REVIEW ON BOVINE TUBERCULOSIS AND ITS PUBLIC IMPORTANCE

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SUMMARY: Tuberculosis is primarily transmitted from infected animals to humans through close contact and the ingestion of raw animal products, especially unpasteurized milk from diseased animals. While Mycobacterium bovis predominantly affects members of the Bovidae family, it can also infect humans. Bovine tuberculosis (bTB) is a zoonotic disease that incurs significant economic burdens due to costly eradication programs and complicates the movement of animals and their products. This chronic infectious disease is characterized by the formation of granulomas in various tissues, particularly the lungs, lymph nodes, liver, intestines, and kidneys. The main etiological agent, *Mycobacterium bovis*, is an acid-fast bacterium distinguished by the presence of mycolic acid in its cell wall. Transmission occurs through both aerogenous and enterogenous routes. Although *M. bovis* is not the primary cause of human tuberculosis, it still poses a threat to human health through the consumption of raw milk, meat, and other products from infected animals or via inhalation of infectious droplets. In Ethiopia, bovine tuberculosis is endemic, with transmission primarily occurring through the ingestion of unpasteurized contaminated milk and contact with infected animals. The disease is associated with the development of miliary tubercular lesions, chronic cough, obstructions of air passages, and enlargement of lymph nodes. The objective of this review is to highlight the significance of tuberculosis as a critical bacterial disease affecting both humans and animals worldwide, with a particular focus on its complex and multi-species nature, including bovine, avian, and human TB.
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1. INTRODUCTION

1.1. Background

Tuberculosis (TB) is an infectious disease caused by the bacillus *Mycobacterium tuberculosis* (M.tb). It is the most dangerous bacterial infection responsible for severe increase in death cases. The tubercle bacillus was discovered by Robert Koch in 1882. There are several reports indicating that tuberculosis (TB) is an age old dreadful disease even from ancient times. The disease was called "consumption" in the past because of the way it would consume from within anyone who became infected. Tuberculosis is a chronic granulomatous infectious disease. Infection occurs via aerosol, and inhalation of a few droplets containing M. tuberculosis bacilli. After infection, M. tuberculosis pathogenesis occurs in two stages. The first stage is an asymptomatic state that can persist for many years in the host, called latent TB (Kaufman, 2014.)

The burden of TB is highest in Asia and Africa. In 2011, largest number of cases was reported from India, China, South Africa, Indonesia and Pakistan. India and China alone accounted for 26% and 12% of global cases, respectively. Of the 8.7 million TB incident cases reported in 2011, about 1.2 million people are also suffering from HIV. In the African region, 39% of TB cases were estimated to be coinfected with HIV (Kaufman, 2014). Most cases of TB are caused by M. Tuberculosis and the reservoir of infection is humans with active TB. Most cases of TB are pulmonary and acquired by person to person transmission of air-borne droplets of organisms. Oropharyngeal and intestinal TB contracted by drinking dairy milk contaminated with *M. Bovis* rarely seen nowadays and usually in countries with tuberculosis dairy cows and unpasteurized milk (Hachart*et al.*, 2016).

Tuberculosis is a common disease prevalent throughout the world.Prevalence data on BTB infection in Africa is scarce .There is, however, sufficient evidence to indicate that disease is widely distributed in almost all African countries and even is found at high prevalence in some animal populations (Ayele *et al.*, 2004). However, in the tropical countries including Ethiopia, BTB has been found to affect a higher proportion of exotic breeds than local zebus (Ameni,2006). Thus BTB is still a great concern in many developing countries and Ethiopia is one of those where BTB is considered as prevalent disease in cattle populations. Its zoonotic implication has also significantly indicated an increasing trend to be of public health hazards (Regassa, 2005). Therefore this seminar paper is prepared with the following objective.

1.2. Objective

- To review Bovine Tuberculosis and the Public health importance of the disease

2. OVERVIEW OF BOVINE TUBERCULOSIS

2.1. Etiology

Genus mycobacterium is characterized phenotypically as non-motile, no capsular, non-spore forming, obligate aerobic, thin rod usually straight or slightly curved having 1-10 μm length and 0.2 - 0.6 μm widths, 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 (Birhanu *et al.,* 2015).

Mycobacterium bovis is the main etiological agent of bTB. It is found that *M. bovis* best survive in frozen tissue and there is adverse effects of tissue preservative i.e. sodium tetra borate on viability (Verma*et al.,* 2014). In the environment *M. bovis* can survive for various months especially in cold as well as dark and conditions which is moist. The survival period varies from 18 - 332 days at 12˚C - 24˚C (54˚F - 75˚F) which is dependent of sunlight exposure. From soil or grazing pasture there is infrequent isolation of this organism. It has been found that culture of the organism can be done for approximately twoyears in samples that are stored artificially. The viability of the organism has been found more recently to be between 4 - 8 weeks in 80% shade whereas it can get destroyed in either summer or winter on New Zealand pastures (Birhanu,*et al.,* 2015; Verma*et al.,* 2014).

2.2. Sources of Infection and Ways of Transmission

Bovine Tuberculosis can be transmitted in various ways. For instance in air that is exhaled; sputum and urine, feces as well as pus the bacteria can spread. Either direct contact or contact with infected animal excreta, aerosol inhalation can spread the disease that depends on the involvement of the species (Phillips*et al.,* 2008) .The common mode of transmission is inhalation or ingestion. Aerogenous or inhalation: it is mainly by droplet infection, inhalation of dust contaminated by sputum, faces, urine of infected animals. Thus close housing and overcrowding along with improper management predisposes to the disease. Zebu (Brahman) type cattle are thought to be much more resistant to tuberculosis than European cattle. The dynamics of *M. bovis* transmission from an effective disseminator tuberculous animal to susceptible hosts are currently not clearly identified and are meagerly understood. Though, infection is principally confined to the respiratory system as bacteria aim to establish the infection within the lung. Infected cattle are considered as possible source of infection as they shed significant amount of *M. bovis* through droplet nuclei in to the environmental and may act as source of intra- herd transmission (Van rhijn*et al.,* 1998; Raviglionn*et al.,* 2011).

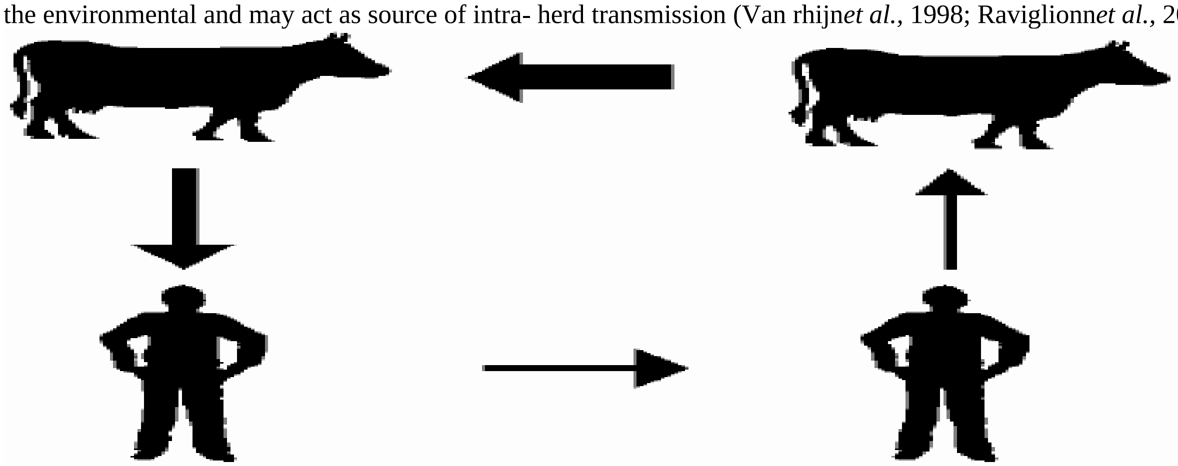

Figure 1: Cycle of M. bovis transmission between cattle and humans

Primarily, tuberculosis is a respiratory disease and is transmitted through mainly by air born route within and between species during close contact (Phillips *et al.,* 2008). In case of enterogenous route or ingestion through buccal mucosa, pharyngeal mucosa and intestinal mucosa the organism may enter into the animal body. It is also through the congenital route but is less common mode of acquiring infection (Radostits *et al.*, 2008).The infected bull may also transmit disease or through artificial insemination with the use of infected semen (Phillips *et al.*, 2008).The *M. bovis* is transmitted from animal to man through ingestion of unpasteurized dairy product, milk of infected cattle and undercooked meat which was recognized as a major public health problem (Phillips *et al.*, 2000).

2.3 Clinical Signs

Mycobacterium bovis is considered to be a slow growing microbe with a doubling time of around sixteen hours. This may account for why the host which is infected could take months to show the effects of the infection. TB caused by this strain of Mycobacterium can cause different symptoms depending on where the infection is taking place. If the infection is in the GI tract for example a main symptoms is extreme abominable discomfort, an infection in the lungs causes an almost uncontrollable cough. It is has been believed that the symptoms can be more closely related to the genome of this strain than the species. Mycobacterium all produces mycolic acids in their cell walls. These acids could cause the symptoms seen from the infection of *M. bovis*(Koehler *et al.*, 2010.) When present, clinical signs can include variable pyrexia, weakness, anorexia, emaciation, dyspnea, enlargement of lymph nodes and coughing, particularly with advanced TB. These signs are not unique to bovineTB. Although normally a chronic debilitating disease, bovine TB can assume a more acute, rapidly progressive course (Raghvendra*et al.*, 2010; Peters, D., 2010).

2.3.1. In animal

Bovine TB is a chronic debilitating disease, and signs may be lacking, or vary when present. Clinical signs of tuberculosis include weight loss and mild respiratory signs. Early in the course of the disease, affected animals exhibit a deep, moist-sounding, chronic cough. As the disease progresses, tachypnea, dyspnea, and abnormal lung sounddevelop (Radostits*et al*., 2007; Raviglione*et al*., 2011). Bovine tuberculosis should be considered in cases of chronic loss of condition and appetite, reduced milk yieldand debilitating disease with or without respiratory signs (Matthews, 2016).

Figure 2: Picture shows clinical sin of bTB in Animal

2.3.2. In humans

M.bovis is a chronic debilitating disease that occurs in humans. No symptoms occur in the early stage of the disease that is asymptomatic. However, in the late stage, there is progressive emaciation, a mild fluctuating fever, weakness, and in-appetence. When infection is present in the lung then dyspnea, moist cough, or tachypnea may occur a capricious appetite and fluctuating temperature are commonly associated with the disease (Riccardo *et al.*, 2014; Romha*et al.*, 2013).

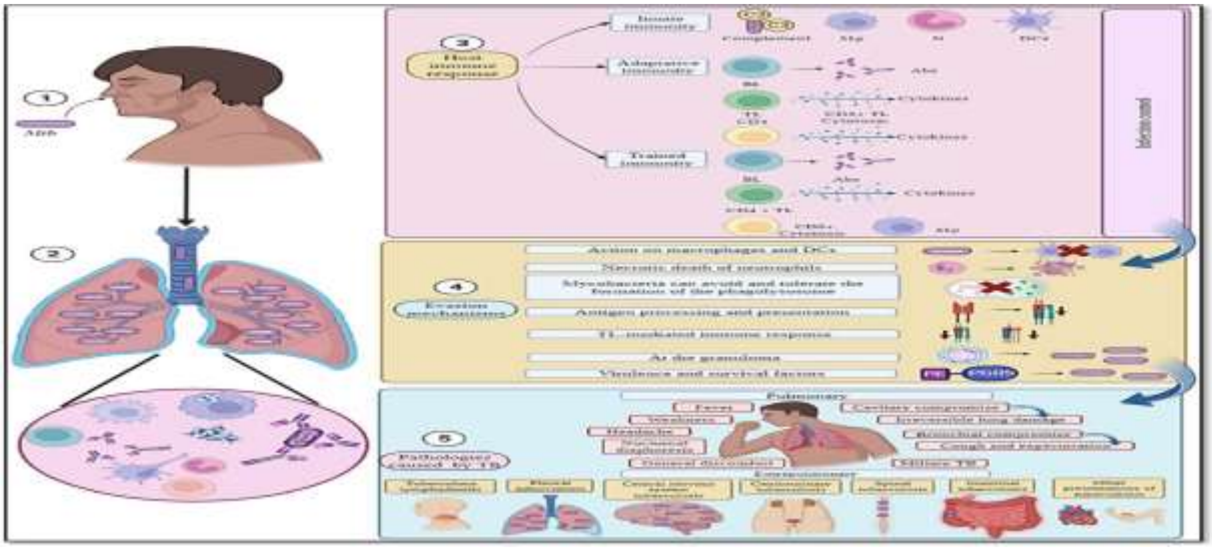

Figure 3: Picture shows clinical sin of bTB in human

2.4. Risk Factors

Tuberculosis has been considered as a disease of poverty so, lack of basic health Services, malnutrition, social disruption, low awareness to diseases and cause of all contribute to the dissemination of TB and its impact in the community (Ratu, 2022). The observed increase in TB incidence in sub-Saharan Africa may have resulted from several of these risk factors (Liu *et al*., 2015). Risk factors contributing to difficulties in controlling bovine tuberculosis in cattle across continents can have their origin at farm-level, e.g. cattle breed, age, behavior and nutrition of animals. However, host independent factors are considered more important in most case include, amongst others, production types, management practices, environmental variables, anthropogenic variables and seasonality. Cattle movement, existence of a wildlife reservoir and possibly strain related differences are of additional significance. Tuberculosis in wildlife can also pose difficulties for bovine tuberculosis eradication (O' Brien *et al*., 2023).

Sub Saharan Africa, which is home to more than half of the world' s cattle population, has been the hardest hit for various reasons. Firstly, in most African countries cattle are used to show economic status in the society and secondly they serve as the main source of income for many farmers. Moreover, countries in Africa are yet to fully implement the TS policy; this is mainly because of the lack of financial commitment on the part of governments to compensate farmers with infected animals (Asante-Poku *et al*., 2023). So far, different studies have indicated a critical knowledge gaps and the associated risky practice towards BTB in Ethiopia .In fact, educational effort among young in Ethiopia were reserved to addressing human to human transmissions (Kidane *et al*., 2015).

2.4.1. Demography, socio-economic status and feeding habits

From the total population of Ethiopia, about 85% of the people are engaged in agriculture. To this effect, very close contact with potentially infected animals may be high, which eventually leads to exposure of the BTB infection. For the urban residents, milk is considered as the main source of BTB infection, while abattoir workers and farmers are predominantly exposed to the aerosol infection as a result of close contact with infected animals (Shitaye *et al*., 2007). The major factors among which contribute to the acquisition of the infection in both urban and rural populations are family ownership of cattle, previous livestock ownership, sharing of the house with animals, consumption of non-pasteurized milk (raw milk) or poorly cooked meat (Asebe and Gudina, 2018). All these causalities and/or habits are the daily practices most notably of rural communities in Ethiopia. In particular, milk borne infection is the main cause of non-pulmonary tuberculosis in areas where bTB is common and uncontrolled (Kwaghe *et al*., 2016).

Professional occupation or workers such as, abattoir workers, veterinarians and laboratory technicians, animal care taker in zoos and those who are working in animals reservations and at national parks can also acquire the infection in due course of regular work (Kwaghe *et al*., 2016). Furthermore demographic factors, such as income, education, age, number of family, number of individuals dwelling per m2 and sanitation etc are also contributing to the epidemiology of BTB (Azeez, 2021). Families with low income often face malnutrition which, when associated with the burden of HIV/AIDS infection, increases susceptibility to various infectious diseases such as tuberculosis by the impaired immune system, in particular the lymphocyte function which plays an important role in containing mycobacterial infections (Kilale *et al*., 2022). Moreover, reports indicated that infants are more vulnerable to food-

borne *M. bovis* infection, whereas older individuals averting BTB may occur as a result of endogenous reactivation (Hadi, 2022).
2.4. 2. Wild Life Reservoirs Role
In Africa a high prevalence of TBC was reported in monkeys (Rosenbaum *et al*., 2015), in buffaloes (Dwyer *et al*., 2020) and deer (Schöning *et al*., 2013). Recent reports in South Africa indicated that there were four outbreaks of BTB in the buffaloes during the years 1996 to 2003. In addition to this, the disease has been prevalent in an Eastern province of South Africa in the 1930s and there are strong indications that greater kudu act as maintenance hosts (Arnot and Michel, 2020), Despite this, kudu have been the source of *M. bovis* infection in one wildlife reserve in Kwazulu-Natal in a group of bTB-free African buffaloes (Michel and van Helden, 2019). So far, to our knowledge, no bTB cases have been reported in Ethiopia in the wildlife population (Kemal *et al*., 2019). However, the presence of the aforementioned animals in different wildlife reserves and even in free ranging forests may have an epidemiological role in the spread of the disease among other wild and domestic animal species. Moreover, (Mohamed, 2020) suggested that the widely distributed Rock hyrax (Procaviacapensis) might also be a possible reservoir of bTB in Ethiopia.

2.5. Epidemiology

Geographically, *M.bovis*is distributed worldwide. According to the Worldwide Animal Health Information Database of OIE (Javaid, 2018), 91 out of 182 countries reported the presence of BTB infection in cattle during the 2015– 2017 period. In Africa, 30 of 59 countries reported the presence of the disease in the same period. The disease is also widespread in Central and South America, partsof Asia, and Middle East countries. While BTB has been controlled successfully in most developed countries through the implementation of test-and slaughter schemes, meat inspection at abattoirs, and pasteurization of milk, BTB remains a problem in some developed countries (e.g., UK, Ireland, New Zealand) (Allen,2018), and in most developing countries where the practice of control programs are either at an early stage or non-existent(Jones *et al.*,2008; Kathy *et al.*,2014).

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; Kahn *et al.*,2007;Katale,2012). However, only little is done particularly in developingcountries on the epidemiology of this organism and the epidemiological requirements for its control. The *M. bovis* is transmitted from animal to man through ingestion of the unpasteurized dairy product, milk of infected cattle, and undercooked meat which was recognized as a major public health problem (Ketema*et al.,* 2019).

Infected cattle are considered a possible source of infection as they shed a significant amount of *M. bovis* through droplet nuclei into the environment and may act as a source of intra herd transmission(Kriek,2006). The main source of infection is untreated smear-positive patients. It typically affects the lungs (PTB) but can also affect other sites as well (extra PTB) (FMOH, 2016) .Infectious organisms can be found in respiratory secretions, feces, milk, urine, vaginal secretions, semen, and draining lymph nodes (Li,2013).

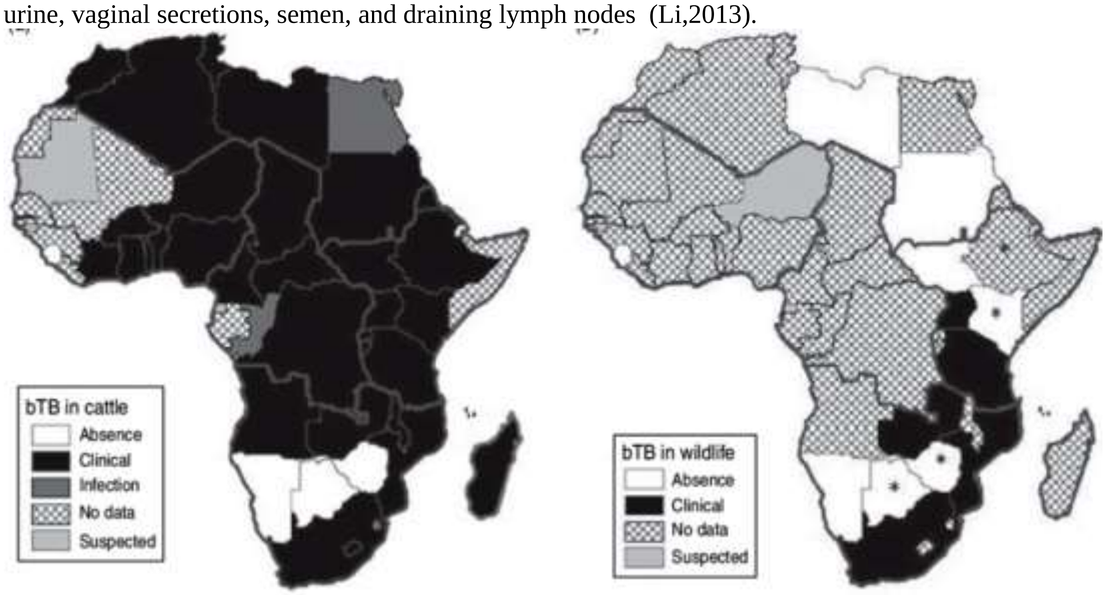

Figure 4: Map shows distribution of bTB in Africa

2.6. Pathogenesis

The bacteria usually enter the respiratory system of a cow and settles in the lungs. After then, the organism is phagocytized by lung macrophages. The bacterium becomes entrenched when it enters a herd of cattle via aerosolized droplets or ingestion. Depending on the severity of the infection and the immune system of the individual animal, the incubation period could last months or years (OIE, 2009) .The organism replicates intracellular after being taken over by macrophages. Granuloma or tubercle is formed as the body tries to draw on infected macrophages through the tissue. Granuloma is usually 1-3 cm wide, yellow or gray, round and solid. In the cut section, the root of the granuloma consists of dry, yellow, or necrotic dry matter. The infection can spread excessively to the lymph nodes and other parts of the body and cause 2-3 mm wide, tubercles. The formation of these tiny tubercles is known as military tuberculosis (OIE, 2009).

2.7. Diagnosis

The global prevalence of human TB caused by *M. bovis* was estimated to be 3.1% of all human TB cases worldwide, accounting for 2.1% and 9.4% of pulmonary and extra pulmonary TB cases, respectively (Ayele *et al.,2004*) and different method used for both animal and human..

2.7.1. Clinical examination

Bovine tuberculosis can be clinically characterized, by progressive emaciation, a low grade fluctuating fever, weakness and in appetence. TB lesions may be found in any organ or body cavity of diseased animals. In early stages of the disease, these lesions are difficult to find, even during post mortem examination. But in later stages, the nodules or lumps caused by bovine TB become very evident in the lungs and associated lymph nodes and in the lymph nodes of the head and intestinal tract. Lesions may also appear in the abdominal organs, reproductive organs, nervous system, superficial body lymph nodes, and bones. Humans and animals with TB develop an immune response, which can be detected by the tuberculin skin test (Raghvendra*et al.,* 2010).

2.7.2. Tuberculin test

Tuberculin is a sterile laboratory product made by growing TB bacteria, killing them with heat, removing them from the substance on which they were grown, and properly diluting and preserving the remaining mixture. About 72 hours after tuberculin is injected into animals affected with TB, a characteristic swelling reaction appears at the point of injection. This reaction is a positive test result, indicating exposure to one type of mycobacteria. Further diagnostic methods are necessary to confirm the presence of bovine TB. 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). Intradermal test is the standard method for the diagnosis of tuberculosis in live bovine. In the past, heat-concentrated synthetic medium tuberculin was preferred to use as a diagnostic reagent; however, now adays it has been replaced by purified protein derivative (PPD) tuberculin because it is more specific and widely used as well as commercially available. For the diagnosis of bTB, single intradermal test using bovine tuberculin or intradermal comparative test using avian tuberculin combined with bovine tuberculin can be used for the test. The preferred position for intradermal test is mid-neck as it is more sensitive than the caudal fold of tail. However, the caudal fold of tail can be applied by increasing the amount of the reagent (Skuce*et al*., 2011).

2.7.3. Differential staining

Mycobacterium bovis can be demonstrated microscopically on direct smears from clinical samples and on prepared tissue materials. The acid fastness of *M. bovis* is normally demonstrated with the classic Ziehl– Neelsen stain, but a fluorescent acid-fast stain may also be used (OIE, 2009).

2.7.4. Serological examination

Serological assays are considered to be useful tools for the diagnosis of bovine tuberculosis although limited to those periods when antibodies are a feature of the disease. There is a switch in the nature of the immune response against *M. bovis* as the infection progresses. It is known that during the later stages of infection, there is a strong humeral response and assays based on the cell-im¬mune response can be either negative or inconclusive. In addition, serological assays are relatively easy to perform and can be used to rapidly test a large number of samples (Surujbali*et al.,* 2002, Medeiros *et al.,* 2010).

2.7.5. Culture detection methods

Mycobacterial culture can be performed on either a solid or a liquid medium. The yield of M. tuberculosis isolated from a liquid medium (e.g., Middlebrook7H9) is greater than that from a solid egg-based medium (e.g., Lowenstein-Jensen) or a solid agar-based medium (e.g., Middlebrook 7H11) (Pfyffer,2015).

2.7.6. Molecular detection methods

In 1995, the amplified mycobacterium direct test (AMTD) (Hologic, San Diego, CA) was the first nucleic acid-based amplification test (NAAT) to be cleared by the Food and Drug Administration for the detection and identification of M. tuberculosis from direct specimens. This assay utilizes transcription-mediated amplification of a portion of the 16S rRNA gene-specific to the M. tuberculosis complex to identify the organism (Papaventsis*et al.*, 2012).

2.8. Impacts

The disease has also significant global economic impacts within the context of animal health particularly in most developing countries, as it directly affects animal productivity and also influences international trade of animal products (Shewatatek, 2015). It remains an epicenter for potential zoonotic diseases such as (BTB) putting public healthy and livestock sector in jeopardy (Bihon *et al*., 2020). Ethiopia is one of the high burdened countries in the world with human TB that estimate 10-15% TB prevalence is due to *M.bovis*(Mulatu and Mohamed, 2023). With every growing population of the country, there is high effort by the livestock sector to cope with proteins demands and hence, high productive animals are reared under intensive farming system in urban and peri urban parts of the county it creates favorable environment for it (Kidane *et al*., 2015). *M.bovis* in cattle is pervasive through different agro ecological zones of Ethiopia where the BTB prevalence in cattle ranged from 16.2%-65.8% in different farming system (Kidane *etal*., 2015).

2.8.1. Economic Impact

Financial losses are encountered through the costs for the control of the disease (testing and compensation expenses, losses from animal movement and sale restrictions) as well as decreased milk and meat production (Zinsstag *et al*., 2006). In contrast, bovine tuberculosis is endemic in numerous developing countries and can have devastating impacts on the livelihood of millions of the world’ s most vulnerable communities as the disease compromises their sustainable food supply, income, social status and potentially their health in the mainly rural livestock producing areas (Dejene, 2017). Ethiopia few abattoir meat inspection surveillances have shown the condemnation rate of the total or partial carcass and organs. It causes ill-health among millions of people each year and ranks as the second leading cause of death from an infectious disease globally next to the human immunodeficiency virus (Aylate *et al*., 2013).

According to World Health Organization (WHO) in 2013, there were an estimated 9.0 million incident cases of TB (ranging from 8.6 million– 9.4 million) and 11.0 million prevalent cases (range, 10 million– 13 million) of global populations. Most of the figured number of cases in 2013 occurred in Asia (56%) and the African Region (29%). Tuberculosis is also one of the major diseases that cause tremendous economic crisis in low income countries (Millet *et al*., 2013). It represents financial burden due to lose of productivity to the livestock sector that can be accounted though reduction of milk production, carcass condemnation and death of animals due to it (Tschopp *et al*., 2021).

2.8.2. Public Health Significance

Human tuberculosis due to *M. bovis* is usually underestimated or under diagnosed because of no clinical, radio graphical and histopathological differentiation 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 it can infect human beings too either by consuming raw milk, meat and their products from infected animals (Malama, *et al* .,2013) , or by inhaling infective droplets or direct exposure to infected animals (Verma*etal.*,2014) . In an estimate, about 10% cases of human tuberculosis are caused by *M. bovis*, while majority are caused by M. tuberculosis (Perez-Lago *et al.*, 2013). In countries where milk is pasteurized and there is effective implementation of bovine tuberculosis program, tuberculosis in human due to *M. bovis* is very rare. But in areas where the disease in bovine is poorly controlled the reporting of the disease is more frequently done. In farmers as well as abattoir workers and others the incidence rate is higher. Exposure to other species apart from cattle can cause infection in human. It has been documented that goats as well as seals, farmed elk and rhinoceros can also act as sources of bovine tuberculosis.

A source of infection may be wildlife especially in countries where people use to take bush meat (Etter*et al*., 2006; Evans *et al.,* 2007). If the whole carcass is condemned then it indicates a high degree of tuberculosis infection and its transmission so it requires immediate attention from both the economic and public health point of viewmeat (Assegede*et al.,* 2004;Torgerson, 2010). Being cause of chronic granulomatous disease tubercle bacilli increases susceptibility to bladder and lung cancer. Though BCG induced cytotoxicity of bladder has paved the way towards initiation of BCG immunotherapy for treatment of bladder cancer (Atkinson *et al.,* 2000; Vento *et al.,* 2011).

2.9. Bovine Tuberculosis Status

2.9.1. 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).

2.9.2. 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 bTB 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 bTB 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).

2.10. Treatment, Prevention, and Control

TB is rarely treated in domestic livestock except in rare cases of valuable animals as zoological exhibits. Anti-tuberculous first-line chemotherapies that have the greatest activity include INH, RIF, PZA, ethambutol (EMB), and streptomycin (SM). Second line drugs include capreomycin (CAP), ethionamide (ETH), cycloserine, and thioacetazone(Waters, 2015). Primary control strategies of bTB depend on testing of infected animals by TST and/or IGRA, isolation of the infected animals within the infected herds, routine slaughter surveillance, slaughtering the infected animals, movement restriction of the affected herds, and removing the TB test-positive animals (reactors). In addition, movement/border testing policies, thorough epidemiological investigation of reported cases, and certification of a negative TB test(s) prior to entry of animals to countries, particularly for animals emerging from bTB-affected regions, are important procedures for controlling bTB (Waters, 2015).

The control system for identification of bTB comprises TST, abattoir surveillance and PM confirmation. There is a dynamic link between these three arms and they could not be considered independent because the deficiencies in TST will manifest in an increased number of lesions at abattoirs. Likewise, missed lesioned animals at slaughter houses will delay the detection of undisclosed transmission within herd (McKinley *et al.,* 2018).

Complete eradication of bTB has not been achieved in any country due to the presence of major problems facing the eradication: (1) Breakdowns: disclosure of bTB affected animals either through detection of TST-positive animals after a successive number of free tests within herds or through confirmation of the infection within abattoirs by bacteriological culture. Breakdowns are caused by anergic carrier or a break in the security of the herd or infection from animals newly introduced to free herds. (2) Non-Visible Reactors (NVL) that create administrative and public relations difficulties. (3) Presence of wildlife reservoirs. (4) Large herds: as in North America and South America where cattle are run under very extensive conditions on large ranches or stations. Also, in intensive dairies where the complete depopulation of herds cannot be performed (Constable, McKinley *et al., 2018*).

Positive TST results are sometimes neglected in countries with rare TB cases. It is unacceptable, but some vets Pathogens 2022, 11, 715 17 of 25 assume that the positive result for bovine tuberculin is a reaction against *M. avium* and do not follow the mandatory CITT procedure, in which both bovine and avian PPDs tuberculin are tested for. Vaccination against bTB is rarely used for controlling the disease in areas with official control programs because BCG can induce a cellular immune response producing interference with the testing strategies using PPD as antigen (TST and IGRA). Lack of the available diagnostic tests to differentiate between infected and vaccinated animals is the main impediment (Chambers *et al.*, 2014). In addition, the live attenuated BCG vaccine has some problems, such as uncertain stability in natural conditions and its possible survival in tissues, secretions, and environment (Balseiro, *et al.,* 2020).

However, some recent experimental trials with bacillus Calmette Guerin (BCG) in cattle demonstrated that it was particularly effective when administered to neonates (Liao *et al.*, 2022). (Chandran,*et al.*, 2019) demonstrated a novel BCG vaccine to protect animals against bTB. The authors also demonstrated a novel skin test for differentiating infected from vaccinated animals (DIVA) that will detect bTB (Chandran,*et al.*, 2019).Nevertheless, several trials have been used in many animal models using heat-inactivated and formalin-killed vaccines with variable results, and great challenges still remain toward production of effective, safe, and easilyimplemented vaccines in domestic animals (Balseiro, *et al.*, 2020). Being zoonotic and causing a severe public health hazard, many prominent organizations as OIE, WHO, FAO endorsed the One Health approach of TB to comprehensively address the challenges at the animal– human interface (Olea-Popelka, *et al.*, 2017).

3. CONCLUSION AND RECOMMENDATIONS

The transmission of tuberculosis (TB) from animals to humans, particularly through infected milk, poses a significant public health concern in developing countries that requires urgent attention. Given the limited access to pasteurization infrastructure, educating rural communities on the importance of boiling milk before consumption is crucial. The challenges associated with extra-pulmonary TB, including bovine TB (BTB), are exacerbated by high rates of HIV infection and the zoonotic nature of the disease. While antimicrobial treatments have been attempted in some animal populations, the long-term nature of such treatments proves impractical in regions focused on eradication. Effective control programs must involve robust post-mortem meat inspections, comprehensive surveillance, systematic testing of cattle and the removal of infected animals. Collaboration between veterinary professionals and government authorities is essential to enhance access to diagnostics and vaccination efforts, especially as ongoing research into new vaccine candidates shows promise for more effective TB control.

Based on the above conclusion the following recommendations are forwarded:-

- ❖ **Implement Vaccination**: Ensure the availability of tuberculosis vaccinations for both humans and animals, recognizing its zoonotic nature.
- ❖ **Enhance Biosecurity Measures**: Strengthen biosecurity protocols on farms to reduce interactions between domestic and wildlife animals.
- ❖ **Ensure Protective Practices**: Mandate the use of protective clothing when handling diseased animals or infected carcasses.
- ❖ **Establish Quarantine Protocols**: Enforce strict quarantine measures for animals imported from other states or countries.
- ❖ **Education and Training**: Provide training for personnel involved in control programs and promote educational initiatives to enhance awareness of TB control measures.

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