG, *Mycobacterium leprae* and the very recently discovered *Mycobacterium mungi* (Egbe *et al*., 2017). Pathogenesis of Mycobacteria can be attributed to its thick cell wall which contains a complex hydrophobic lipid. The core of the cell wall is made up of three attached molecules, i.e., peptidoglycan, arabinogalactan and mycolic acide that together constitute mycolylarabinogalactan, a peptidoglycan complex. The said complex is underneath a sheet of glycolipids buildup of several constituents like cord factor, mycosides, wax D, sulfatides and sulfolipid. This complex imparts some special features to the bacillus like acid fastness, able to form granuloma, ability to grow on lipid media (due to aggregation of complex lipids), impermeable to chemical agents and development of resistance to disinfecting agents, immune system of host and antitubercular drugs (Jaouad, 1993; Charles *et al.*, 2006; Kuria, 2019)

The survival of the organism in the environment depends on the amount of sunlight, environmental temperature, humidity and concentration of the organism. In cold, dark and moist conditions, it can persist up to several months (Broughan *et al.*, 2016). The organism perishes within weeks on exposure to high environmental temperature, sunlight and dry conditions. They die at temperature of 65oC or above for 30 mins. They can also be killed by UV light (McCallan *et al.*, 2014). Quaternary ammonium compounds like hexachlorophene and chlorhexidine have shown bacteriostatic effect while bactericidal effect on M. Bovis is shown by formaldehyde vapor, 70% ethanol, chlorine compounds, hydrogen peroxide, 5% phenol and alkaline glutaldehyde (Kuria, 2019).

Risk factors and transmission of *Mycobacterium* bovis

It is more common in children who consume unpasteurized milk. Mortality rates are high in immune compromised patients. Cattles though regarded as the true host of *M. Bovis*, the organism have also been isolated from buffaloes, bisons, white tailed deers, wild boars and other domestic and wild animals. Therefore, extensive interfaces amongst different groups pave the way for transmission of *M. Bovis*, making it a significant risk factor (Krajewska-Wedzina *et al*., 2020)

Risk factors can be categorized into four groups:

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(A) Animal associated risk factors: genetics, sex, breed, age, nutritional status, reproductive status, milk yield and behavioral factors, etc

(B) Herd level risk factors: herd type, herd size, farm management, farm area, contact with neighboring herds, cattle movement, etc.

(C) Environmental risk factors: weather, soil type, source of water, presence of invertebrates and birds.

(D) Wildlife Reservoir: Wild Boar, Badgers and Deer (Brougham *et al*., 2016)

Studies have demonstrated that *Acanthamoeba castellanii*, a protozoon that harbours *M. Bovis* facilitates its transmission by extending the survival of the tubercle bacillus in the soil (Taylor *et al.*, 2003). Tuberculosis associated with M. bovis affect lungs, lymph nodes and other parts of the body. *Mycobacterium tuberculosis* infection is occupational in nature. People engaged in cattle, bison or cervids husbandry, dairy farm workers, abattoir workers, butchers, veterinary personnel, zoo staff are at greatest risk of acquiring the infection. Several ways of transmission is clanged to the spread of *M. bovis* infection. Direct contact is one major route as the load of organism is high in exhaled droplets, saliva, milk, urine, faeces, discharge from open peripheral lymph nodes, etc. Ingestion can follow through inhalation, ingestion of contaminated feed, etc. Consumption of raw, contaminated and unpasteurised milk can lead to infection with *M. bovis*. The infection can be easily transmitted from man to man through cough or sneeze (Mukundan *et al*., 2015; Constable *et al.*, 2016; Domingo *et al.*, 2014).

Immunopathogenesis

Once inside the body, Mycobacteria are phagocytosed by macrophages which through the lining of bronchioles get entry into the circulation and are carried to lymph nodes, the parenchyma of lungs and other sites of predilections. The bacillus has the inherent capacity to escape the killing process of macrophages due to lipoarabinomannan and mycobacterial proteins of the antigen 85 complexes. The bacteria that have escaped phagocytosis by macrophages survive and multiply within the phagosomes and destroy them (Charles *et al.*, 2006). Following initial infection, the Mycobacteria travels through the lymphatic capillary vessels to the draining lymph nodes, where they develop new infection foci (Domingo *et al.*, 2014).

Caseonecrotic granuloma, the hallmark of tuberculosis is body's attempt to localize the infection and to let the inflammatory and immune mechanisms kill the bacteria and known as tubercle. ESAT-6, the virulence factor secreted by Mycobacteia facilitates the formation of granuloma by direct action (Osman *et al.*, 2022).

Symptoms

TB usually lasts for a protracted period and takes months or years for symptoms to appear. The clinical presentations of the *M. bovis* infections are fluctuating fever, malaise, night sweats, large

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prominent lymph node and weight loss. Symptoms of the disease depend on the system of the body that is affected. If the organism gets lodged in the lungs, it will present intermittent hacking cough, chest pain, hemoptysis or respiratory distress. On the other hand, gastrointestinal diseases will manifest abdominal pain and diarrhoea. Cervical lymphadenopathy is a common feature in children. Cutaneous lesion may appear as papule, ulcer or suppurative lesion; reddish brown gradually enlarged subcutaneous nodule or a vegetative lesion that resembles a tumour. Fatality may result if cases do not receive proper treatment at proper time. It leads to economic loss in livestock resulting from death, diseases, lost productivity and trade restrictions. Oral routes effect cervical and mesenteric nodes while aerogenous infection causes pulmonary TB. Immunosuppressive individual which HIV/AIDS and those receiving corticosteroids are at greater risk (Ayele *et al*., 2004).

Diagnosis

TB can be diagnosed by:

(a) Tuberculin test
(b) Meat inspection
(c) IFN-Gamma Release Assay (IGRA)
(d) ELISA
(e) Mycobacterial culture
(f) Histopathology
(g) Molecular diagnosis

Management and Control:

As per WHO, the most important strategy in reducing the incidence of TB in high risked communities is by curing with DOTS (Directly Observed Treatment Short Course). The five main commitment of DOTS include Government commitment, case detection by sputum spear microscopy, standardized treatment regimen for a duration of six to nine months, drug supply and recording and reporting of treatment results.

Unpasteurized milk and dairy products are the major source of *M. Bovis* infection to man. Milk should be pasteurized to a sufficient temperature for a definite period of time. While purchasing dairy products, ensure that the word ‘pasteurized’ is listed on the label. People at risk of contracting disease should seek medical attention for any symptoms resembling TB. People living in endemic areas should be administered with BCG vaccine containing an attenuated strain of *M. bovis.* The BCG vaccine provides protection against both *Mycobacterium tuberculosis* and *Mycobacterium bovis* infection.

Complete eradication of bovine tuberculosis is challenging due to breakdowns, non-visible reactors, presence of wildlife reservoirs and large herds (Constable *et al.,* 2016). Disease eradication programme of *Mycobacterium bovis* infection in animals include regular disinfection, meat inspection (formation of granuloma), intensive surveillance, on farm visit, testing (tuberculin skin test) and

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removal of infected and in contact animals (Waters *et al.*, 2015)

Conclusion

Although many countries have curbed *M. bovis* infection toba great extent, but the total elimination has not been achieved due to consistent presence of the infection in wild animals such as Badgers, white tailed deer, brush tailed possum etc. So, effort should be put to control the disease in wilds so that it's influence over domesticated animals as well as humans can be contained. Therapeutic and preventive measures have to be equally implicated to all living forms likely to get infected, in order to make the world TB free. Eradication of TB is a tedious job and requires one health approach. Albeit, with all the stakeholders coming together and acting for the cause, we can definitely end TB in near future.

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