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Review on the Epidemiology, Public Health and Economic Importance of Bovine Tuberculosis

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Abstract
Bovine tuberculosis has been widely distributed throughout the world and it has been a cause for great economic loss in animal production and productivity. 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 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 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 rigorous control measures to reduce the risk of the disease in human and animal populations. The introduction of proper food hygiene practices and stronger inter sectorial collaboration between the medical and veterinary professions is vital to the control of the disease. Since it is chronic bacterial disease which requires a rigorous and lengthy anti-bacterial treatment which is costly to treat, prevention of the disease is better than curing the diseased one.
Keywords: Bovine Tuberculosis, Epidemiology, Public health important**.**

1. Introduction

Tuberculosis is recognized as one of the most important threat to human and animal health causing mortality, morbidity and economic losses (Smith, 2006). It remains a major global health problem and cause health among millions of peoples each year and ranks as second leading cause of death from an infectious disease worldwide after Acquired Immune Deficiency Syndrome disease (WHO, 2014).

The genus mycobacterium is characterized phenotypically as non-motile, non-capsular, non-spore forming, obligate aerobic, thin rod usually straight or slightly curved having 1-10μm length and 0.2-0.6μm 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 for the bacterium resistance to many disinfectants, common laboratory stains, antibiotics and physical injuries. It probably also contributes to the slow growth rate of some species by restricting the uptake of nutrients (Quinn *et al.,* 1999).

In developing countries the socio economic situation and low standard living area for both animals and humans are more contributing in bovine tuberculosis transmission between human to human and human to cattle or vice versa (Ameni *et al.,* 2010). Human infection due to *M. bovis* is thought to be mainly through drinking of contaminated or unpasteurized raw milk and under cooked 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 Mycobacteria between cattle and humans (Shitaye *et al*. 2007).

Even if bovine tuberculosis represents a potential health hazard to both animal and human populations interms of health and economics, *M. bovis* infection remains largely uninvestigated, its epidemiology and public health significance remains largely unknown and has not received much attention like human tuberculosis. As a result, current review will be helpful to provide useful epidemiological data and a basis to adopt the control measures against the diseases in bovine as well as humans.

Therefore, the objectives of this review paper are: to compile the available literature on the epidemiology, zoonotic and economic importance of bovine tuberculosis and highlight some possible approaches for bovine tuberculosis control and prevention as a basis for designing further effective control strategies.

2. General Aspect of Mycobacterium

Mycobacterium tuberculosis complex consists of *Mycobacterium africanum, Mycobacterium bovis, Mycobacterium Canetti, Mycobacterium microti, mycrobacterium BCG, mycrobacterium caprae Mycobacterium* *tuberculosis (*Quinn *et al.,* 2002). Characteristics used to define mycobacteria were the absence of motility, the morphology of the bacilli (slightly curved and rod-shaped), and the characteristic resistance to acid-alcohol following coloration with phenicated fuchsin (Ziehl-Neelsen stain) (Lehman and Neuman, 1896). Mycobacterium species grows on medium containing serum, potato and egg. The most commonly used media are Lowenstein-Jensen (LJ) that contains egg, glycerol, asparagine, mineral salt and malachite green and stone brinks medium. *M. bovis* grows more slowly than *M. tuberculosis,* which needs more than 8 weeks to appear on primary culture and the optimal growth temperature is 37^0C (Simons *et al.,* 2011).

3. Epidemiology of Bovine Tuberculosis

The disease affects cattle throughout the globe, but some countries have been able to reduce or limit the incidence of the disease through 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 (Abubakar *et al.,* 2011). *Mycobacterium bovis* combines one of the widest host ranges of all pathogens with a complex epidemiological pattern, which involves interaction of infection among human beings, domestic animals and wild animals (Gemechu *et al.,* 2013). However, only little is done particularly in developing countries on the epidemiology of this disease and the epidemiological requirements for its control (Ali, 2006).

3.1. 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 (Girmay *et al.,* 2012). 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 (Radostits *et al.,* 2000). Inter-human transmission of *M. bovis* is possible, but few cases have been confirmed (Acha and Szyfres, 2001). 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 (Manzies and Neill 2000), however it is an important pathway in introduction of wildlife (wie *et al*., 2004). There are three routes of infection with *M. bovis* in human hosts: ingestion, inhalation or direct contact with mucous membranes and skin abrasions. 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 (Rua-Domenech, 2006).

3.2. Risk factors

The small holders and intensive production systems in particular meet their target for milk and milk products production 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 a conducive environment for the spread of BTB that puts the people, most notably those who drink raw milk, under the risk of bovine tuberculosis infection(Ameni *et al.,* 2003b). Susceptibility to *M. bovis* may be as well enhanced in cattle infected with immunosuppressive viruses such as bovine viral diarrhea or immunodeficiency viruses (Rua-Domenech, 2006).
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 (Srivastava *et al.,* 2008). 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 (Flynn and Chan, 2001). 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 a more enhanced pH sensitivity. Bovine tuberculosis can be controlled and eliminated from a country or region by implementing the test and slaughter policy (Kremer, 2005). However, because of financial constraints, scarcity of trained man power as well as the under estimation of the importance of bovine tuberculosis by national governments and donor agencies, control measures are not applied or are applied inadequately in most developing countries (Cosivi *et al.,* 1998). 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 (Tamiru *et al.,* 2013). 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 course of their regular work (Shitaye *et al.,*2007).

3.3. Pathogenesis

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 military tuberculosis, discrete nodular lesion in various organ or chronic organ tuberculosis (Radostits *et al*., 2007).

The macrophage are the primary host cell for intracellular growth *mycobacterium bovis* following an infection (Pollock *et al.,* 2006). 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 (Quinn *et al*., 2002). The characteristic lesion caused by *mycobacterium bovis* in cattle is described as having a center of caseous necrosis, usually with some of calcification, with boundaries of epithelioid cells, some of which form multi nucleated giant cell and a few to numerous lymphocyte and neutrophils. In cattle lesion most frequently occur in lymphatic tissue of the thoracic cavity, usually the bronchial and mediastinal lymph node. Lymph node of head region are the second most frequent site and in many instances lesion in retropharyngeal and sub maxillary lymph node in the absence of detectable lung lesion. Less frequently lesions are found in both region simultaneously (Neill *et a*l., 1994).

3.4. Clinical finding

Tuberculosis is chronic disease occurs in cattle with no symptom at early stage. However in later stage there is a capricious appetite and fluctuating temperature are 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 (Radostits *et al.,* 2007).

In chronic stages animal become emaciated and develop acute respiratory distress, cough occurs once or twice at a time and is common during morning and cold weather. Involvement of digestive tract is manifested by intermittent diarrhea and constipation. In advanced case, air passage, digestive tract and blood vessel become obstructed because of enlarged lymph node. Tuberculosis mastitis is major importance because of danger to public health (Radostits *et al.,* 2000).

In humans, tuberculosis due to *M. bovis* is indistinguishable from that due to *M. tuberculosis* in terms of clinical signs, radiological and pathological features (Ayele *et al.,* 2004). Pulmonary TB 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 (Davis and Danker, 2000). In developing countries, tuberculous lymphadenitis is one of the most frequent causes of lymphadenopathy and the most common form of extra pulmonary tuberculosis. In terminal stages of bovine tuberculosis, extreme emaciation and weakness may occur (Nishi *et al.,* 2006).

3.5. Diagnosis of bovine tuberculosis

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 (Tsegaye *et al.,* 2010). 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 (Smith *et al.,* 2006).

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 (Cousins and Florisson, 2005). 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 (Legesse *et al.,* 2012).

With the advance of 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 (Palomino *et al.,* 2007).

3.6. Prevention and control

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 under estimation 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 (Cosivi *et al.,* 1998). Cattle should not be treated at all and as such farm animals with tuberculosis must be slaughtered (culled) (Krauss *et al.,* 2003).

Testing of cattle with an intradermal 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, practical elimination of human infection can be achieved with a control programme targeting only domestic animals. (Morris *et al.,* 1994). 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 (WHO, 2014).

4. Public Health Significance

Human tuberculosis is usually under estimated or under diagnosed because of no clinical, radiological and histopathological differential of tuberculosis caused by *M. tuberculosis* and *M. bovis* (Perez-Lago *et al.,* 2013). *M. bovis* is not the major cause of human tuberculosis but infect human too by either consuming raw milk, meat, their product from infected animals or by inhaling infective droplet (Malama *et al.,* 2013).

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 (Pal *et al.,* 2014 ;). In the developing world, *M. bovis* is responsible for 5-10% of human tuberculosis cases but this varies between countries (Parmar *et al.,* 2014).

The current increasing incidence of tuberculosis in humans, particularly in immune compromised persons, has given a renewed interest in the zoonotic importance of *Mycobacterium bovis*, especially in developing countries (Pal, 2007).

The human form of *M. bovis* infection has similar clinical forms as that caused by *M. tuberculosis* (Ofukwu, 2006). 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 (Pullock *et al.,* 2006). Though animals with tuberculosis pose some risk to humans, this risk is extremely remote in developed countries due to introduction of milk pasteurization and effective bovine tuberculosis control program (Shitaye *et al.,* 2006). In contrast, spread from animals to humans in developing countries remains a very real danger, mostly from infected milk (Gemechu *et al.,* 2013).

5. Economic Significance of Bovine Tuberculosis

Bovine tuberculosis has great importance regarding the economy of livestock industry because it can infect the human population due to its zoonotic nature, therefore it is an important public health issue (O`Reilly and Daborn, 1995). The disease decreases livestock productivity and may be economically devastating for the cattle industry, especially the dairy sector, milk yields and draft power can be significantly reduced, with direct effects on the livelihoods of poor livestock holders (Asseged *et al.,* 2004). Most important is the impact of infection in humans particularly women and children, who appear to be more susceptible to the disease in countries with poor socio-economic conditions and weak veterinary and public health services. Although estimates of the costs associated with bovine tuberculosis and its control refer only to specific countries, all data suggest that worldwide economic losses due to the disease are significant. These losses include those related to mortality, animal production, markets and trade restriction, carcass condemnation, losses of tourism, as well as the costs of implementing surveillance and control programs (Zinsstag *et al.,* 2006).

In Argentina, the annual loss due to bovine tuberculosis is approximately 63 million USD (Ashford, 2001). The socio-economic impact of bovine tuberculosis to the agriculture and health sector in Turkey has been estimated between 15 and 59 million USD per year (cosivi *et al*., 1998). Even in some industrialized countries, where bovine tuberculosis has been eradicated by expensive schemes for control, eradication and compensation for farmers, the disease still has a major economic impact, mainly due to the existence of permanent wildlife reservoirs that reduces the efficiency of control strategies. In the United Kingdom, where badger and other wildlife such as deer remain an important source of infection for livestock, approximately 100 million pound is spent annually in efforts to control the disease (Mathews *et al*, 2006). In Africa, the economic losses associated with livestock infected with bovine tuberculosis have not been examined sufficiently, or have not been studied at all (Ayele *et al*., 2004). For the public health sector, WHO estimates total tuberculosis control costs in Ethiopia of USD 14.2 million per year and USD 129 per patient (WHO, 2004).

6. Status of Bovine Tuberculosis

6.1. Global status

The global prevalence of human tuberculosis due to *M. bovis* has been estimated at 3.1% of all human tuberculosis cases, accounting for respectively 2.1 and 9.4 % of pulmonary and extra pulmonary tuberculosis case. Human tuberculosis due to *M. bovis* in developing countries today is analogous to condition in 1930s and 1940s in Europe, where more than 50% of cervical lymphadenitis case in children where due to *M. bovis* (Cosivi *et al.,* 2013). Eradication programs based on test-and-slaughter policies to clear herds of infected animals virtually eliminated tuberculosis from livestock in many developed countries. However, the maintenance of *M. bovis* infection by wildlife species has compromise eradication efforts in countries such as in the United Kingdom, Ireland, New Zealand and parts of the United States of America (Thoen *et al.,* 2009).

6.2. Ethiopian status

Study done in and around Addis Ababa indicated that there was 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.,*2000) 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%) (Sisay *et al.,* 2013), 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 (Awah-Ndukum *et al.*, 2012).

A comprehensive investigation on bovine tuberculosis in Ethiopia showed a wide spread distribution of the disease at an average prevalence of approximately 5% (Mekibeb *et al.,* 2013). Recently, studies has indicated that the individual level prevalence of bovine tuberculosis via comparative intradermal tuberculin test as reported by (Haimanot *et al*., 2016) and (Sintayehu *et al*., 2016) 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 study carried out at Elfora export abattoir and Bishoftu municipal abattoir in Ethiopia (Wagari, 2016).

7. Conclusions and Recommendations

Bovine tuberculosis is caused by a group of closely related acid fast bacilli forming the Mycobacterium tuberculosis complex specifically *M .bovis*, which has great tendency to infect human and other animals due to its wide host range. The BTB is a chronic and progressive disease with cosmopolitan distribution. 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 some 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 TB 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 TB 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 and each epidemiological context. This provides an ideal policy for the One Health approach, which can be operationalized through adapted approaches for improving surveillance and meat inspection, enhancing community awareness, promoting milk pasteurization at the community level, and strengthening inter sectorial collaboration.

Based on the above review, the following recommendations are forwarded;

- ✓ Educating the people about the risk of BTB transmission through consumption of raw/under cooked meat and unpasteurized milk; and the public health implication, route of reverse zoonosis are of extreme importance for effective implementation of TB control measures.
- ✓ There should be a co-operation between human as well as veterinary health care professionals which will ultimately help in assessment of the risk factors there by paving the way to the eradication of bovine tuberculosis.
- ✓ Based on a proper strategy, regular tuberculin skin testing should be continued in large with significant efforts in all animal production systems nationwide. It is equally important to take strict control and

quarantine measures during the importation of animals and animal products.

- ✓ Creating awareness among the people, to meet the standard hygienic requirement and to improve husbandry practices is of paramount importance.
- ✓ Bio-security measures should be followed on farm at different level which helps in decreasing the interaction between domestic animals and wild life animals.

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