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Zoonotic Tuberculosis: Developing Countries Scenario on Epidemiology and Management

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Abstract: Bovine tuberculosis has been widely distributed throughout the world and it has been a cause for the great economic loss in animal production and productivity in developing countries in particular. In a large number of countries, bovine tuberculosis is a major infectious disease among cattle, other domesticated animals and certain wildlife reservoirs. Transmission to humans constitutes a public health problem and conditions such as the culture of consuming raw milk, keeping cattle in close proximity to the owner house and immune suppressive disease can exacerbate the disease. Bovine tuberculosis is characterized by the formation of granulomas in tissue especially the lungs, lymph nodes, liver, intestines and kidneys. Infection in cattle is usually diagnosed in the live animal on the basis of delayed hypersensitivity reactions, necropsy, histopathological and bacteriological techniques. Rapid nucleic acid methodologies, such as the polymerase chain reaction, may also be used although these are demanding techniques and should only be used when appropriately validated. Due to the grave consequences of Mycobacterium bovis infection on animal and human health, it is necessary to introduce proper food hygiene practices and stronger inter-sectorial collaboration between the environmental, medical and veterinary professions is vital to the control of the disease.

Key words: Bovine Tuberculosis · Developing Countries · Epidemiology · Management

INTRODUCTION

Tuberculosis is recognized as one of the most important threats to human and animal health causing mortality, morbidity and economic losses [1]. It remains a major global health problem among millions of peoples each year and ranks the second leading cause of death from an infectious disease worldwide after Acquired Immune Deficiency Syndrome disease [2].

The genus Mycobacterium is characterized phenotypically as non-motile, non-capsular, non-spore forming, obligate aerobic, thin rod usually straight or slightly curved having 1-10 µm length and 0.2-0.6 µm width, facultative intracellular microbe and has a slow generation time about 15-20 hours. Its cell wall is rich in lipids (Mycolic acid) that provide it the thick waxy coat which is responsible for acid fastness and hydrophobicity. This waxy coat (Mycolic acid) is also greatly contributing to the bacterium resistance to many disinfectants, common laboratory stains, antibiotics and physical injuries [2].

In developing countries, the socio-economic situation and low standard living area for both animals and humans are more contributing to bovine tuberculosis transmission between human to cattle or vice versa [3]. Human infection due to *M. bovis* is thought to be mainly through drinking of contaminated or unpasteurized raw milk and undercooked meat. The high prevalence of TB in cattle, close contact of cattle and humans, the habit of raw milk and meat consumption and the increasing prevalence of HIV may all increase the potential for transmission of *M. bovis* and other Mycobacterium between cattle and humans [4].

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Even if bovine tuberculosis represents a potential health hazard to both animal and human populations in terms of health and economics, only little is done particularly in developing countries on the epidemiology of this disease and the epidemiological requirements for its control. Therefore current review aimed to compile and provide updated epidemiological data which is a basis to adopt the control measures against the diseases in bovine as well as humans.

Epidemiology of Zoonotic Tuberculosis: The disease affects cattle throughout the globe, but some countries have been able to reduce or limit the incidence of the disease through the process of 'test and cull' of the cattle stock. Most of Europe and several Caribbean countries are virtually free of M. bovis. Bovine tuberculosis is endemic to many developing countries particularly African countries [5]. Mycobacterium Bovis combines one of the widest host ranges of all pathogens with a complex epidemiological pattern, which involves the interaction of infection among human beings, domestic animals and wild animals [6].

Source of Infection and Mode of Transmission: Cattle serve as the principal reservoir of M. bovis and human can be infected with M. bovis where cattle are reared for milk production [7]. Organisms are excreted in the exhaled air, nasal discharge, milk, urine, vaginal and uterine discharges and discharges from open peripheral lymph nodes. Animals with gross lesions that communicate with airways, skin or intestinal lumen are obvious disseminators of infection. In the early stages of the disease, before any lesions are visible, cattle may also exert viable mycobacterium in nasal and tracheal mucus. In experimentally infected cattle excretion of the organism commences about 90 days after infection [8].

Inter-human transmission of M. bovis is possible, but few cases have been confirmed [9]. Close contact between animals (Example: intensive farming practice, water points, salt licks, market places, transports, auctions) contributes to the effective spread of M. bovis. Ingestion of contaminated products (Example: carcasses of prey, pastures and water) is considered as a secondary way to spread the disease in cattle [10] however, it is an important pathway in the introduction of wildlife. There are three routes of infection with M. bovis in human hosts: ingestion, inhalation or direct contact with mucous membranes and skin abrasions. The contribution of humans as a source of M. bovis infection to cattle is insignificant compared to the much more prevalent reservoirs of infection in cattle, badgers and other animal populations [11].

Possible Risk Factors: The smallholders and intensive production systems, in particular, meet their target for milk and milk products produced through the introduction of exotic breeds. However, in contrast, this introduction of exotic and cross-bred cattle, into the central highlands of Ethiopia, in particular, has created conducive environment for the spread that puts the people, most notably those who drink raw milk, under the risk of bovine tuberculosis infection [12]. Susceptibility to M. bovis may be as well enhanced in cattle infected with immunosuppressive viruses such as bovine viral diarrhea or immunodeficiency viruses [13].

The causative organism is moderately resistant to heat, desiccation and many disinfectants. It is readily destroyed by direct sunlight unless it is in a moist environment. In warm, moist, protected positions, it may remain viable for weeks [13]. The success of tubercle bacilli as pathogens comes mainly from its ability to persist in the host for long periods and cause disease by overcoming host immune responses. Nevertheless, the possibility of surviving for long periods in the environment is explained by the Mycobacterial impermeable cell wall and slow growth. In contrast, other features render these species more sensitive to environmental survival, like more enhanced pH sensitivity [14].

Consumption of raw or soured milk is mainly practiced in some parts of the world, approximately 90% of the total volume of milk produced in sub-Saharan Africa is consumed fresh or soured and only a very small proportion follows official marketing channels [15]. Professional occupation involving workers such as abattoir personnel, veterinarians and laboratory technicians, animals caretaker in zoos and those who are working in animal reservations and at national parks can also acquire the infection due to the course of their regular work [4].

Pathogenesis and Clinical Manifestations: Tuberculosis spreads through the body in two stages, the primary complex and post-primary dissemination. The primary complex consists of the lesion of the point of entry and local lymph node. Post-primary dissemination from the primary complex may take the form of acute miliary tuberculosis, discrete nodular lesion in various organs or chronic organ tuberculosis [16].

The macrophages are the primary host cell for intracellular growth M. bovis following infection [17]. The gradual accumulation of macrophages in the lesion and the formation of macrophage in the lesion and the formation granulomatous response lead to the developments of tubercle. The characteristic lesion caused by M. bovis in cattle is described as having a center of caseous necrosis, usually with some of the calcification, with boundaries of epithelioid cells, some of which form the multinucleated giant cell and a few to numerous lymphocyte and neutrophils. In cattle lesion most frequently occurs in lymphatic tissue of the thoracic cavity, usually the bronchial and mediastinal lymph node. Lymph node of the head region is the second most frequent site and in many instances lesion in a retropharyngeal and sub-maxillary lymph nodes in the absence of detectable lung lesion. Less frequently lesions are found in both regions simultaneously [18].

Tuberculosis is a chronic disease which occurs in cattle with no symptom at an early stage. However, in a later stage, there is a capricious appetite and fluctuating temperature commonly associated with the disease. The hair coat may be rough or sleek. Affected animals tend to become more docile and sluggish but the eyes remain bright and alert [16].

In chronic stages animal become emaciated and develop acute respiratory distress, cough occurs once or twice at a time and is common during the morning and cold weather. Involvement of the digestive tract is manifested by intermittent diarrhea and constipation. In an advanced case, air passage, digestive tract and blood vessels become obstructed because of the enlarged lymph node. Tuberculosis mastitis is of major importance because of danger to public health [8].

In humans, tuberculosis due to M. bovis is indistinguishable from that due to M. tuberculosis in terms of clinical signs, radiological and pathological features. Pulmonary tuberculosis may result in cough, dyspnea and respiratory distress. Extra pulmonary tuberculosis may lead to various clinical signs, depending on which organs are affected. Enlarged lymph nodes may obstruct air passages, the alimentary tract or blood vessels. Cervical lymphadenitis (Scrofula) is typically found in milk-borne tuberculosis infection in humans and is characterized by visually enlarged lymph nodes of the head and neck, which can sometimes rupture and drain. In developing countries, tuberculous lymphadenitis is one of the most frequent causes of lymphadenopathy and the most common form of extra pulmonary tuberculosis [19].

Diagnostic Modalities: Because of the chronic nature of the disease and the multiplicity of signs caused by the variable localization of the infection, bovine tuberculosis is difficult to diagnose on clinical examination [20]. Enlarged superficial lymph nodes provide a useful diagnostic sign when lungs are extensively involved; there is commonly an intermittent cough. The principal sign of tuberculosis is commonly chronic wasting or emaciation that occurs despite good nutrition and care [21].

Humans and animals with bovine tuberculosis develop an immune response, which can be detected by the tuberculin skin test and further diagnostic methods are necessary to confirm the presence of bovine tuberculosis. In humans, these tests include chest x-rays and sputum cultures. For animals, the comparative cervical tuberculin test, serological tests, post mortem examinations and other laboratory procedures are used [22]. This allows for better separation of in vitro blood test responses leading to greater test accuracy. In serological study gamma interferon assay and the lymphocyte proliferation assay measure cellular immunity, while the ELISA measures humoral immunity [23].

With the advance of a molecular diagnosis, various PCR methods in diverse clinical specimens have been introduced to identify M. bovis more easily and quickly. PCR has several advantages over culture, including confirmation of the presence of M. bovis within 1 to 3 days as compared to 6 weeks with conventional culture techniques. Additional advantages of PCR over conventional methods include its high sensitivity, performance in few hours and depending on the assay design, ability to differentiate between Mycobacterium tuberculosis complex and Mycobacterial species other than tuberculosis and identification of gene mutations associated with drug resistance [24].

Management of Zoonotic Tuberculosis: The basic strategies required for control and elimination of bovine tuberculosis are well known and well defined. However, because of financial constraints, scarcity of trained professionals, lack of political will, as well as the underestimation of the importance of zoonotic tuberculosis in both the animal and public health sectors by national governments and donor agencies, control measures are not applied or are applied inadequately in most developing countries. Cattle should be treated at all and as such farm animals with tuberculosis must be slaughtered (Culled) [25].

Testing of cattle with intra-dermal tuberculosis test and by inspection at slaughter, combined with removal or quarantine of infected herds and pasteurization of milk, has proven very effective in reducing the incidence of M. bovis infection in humans. Elimination is complicated by the several wildlife reservoirs of M. bovis present in most countries of the world. However, the practical elimination of human infection can be achieved with a control program targeting only domestic animals. Milk should be pasteurized or effectively treated with heat prior to human consumption or further processing, as this is the generally agreed critical and effective control measure to prevent transmission of zoonotic tuberculosis through milk. Farmers and other occupationally at-risk individuals should be required to adopt appropriate measures to minimize exposure of employees and farm visitors to infections that can be transmitted to humans from animals [2].

Public Health Implication: Human tuberculosis is usually underestimated or underdiagnosed because of no clinical, radiological and histopathological differential of tuberculosis caused by M. tuberculosis and M. bovis [26]. M. bovis is not the major cause of human tuberculosis but infects human too by either consuming raw milk, meat, their product from infected animals or by inhaling infective droplet [27].

Human tuberculosis caused by M. bovis is unusual in countries in the developed world, due to the implementation of eradication programs for domesticated animals, accounting for 1% of tuberculosis infections. In developing world, M. bovis is responsible for 5-10% of human tuberculosis cases but this varies between countries [28]. The current increasing incidence of tuberculosis in humans, particularly in immune compromised persons, has given a renewed interest in the zoonotic importance of M. bovis, especially in developing countries [29].

The human form of M. bovis infection has similar clinical forms as that caused by M. tuberculosis [30]. Following ingestion of the organism, the primary infection in the intestine may heal, it may progress in the intestines, or it may disseminate to other organs. Cervical lymphadenopathy which primarily affects the tonsillar and pre-auricular lymph node was once a very common form of tuberculosis in children that took infected milk [31]. Though animals with tuberculosis pose some risk to humans, this risk is extremely remote in developed countries due to the introduction of milk pasteurization and effective bovine tuberculosis control program [4]. In contrast, spread from animals to humans in developing countries remains a very real danger, mostly from infected milk [7].

Status of Bovine Tuberculosis in Ethiopia: Study done in and around Addis Ababa indicated that there was a corresponding increase in the prevalence of bovine tuberculosis as herd size increased, thus the prevalence of bovine tuberculosis was 4.6, 6.4 and 10.5% for small, medium and large herd size respectively. Asseged *et al.* [32] also indicated that bovine tuberculosis is a disease of overcrowding. Thus, when the number of animals in a herd increases, the transmission of the bacillus is promoted. Animals with no grazing are at a higher risk of infection than those kept on free grazing and mixed grazing. The prevalence of bovine tuberculosis is higher in Holstein, Cross [HFxZebu] and Begait cattle than pure Zebu breed. Fewer reactor animals have been recorded in the younger age groups (3.5%) and reactivity to the CIDT test increased with age, up to six years of age adult (9.1%) [33] after which it declined old (6.8%).

It is possible that the infection may not become established in young animals but, as they get older, their chance of acquiring infection also increases, due to the increased time of exposure. Infection of cattle with M. bovis constitutes a human health hazard as well as an animal welfare problem. Furthermore, the economic implications in terms of trade restrictions and productivity losses have direct and indirect implications for human health and the food supply [34]. A comprehensive investigation of bovine tuberculosis in Ethiopia showed a widespread distribution of the disease at an average prevalence of approximately 5% [34].

Recently, studies have indicated that the individual level prevalence of bovine tuberculosis via comparative intradermal tuberculin test as reported by Mekibeb *et al.* [35] and Haimanot *et al.* [36] was 8.14% in Afar region, North Eastern Ethiopia and 5.5% in Wollega zone, Western Ethiopia respectively. Accordingly, 2.9% of overall prevalence was reported by a study carried out at Elfora export abattoir and Bishoftu municipal abattoir in Ethiopia [37].

CONCLUSIONS AND FUTURE CONSIDERATION

In developed countries, significant progress has been made in controlling and eradicating the disease in cattle primarily via test and slaughter strategies and in humans via improved hygiene practices and pasteurization of milk. However, eradication programs in developing countries are constrained by the presence of endemic infection in wildlife reservoir hosts with implications for food security and trade restriction. In the absence of effective surveillance and control strategies, Bovine tuberculosis continues to be a major public health problem, especially in countries where the prevalence of infection in cattle is high, consumption of raw milk products is common and malnutrition and other immune depressive conditions exacerbate the danger of the infection. From successful experience in many developed countries, it can be concluded that Bovine tuberculosis can be controlled only when there is a strong political and producer support, an appropriate legal framework to enforce control measures and active participation of all concerned in finding practical and affordable control options that are suitable for each country, this provides an ideal policy for the One Health approach. Educating the people about the risk of the disease transmission through consumption of raw/undercooked meat and unpasteurized milk; and the public health implication, route of reverse zoonosis are of extreme importance for effective implementation of Bovine tuberculosis control measures.

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