DOI: https://doi.org/10.20372/afnr.v3i1.1161
Journal of Agriculture, Food and Natural Resources
J. Agric. Food Nat. Resour. Jan-Apr 2025,3(1):50-63
Journal Home page: https://journals.wgu.edu.et

Review Article

Bovine Tuberculosis and Drivers for Initiating Its Control in Ethiopia:

Mitiku Wamile[1]*, Yismaw Alemie [1], Megarsa Gemechu [1], and Buzunesh Tesfaye[1]

[1]Department of Animal Science, Faculty of Agriculture, Wollega University, Shambu, Ethiopia

Abstract

Bovine tuberculosis (bTB) is a zoonotic bacterial infection caused by *Mycobacterium bovis.* This paper reviews the status and drivers for controlling bovine tuberculosis (bTB) in Ethiopia. Bovine tuberculosis, caused by *Mycobacterium bovis*, is a zoonotic bacterial disease that is endemic and widespread in Ethiopia. The most common route of transmission between cattle is inhalation whereas from animals to humans is through the consumption of raw animal products especially milk. Close contact between humans and animals is another significant risk factor for the spread of zoonotic TB. Bovine TB poses a serious threat to animal production; particularly affecting exotic breeds kept under intensive or semi-intensive production systems, and has considerable public health implications. In humans, zoonotic TB often presents as extra-pulmonary TB, making it clinically and radiologically indistinguishable from TB caused by *M. tuberculosis*. Misdiagnosis and delayed treatment initiation are common challenges. Moreover, *M. bovis* is naturally resistant to pyrazinamide, complicating treatment outcomes when healthcare providers initiate therapy without drug susceptibility testing. The challenges in combating zoonotic TB in developing countries include the involvement of multiple hosts, lack of early diagnostic tools, and socio-cultural barriers. While treatment in animals is generally not recommended, vaccination is practiced in human medicine but is not widely used as a preventive measure in animals. In industrialized countries, *M. bovis* has been significantly reduced through measures such as strict test-and-slaughter policies, meat inspection, milk pasteurization, and financial compensation for farmers. Globally, the End TB Strategy aims to end the TB epidemic by reducing TB deaths by 95% and new cases by 90% between 2015 and 2035 while eliminating catastrophic economic burdens on affected families. However, Ethiopia lacks a national bTB control program. Given the severe impact of *M. bovis* on both animal and human health, implementing sustainable bTB control and prevention measures in Ethiopia is essential to reduce the disease's burden on both populations.

Article Information

Article History:
Received : 19-09- 2024
Revised : 24-02-2025
Accepted : 24-03-2025

Keywords:
Bovine tuberculosis
Cattle, Drivers, Ethiopia
Mycobacterium bovis

***Corresponding Author:**
E-mail:
mwamile@yahoo.com

INTRODUCTION

Bovine tuberculosis (bTB) is a zoonotic bacterial infection caused by *Mycobacterium bovis*. It belongs to a group of well-known and newer mycobacteria, together with *Mycobacterium tuberculosis*, all of which were derive from a common ancestor forming the *Mycobacterium tuberculosis complex (MTBC)* (Wirth *et al .,* 2008*;* Langer and LoBue, 2014)*. M. bovis* is capable of infecting a broad range of hosts, including ruminants (predominantly domestic cattle), humans and other primates. The most common route of transmission between cattle is aerosol inhalation (Teppawar *et al.,*2018).

Globally, TB is one of the top 10 causes of death and the leading cause from a single infectious agent (above *HIV/AIDS*) (WHO, 2018). Millions of people continue to fall sick with TB each year. In 2017, TB caused an estimated 1.3 million deaths (range, 1.2–1.4 million) among *HIV*-negative people and there were an additional 300,000 deaths from TB (range, 266, 000–335, 000) among HIV-positive people (WHO, 2018).

Globally, most cases of zoonotic TB are caused by *M. bovis*, and cattle are the major reservoir (Ameni and Wudie, 2003 ; Ayele *et al .,* 2004 ; Nuru *et al .,* 2015). 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 and Boru, 2012).

Bovine tuberculosis is widely distributed across major livestock producing regions of Ethiopia. The prevalence of bovine tuberculosis in Holstein-Friesians was higher than the prevalence in local zebus and crosses. Cattle kept under intensive and semi-intensive production systems had higher prevalence of bTB than those kept in extensive livestock production system (Sibhat *et al.,* 2017)

Disease caused by either *M.bovis* or *M.tuberculosis* is considered clini cally and radiologically indistinguishable from each other. An increased risk of infection for humans exists especially in rural communities due to close contact between people and infected livestock and consumption of improperly cooked beef and drinking of unpasteurized milk and milk products or by inhaling infected aerosol (Mamo *et al.,* 2013). In countries where pasteurization of milk is rare and bTB in cattle is common, 10% to 15% of human TB cases is caused by *M. bovis* (Ashford *et al .,* 2001 ; Michel *et al .,* 2010). Bovine tuberculosis (bTB) has a potential public health risk and economic impact in pastoralist community whose livelihood depends on their livestock (Gumi *et al .,* 2012; Mamo *et al .,* 2013).

Control and elimination measures for animal tuberculosis are lacking in most African countries. The present situation is most probably due to the chronic lack of funds, trained professionals and political will, but also to the under-estimation of the economic and zoonotic consequences of animal tuberculosis by African governments and donor agencies. The time is right for a bold and concerted effort to collectively address zoonotic and bovine TB, framed within the multidisciplinary United Nations Sustainable Development Goals (SDGs) 2016–2030 and WHO's *End TB Strategy* which seek to end the global TB epidemic by 2030. The *Strategy* calls for diagnosis and treatment of every person with TB, and this must include zoonotic TB. This is supported by the Stop TB Partnership's *Global Plan to End TB 2016–2020 – The Paradigm Shift*, which identifies people at risk of zoonotic TB as a neglected population deserving greater attention (Global Plan to End TB, 2016:Olea-Popelka *et al.,* 2017).

Nowadays, national TB control strategy, incorporating directly observed treatment short course (DOTS) in Ethiopia has been practicing exclusively on human, neglecting the disease in animals, even though it seems difficult for the program to be effective without the taking part of animal health professionals. The DOTS strategy existing in human will not directly influence the control of bTB (Firdessa *et al.,* 2012). bTB is a neglected tropical zoonotic disease which is underestimated and has not been receiving scientific attention and resources as compared to its impacts (Olea-Popelka *et al.,* 2017; WHO/FAO/OIE, 2017). A national bTB control program in Ethiopia is absent and there is no consideration for implementing effective control strategies. In order to seek for appropriate control strategy, information on the current status and drivers for initiating control of Bovine Tuberculosis is required. Therefore, the objective of this review is to review the status and drivers for initiating control of Bovine tuberculosis in Ethiopia.

OVERVIEW OF BOVINE TUBERCULOSIS

Etiology, Taxonomy of Mycobacteria and Physical and biochemical characteristics

Bovine tuberculosis (bTB) is a chronic wasting diseases of cattle caused *by M. bovis,* within the *Mycobacterium tuberculosis-complex* (MTC) (Bezos *et al .,* 2012). By far, the most important etiologic agents of bTB in cattle are *M. bovis* and, to a lesser extent, *M. caprae*, which were recognized as an independent mycobacterial species since 2003 (Schiller *et al .,* 2010). *M. bovis* and *M. caprae* can also affect other domestic and wild animals as well as humans (Amanfu, 2006).

The *Mycobacterium tuberculosis-complex* represents one of the three groups into the genus *Mycobacterium* together with *M. leprae* and the group of *non-tuberculous mycobacteria (*NTM) (i.e., mycobacteria other than the MTC and *M. leprae*). It comprises a range of mycobacterial species causing tuberculosis in humans and animals that are highly related among them (i.e., 99.9% homogeneity in the nucleotides sequence and virtually identical 16S rRNA sequences). Despite their great genetic relatedness, MTC species differ in terms of pathogenicity, geographical distribution and preferred host. Moreover, they also differ in some biochemical characteristics, cultural requirements and for several molecular markers (Rodriguez-Campos *et al .,* 2014).

Mycobacteria are non-motile, non-spore forming, non-capsular, pleomorphic bacilli or coccobacilli, 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 of about 15- 20 hours. They occur singly, in pairs or as small bundles. On laboratory media they may appear as cocci or rods measuring 6-8μm. The Mycobacterial cell wall is triple layered comprising a basal peptidoglycan layer and an intermediate arabinogalactan mycolate complex. The outer layer is lipid rich; comprising surface rope like structure of peptidoglycolipid. 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. Mycolic acid is the major component of the cell wall envelope, greater than 50% by weight, a significant number which are responsible for their resistance to humoral defense mechanism, disinfectants, acids and alkalis. The staining characteristic of *M. tuberculosis* is due to the mycolic acid which resists decolorization by acid alcohol. *Mycobacteria* when stained are acid fast as they resist decolorizing with strong acid/alcohol solutions (Chukwu *et al .,* 2013) .

Pathogenesis and Pathology

Mycobacterium tuberculosis-complex species lack toxins; they have several virulence genes, which mostly encode for enzymes of lipid pathways, cell surface proteins, regulators, or proteins of the signal transduction system. Moreover, other genes are involved in Mycobacterial survival inside the host macrophages, encoding for proteins inhibiting the antimicrobial effect of macrophages, including phagosome arrest and inhibition of apoptosis (Forrellad *et al .,* 2013). Therefore, the tuberculous infection is characterized by the activation of an exacerbated inflammatory process (i.e., caseous-necrotising), as host response to virulence factors and antigen stimulation. This process leads to the formation of the typical lesions of the MTC, the granulomas, which represent the intent of the organism to limit tissue damage and restrict microbial dissemination(Waters *et al .,* 2014)

Tuberculosis spreads through the body in two stages, the primary complex and post-primary dissemination. The primary complex consists of the lesion at the point of entry and the local lymph node. Post-primary dissemination from the primary complex may take the form of acute miliary tuberculosis, discrete nodular lesions in various organs, or chronic organ tuberculosis (Radostits *et al .,* 2000). In cattle, the granulomas are characterized by a central core of caseous, often mineralized material, surrounded by infiltrates of epithelioid macrophages, Langhan's type multinucleated giant cells and lymphocytes . This structure is often enclosed by a fibrous capsule with level of fibrous encapsulation depends on the chronicity of infection. The macrophages are the primary host cell for intracellular growth of *M. bovis* following an infection. The gradual accumulation of macrophages in the lesion and the formation of a granulomatous response lead to the development of a tubercule (Quinn *et al.,* 2004). The granuloma prevents the spreading of bacilli resident within macrophages. However, the latent bacilli could be later released if the immunological balance is broken, triggering disease reactivation.

The characteristic lesion caused by *M. bovis* in cattle is described as having a center of caseous necrosis, usually with some calcification, with a boundary of epithelioid cells, some of which form multinucleated giant cells and few to numerous lymphocytes and neutrophils. In cattle, lesions are found most frequently in lymphatic tissues of the thoracic cavity, usually the bronchial and/or mediastinal lymph nodes. Lymph nodes of the head region are the second most frequent site, and in many instances lesions in the retropharyngeal and sub-maxillary nodes exist in the absence of detectable lung lesions(Neill *et al .,* 2001). Within the granuloma, the mycobacteria may remain dormant for decades without any clinical disease (i.e., latent tuberculosis). Subsequent immune suppression could allow activation of the dormant bacteria, followed by replication and spread; consequently, a proportion of infected cases may not develop any active tuberculosis. The mechanisms responsible for latency in tuberculosis are not well understood; potential latent infections are suspected in cattle, thought their occurrence remains unclear (Domingo *et al .,* 2014).

Immunity

Both humoral and cell mediated immune responses can be induced to mycobacterial infection, but the cell mediated immunity is generally accepted to have the most significant role in protection. The macrophages have a central role in processing and subsequent presenting of mycobacterial antigens to antigen specific T-lymphocytes(Ali, 2006) .

Epidemiology of Bovine Tuberculosis

Global Distribution

Mycobacterium bovis is 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 (Pal, 2012 ; Mamo *et al .,* 2012). However, only little is done particularly in developing countries on the epidemiology of this organism and the epidemiological requirements for its control (Romha *et al .,* 2018)

Zoonotic TB is distributed globally and is more prevalent in most of Africa, parts of Asia and of the Americas except Antarctica, Caribbean islands, parts of South America and Australia, Iceland, Denmark, Sweden, Norway, Finland, Austria, Switzerland, Luxembourg, Latvia, Slovakia, Lithuania, Estonia, the Czech Republic, Canada, Singapore, Jamaica, Barbados, and Israel (Teppawar *et al.,* 2018). Although most of the developed countries have reduced or eliminated bovine TB from their cattle population, however, the disease is still present in the wildlife of United Kingdom, Canada, the United States, and New Zealand. Eradication programs are in progress in other European countries, Japan, New Zealand, the United States, Mexico, and some countries of Central and South America where it has been eradicated by following strict test-and-slaughter policies (Teppawar *et al.,* 2018).

The largest decrease in regional bTB trends was observed in Oceania and Europe (ie by more than 45%), followed by Asia (i.e, 38% decrease); where as the decrease in bTB notification was slower in Africa and the Americas, with a reduction of 25% and 18%, respectively, over the period 30 year period (Awada *et al.,* 2018).

Host range

The most important causes of bovine TB in cattle are *M. bovis* and *M. caprae*, both of which cause infectious diseases. *M. bovis* has one of the broadest host ranges of all known pathogens and has been diagnosed worldwide. Cattle are considered to be the true hosts of *M. bovis*. However the isolations of *M. bovis* has also been detected from domestic animals like buffaloes, sheep, goats, pigs, equines, camels (Mamo *et al.,* 2009) and along with other animals like deer, antelopes, bison, wild boars, primates, llamas, kudus, elephants, foxes, mink, ferrets, rats, elands, tapirs, elks, sitatungas, oryxes, addaxes, rhinoceroses, possums, ground squirrels, badgers, otters, seals, hares, moles, raccoons, coyotes and lions, tigers, leopards and lynx . The natural movement of these reservoir animals increases the spread of the disease to domestic animals (Teppawar *et al.,* 2018).

Transmission

Mycobacterium bovis has a wide host ranges that includes most mammalian species. In addition to livestock and wild hoofed mammals, the disease has been reported in elephants, human, non-human primates, and many other species (Teppawar *et al.,*2018). The ability of *M. bovis* to infect such a wide variety of species can be attributed to different routes of transmission by which *M. bovis* can be transmitted from animal to animal (Ameni and Wudie, 2003 ; Mamo *et al .,* 2013).The main reservoir of *M. bovis* is cattle (Pal and Boru, 2012), which can transmit the infection to many mammalian species including man. Organisms live in the host respiratory discharges, faeces, milk, urine, semen and genital discharges. These body excretions may contaminate grazing pasture, drinking water, feed, water and feed troughs or fomites, which may act as source of infection to other animals. Main routes of infection by which tubercle bacilli gain entrance into the host are respiratory and alimentary(Wubit, 2017 ; Teppawar *et al.,* 2018).

The most common route of transmission between cattle is aerosol inhalation (Teppawar *et al.,* 2018). Transmission may also occur by ingestion of water or feed contaminated by feces, or as a result of calves nursing infected dams. The digestive tract is also a route of infection for bovine tuberculosis, especially in calves fed milk from cows with tuberculous mastitis or through ingestion of contaminated water or forage. In this case, the primary complex is located in the digestive organs and lymph nodes (Ameni and Wudie, 2003 ; Mamo *et al .,* 2013).

Less common routes of infection include intrauterine infection, at coitus or through the use of infected semen or contaminated insemination or uterine pipettes, and intramammary infection, by the use of contaminated teat cannulas or contaminated cups of milking machines. Unusual sources of infection are infected cats, goats, or even farm attendants. Under natural conditions, stagnant drinking water may cause infection up to 18 days after its last use by a TB-carrier animal, but a running stream does not represent an important source of infection to cattle in downstream fields. Viable organisms can be isolated from the feces of infected cattle and from the ground in contact with the feces for 6 to 8 weeks after the feces are dropped (King *et al .,* 2015).

On the other hand, studies have also indicated that cattle and other animals can acquire *M. tuberculosis* from humans (Ameni *et al.,* 2011 ; Mamo *et al.,* 2012), which may have implications in the epidemiology and control of human TB. *M. tuberculosis* has also widely been isolated from bovine milk (Mariam, 2014) and tissues of different animal species in Ethiopia (Berg *et al.,* 2009; Ameni *et al.,* 2010, 2013; Aylate *et al.,* 2013; Mamo *et al.,* 2012) using different molecular diagnostic methods such as PCR and spoligotyping. Indeed, transmission of *M. tuberculosis* from humans to other animals has also been suggested (Berg *et al.,* 2009; Ameni *et al.,* 2011; Mamo *et al.,* 2012).

Status of Bovine Tuberculosis in Ethiopia

Ethiopia is among the 22 high TB-burden countries that accounts for 81% of estimated cases (WHO, 2014). Bovine tuberculosis (TB) is an endemic disease of economic significance in Ethiopia where it affects cattle, sheep, goats, and camels. In a recent study in central Ethiopia where commercial dairy farming is widely practiced, 90% of the herds were positive for bTB, and a prevalence of as high as 41.3% was recorded in some of the large dairy herds(Areda *et al.,* 2019).. The dissemination of the disease appears to be dependent on two main practices: pastoralism and the search for and the location of markets. The number of *M. bovis* infections in humans in Ethiopia has been reported to be low, but it is likely to be substantial because of the high prevalence of the diseases in livestock (Areda *et al.,* 2019).The prevalence of bTB in Ethiopia is high and molecular typing of *M. bovis* has also indicated the existence of unique strains of tuberculosis (Zeru *et al.,* 2013). Ethiopia is one of the African countries where tuberculosis is wide spread in both humans and cattle and the endemic nature of tuberculosis in humans and cattle has long been documented (Shitaye *et al.,* 2007).

Currently, conventional and molecular epidemiological studies have provided evidence for the widespread distribution of bTB in cattle populations throughout the country (Gumi *et al.,* 2012; Mamo *et al.,* 2013). Moreover, studies have indicated that zoonotic TB is as an on-going risk to public health in Ethiopia, as rural dwellers live in close contact with their animals as well as due to meat-borne infections as a result of poor meat inspection practices and consumption of unpasteurized dairy products (Firdessa *et al .,* 2012 ; Mamo *et al .,* 2013) . On the other hand, studies have also indicated that cattle and other animals can acquire *M. tuberculosis* from humans (Ameni *et al .,* 2011), which may have implications in the epidemiology and control of human TB. *M. tuberculosis* has also widely been isolated from bovine milk(Mariam, 2014) and tissues of different animal species in Ethiopia.

Prevalence of bTB varies depending on the geographical areas, breeds and husbandry practices. The observed variability of bTB disease frequency in Ethiopia might well be influenced by different livestock production systems (rural/pastoral/peri-urban) and different geographic and climatic contexts. Transmission of bTB seems to be higher in intensive peri-urban settings when compared to extensive rural and pastoral areas (Mamo *et al.,* 2011). Sibhat *et al.,* 2017 reviewed that pooled prevalence estimate of bovine tuberculosis in Ethiopia was found to be 5.8% (ranges of 0 % and 46.9%).The status of bTB in wildlife populations that often share habitat with livestock is unknown (Tschopp *et al.,* 2010a). According to Gelalcha *et al.,* 2019) strain typing of the isolates from cattle and sheep using spoligotyping confirmed that all of the ovine and bovine isolates were *M. bovis* and identified them all as belonging to spoligotype SB0134(Gelalcha *et al.,* 2019).

Diagnosis of Bovine Tuberculosis

Traditionally, the fight against bTB is initiated by the implementation of routine diagnostic tests for certification of free properties. The diagnosis of bTB can be made by direct and indirect methods, in which we can mention clinical diagnosis, *post mortem* and histopathological examination, chemical, immunological, bacteriological and molecular methods. The renewal of scientific interest in tuberculosis in recent year has led to develop and improve methods of diagnosis, prevention, control and eradication of bTB (Ramos *et al .,* 2015). The identification of the closely related members of the *MTBC* has remained a challenging task in diagnostic laboratories. *MTBC* includes a variety of closely related Mycobacteria namely *M. tuberculosis , M. bovis, M. Canetti, M. africanum* and *M. microti*. A panel of classical tests based on microbiological features such as growth rate and phenotypic and biochemical characteristics has conventionally been utilized to distinguish members of *MTBC*

After death, infection is diagnosed by necropsy, histopathological and bacteriological examination and biochemical tests like nitrate reduction, niacin production, deamination of pyrazinamide and urease tests. Immunological diagnostic techniques like tuberculin skin tests: Single intradermal test, comparative intradermal test, short thermal test and stormont test; Blood based diagnostic techniques like gamma interferon assays, Enzyme-linked immune-sorbent assays and lymphocyte proliferation assay, culture of *mycobacterium* and molecular diagnostic techniques which involves polymerase chain reaction, is a method that allows direct identification of the *M. tuberculosis* complex (De la Rua-Domenech *et al .,* 2006).

Spoligotyping, restriction fragment length polymorphism (RFLP), variable number tandem repeats typing (VNTRT) are the techniques used for concurrent detection and typing of *mycobacterium* species at strain level. Its clinical usefulness over the other techniques is determined by its rapidity, both in identifying causative bacteria and in providing molecular epidemiologic information on strains (De la Rua-Domenech *et al .,* 2006).

Economic Importance

Bovine TB is a chronic debilitating disease, characterized by a progressive loss of body condition, reduced milk production, lower reproductive rates, and losses caused by reduced feed utilization, a decrease in the average productive age, a reduced market value due to poor body condition, condemnation of carcasses or portions of carcasses at abattoirs of bTB-infected cattle, and the additional processing costs following condemnation at abattoirs. The presence of bTB in the national herd also prevents participation in international trade in cattle, milk, and milk-derived products (Dibaba *et al.,* 2019). In some situations, bTB may also be a serious threat to endangered species. The infection leads to a decrease from 10 to 20% of milk production, loss of weight and a reduction of fertility. In addition, there is condemnation of carcasses of infected animals, and restrictions to export meat to countries where BTB is controlled (Asseged *et al .,* 2004 ; Ramos *et al .,* 2015). Some data exist, and in Central Ethiopia it was estimated that the milk yield was reduced by 5–13%, the number of services per conception increased from 1.25 to 2.02, and the number of milking days was reduced from 328 days in bTB-negative to 294 days in bTB-positive cows (Ameni *et al.* 2010).

Bovine TB causes fertility losses of 5 % of the annual number of calves born per cow among CIDT positive cows (Tschopp *et al.,* 2012). 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 (Markos and Tadesse, 2017). There is an attempt by the World Trade Organization (WTO) to reduce trade restrictions, considering certain diseases like bTB as trade barriers, to increase globalization and the integration of markets with decreasing border control, as is the case in Western Africa. All these efforts will put additional strain on countries with limited resources to manage livestock diseases (Cousins, 2001). It is probably impossible to quantify the economic losses attributable to bTB in Africa at this stage, but there is no reason to believe that the nature and extent of the losses will be different to those in other countries across the globe. An additional factor on the continent is that the disease also causes an indirect loss in agricultural productivity because of the reduction in animal traction power caused by the debilitation that is characteristic of cattle suffering from bTB.

About 1.7 billion people, 23% of the world's population, are estimated to have a latent TB infection, and are thus at risk of developing active TB disease during their lifetime(WHO, 2018).Funding for the provision of TB prevention, diagnostic treatment services has more than doubled since 2006 but continues to fall short of what is needed. In 119 low- and middle-income countries that reported data (and accounted for 97% of reported TB cases globally) funding reached US$ 6.9 billion in 2018(WHO, 2018). While many industrialized countries eliminated or controlled bTB with massive public funding for test and slaughter of infected animals and compensation to their owners, the resources to do this are not available in developing countries. Prior to embarking on the control of bTB, an estimation of its cost to society including animal production and public health is warranted, particularly in resource poor countries like Ethiopia (Zinsstag *et al.,* 2007)

Zoonotic Importance

Transmission to humans constitutes a public health problem, and conditions such as culture of consuming raw milk, keeping cattle in close to the owner house (Mamo *et al .,* 2011; Gumi *et al.,* 2012 ; Mamo *et al .,* 2013) and immune suppressive disease can exacerbate the disease. The possibility of transmission of this *Mycobacterium* to humans from infected animals could be high in areas where there is close contact between human and animals (Ameni *et al .,* 2011 ; Pal, 2012). Amongst the members of the *Mycobacterium tuberculosis* complex (MTBC), *M. tuberculosis* is mainly a human pathogen, whereas *M. bovis* has a broad host range and is the principal agent responsible for tuberculosis (TB) in domestic and wild mammals (De la Rua-Domenech, 2006). *Mycobacterium bovis* can infect human primarily by consumption of unpasteurized infected milk and ingestion of meat and meat products from slaughtering infected cattle, inhalation of aerosols and through breaks in the skin (Teppawar *et al.,* 2018).

The re-emergence of bovine tuberculosis among animals and humans is a serious worldwide concern, especially in developing countries(El-Sayed *et al .,* 2016). The exact prevalence of *M. bovis* infections in humans is unknown and underdiagnosed, especially in various African countries. In countries where pasteurization of milk is rare and bTB in cattle is common, 10% to 15% of human TB cases were caused by *M. bovis* (Ashford *et al .,* 2001; Michel *et al .,* 2006). It is unknown what the current prevalence of zoonotic bTB is in African countries, or whether its prevalence will change over time, as it did in Europe. Given the high prevalence of HIV-AIDS in Africa, co-morbidity with HIV may alter the situation, but the actual situation is unknown, and the assumption that it may increase the number of zoonotic cases is highly speculative. It is commonly assumed that *M. bovis* is less virulent and has less transmission potential among human populations than *M. tuberculosis.*

Zoonotic TB is indistinguishable clinically or pathologically from TB caused by *M. tuberculosis*. Differentiation between the causative organisms may only be achieved by sophisticated laboratory methods involving bacteriological culture of clinical specimens followed by typing of isolates according to growth characteristics, biochemical properties, routine resistance to pyrazinamide (PZA) and specific non-commercial nucleic acid techniques. All this makes it difficult to accurately estimate the proportion of human TB cases caused by *M. bovis* infection, particularly in developing countries. Distinguishing between the various members of the *MTBC* is essential for epidemiological investigation of human cases and, to a lesser degree, for adequate chemotherapy of the human TB patients (de la Rua-Domenech, 2006).

For Africa, the data are almost non-existent and totally inadequate, and an assessment of the situation there is largely based on small, local studies, and unreliable anecdotal information. No *M. bovis*, for instance, could be detected in humans in some studies (Aylate *et al.* 2013), but a recent study in Ethiopia found that 2 of 70 cases with tuberculous lymphadenitis (2.9%) were caused by *M. bovis* (Nuru *et al.,* 2017). Recently, it was indicated that M. bovis is not the major cause of human TB lymphadenitis in Ethiopia although the transmission of *M. bovis* from animal to human was suggested. The suggestion was supported through isolation of M. bovis from human (Gumi *et al.,* 2012; Firdessa *et al.,* 2013; Nuru *et al.,* 2017) as well as considering the risky socio-cultural conditions and practices such as the habit of consumption of raw meat and milk (Nuru *et al.,* 2017).

According to Gumi and his colleagues total of 161 isolates from sputum (pulmonary TB) and fine-needle aspirate (extrapulmonary TB) samples were reported; three were confirmed to be *M. bovis* (1.9%) from sputum sample of pulmonary TB patients (Gumi *et al.,* 2012). These three *M. bovis* has a spoligotype pattern of SB0133 and SB0303 strains. The study also isolated the same SB0133 strain from cattle in the same area indicating the zoonotic transmission of the strain in the pastoralist communities of south east Ethiopia In south east Ethiopia The three *M. bovis* strain isolated from sputum were of spoligotypes SB0133 and SB0303 in the *M.bovis*.org database (Gumi *et al.,* 2012)**.** Different strains of *M. bovis* are widely distributed in domestic animals predominantly in the Ethiopian cattle and the main strain was found to be SB1176. In addition, the isolation of *M. tuberculosis* from domestic animals in different settings signifies the circulation of the agent between humans and animals in Ethiopia (Ameni *et al.,* 2011).

Humans suffering from active TB are the most probable source of *M. tuberculosis* in animals, with infection spread via sputum, and rarely urine or faeces or respiratory route as in rural area of Ethiopia, grazing cattle are commonly brought into the farmers households at night where they may become infected via aerosol transmission from humans (Ameni *et al.,* 2013). Previous studies in Ethiopia had confirmed transmission of *M. tuberculosis* from farmers to their cattle, goat and camel (Berg *et al.,* 2009; Ameni *et al.,* 2011; Gumi *et al.,* 2012; Mamo *et al.,* 2012).

Identical spoligotypes of *M. bovis* isolates from humans and cattle, as well as collection of *M. tuberculosis* isolates from animals, indicates transmission between livestock, mainly between cattle and humans (Gumi *et al.,* 2012) and the *M. bovis* isolates from human pulmonary TB patients matched with both the dominant spoligotype of the animal isolates in the area (SB0133) and with SB0303, which has been isolated from cattle in central Ethiopia (Berg *et al.,* 2011).

Control and Prevention

Tuberculosis needs to be prevented and controlled because it causes loss of productivity in animals infected and there is risk of infection to humans (Krauss *et al .,* 2003). *Mycobacterium species* is resistant to pyrazinamide, which is widely used in the treatment of infections caused by *MTBC* in humans. Treatment of infected animals is rarely attempted .Cattle should not be treated at all and as such farm animals with tuberculosis must be slaughtered (culled). This is because the risk of shedding the organisms, high cost of treatments, hazards to humans and potential for drug resistance make treatment controversial (Nwanta *et al .,* 2010).

In many countries, routine meat inspection forms part of the surveillance program for bovine tuberculosis(Krauss *et al .,* 2003). Meat inspection system should be strengthened and designed to prevent the consumption of contaminated products by people. All animals entering the food chain should be subjected to ante-mortem and post- mortem inspection. Tuberculin testing followed by isolation/segregation and slaughter of reactor has been implemented as the basis of eradication program. Test and slaughter program may be feasible and appropriate in areas with low prevalence of bTB and effective control of animal movement.

Disease eradication programs consisting of postmortem meat inspection, intensive surveillance including on-farm visits, systematic individual testing of cattle and removal of infected and in contact animals as well as movement controls have been very successful in reducing or eliminating the disease. Pasteurization of milk of infected animals to a temperature sufficient to kill the bacteria has prevented the spread of disease in humans. Hygienic measures to prevent the spread of infection should be instituted as soon as the first group of reactors is removed. Feed troughs should be cleaned and thoroughly disinfected with hot, 5% phenol or equivalent cresol disinfectant. Water troughs and drinking cups should be emptied and similarly disinfected. It is important that calves being reared as herd replacements be fed on tuberculosis-free milk, either from known free animals or pasteurized (OIE, 2015).

To minimize the potential for introduction of bovine TB into cattle herds, pre-entry TB testing must be conducted on all cattle before they come in contact with a herd of dairy cattle, breeding beef cattle, or stocker cattle. Total health management minimizes the potential for introduction of infectious diseases, including bovine TB. These management practices include: annual herd tests, replacement animal tests, tests of emaciated and chronic coughing cattle, postmortem examinations, individual animal identification and record keeping. Although to date no commercial vaccine is available for animals, considerable progress has been made in studying the protective efficacy of BCG (Bacillus Calmette Guerin) in reservoir hosts such as cattle, deer, badgers and brush tail possums. In African buffaloes, however, BCG did not induce significant levels of protection to challenge with *M. bovis*(Bidart, 2011).

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. Testing of cattle with an intradermal tuberculosis test and 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.

The epidemiology of zoonotic TB varies throughout the world depending on the human, livestock, and wildlife populations, and on existing TB control programs, environmental conditions, and the socio-economic status of countries or regions. The relationship between humans, livestock, wildlife, and ecology in the epidemiology of zoonotic TB makes control of the diseases complex (Nishi *et al .,* 2006) . Zoonotic TB is not a new disease but has long been neglected; burden of this disease in humans cannot be fully addressed without considering the animal reservoir and the risk of transmission at the animal-human interface. As with other zoonotic diseases, zoonotic TB cannot be controlled by the human or animal health sector alone. Human health, animal health and food safety sectors must be engaged to address the role of animals in maintaining and transmitting *M. bovis* (Teppawar *et al.,* 2018).

Drivers for Initiation of bTB Control in Ethiopia

Bovine TB has a significant impact on the international trade, and as it is a zoonotic disease-implication for animal and public health. Today, some of developed countries have been certified to be bTB-free, whereas bTB is still a serious challenge in most developing countries. In the developed countries where bTB still exists, the persistence of bTB in wildlife seems to be a major setback in eradicating the disease and also eradicating the disease is hindered by the lack of funding and proper logistics, and inadequate adherence to basic procedures such as ante-mortem and post-mortem inspections. Effective control and management of bTB is essential to eliminate it, but in developing countries the battle against the disease is far from being over due to the lack of funds needed to restrain bTB. In developing countries, the number of laboratories that can diagnose bTB is limited, and diagnosing the disease in humans stops at the smear level making it impossible to estimate the role of *M. bovis* in human infections. There is also a scarcity of data on bTB in the developing countries, which influences the control of the disease(Kwaghe, 2015).

Unique challenges of Bovine Tuberculosis
In Cattle

Vaccination for the control of bovine tuberculosis (bTB) in cattle is not currently used within any international control program, and is illegal within the European Union (EU). Vaccine is used in human medicine, but it is not widely used as a preventive measure in animals because its efficacy is variable and it can interfere with testing to eliminate the disease (Teppawar *et al.,* 2018). Candidate vaccines, based upon *Mycobacterium bovis* bacillus Calmette-Guérin (BCG) all interfere with the action of the tuberculin skin test, which is used to determine if animals, herds and countries are officially bTB-free. Although the *M. bovis* bacille Calmette-Guérin (BCG) vaccine has been used in humans for nearly a century, its use in animals has been limited, principally as protection against TB has been incomplete and vaccination may result in animals reacting in the tuberculin skin test (Buddle *et al.,* 2018).

The tuberculin skin test (TST) has been a useful diagnostic and epidemiological tool for control of bovine tuberculosis for several decades. However, suboptimal specificity of TST has frequently been reported in some bovine tuberculosis eradication programs. This suboptimal specificity could be attributed, in part, to the nature of the poorly characterized antigens of the used tuberculin. These antigens are mycobacterial extracts that contain, the antigens comprises of nonindigenous components in addition to species-specific components. As a result, the current test has failed to single out the individuals infected by tuberculous *mycobactria* from those that are immune to *Mycobacterium spp* as a consequence of exposure to environmental non-tuberculous mycobacteria. In other words, the reported false positive cases and cross-reactions that occur due to exposure or infection with other non-tuberculous environmental mycobacteria are generally attributed to the fact that the PPD of tuberculin has many antigens shared by other non-tuberculous *Mycobacterium* species as *Mycobacterium avium, M. interacellularae, M.scrofulaceum,M. paratub erculosis*, *M.kansasii* and *M. fortuitum (*Whelan *et al.,* 2003).

The test questionable specificity complicates its use as a tool for accurate diagnosis and control of both active and latent diseases. Single intradermal comparative tuberculin test (SICTT) was proposed as an alternative field test to overcome this problem. The SICTT compares skin responses to parallel injections of bovine PPD and avian PPD on the two sides of the animal neck. Animals are considered positive when the responses to bovine PPD is greater than parallel responses to avian PPD Nevertheless, although the results of the SICTT constitute a good indication of mycobacterial exposure, even this test does not always discriminate between cattle with tuberculosis and those exposed to nonpathogenic organisms(Whelan *et al.,*2003). Immature and very old animals rarely react to tuberculin inoculation regardless of the status of infection; the level of reaction is directly related to maturation and wasting of organs of immune system (Buddle *et al.,* 2003).

Importantly, the TST only identifies TB infection, but does not provide any information that can distinguish latent TB infection from active TB disease. TST effectiveness is limited by the need for a return visit, inter-reader variability, cross-reactivity with non-tuberculosis mycobacteria as well as the Bacille Calmette-Guerin (BCG) vaccine, and poor sensitivity in immune-compromised patients (Nahid *et al.,* 2006). The treatment of animals with tuberculosis is not a favored option in eradication-conscious countries and is not economical (Parlane and Buddle, 2015).

The vaccination of animals with BCG is sensitive to the tuberculin skin test, and animals become test positive in the classical skin test at least for a significant period of post-vaccination. This is the reason why the test and slaughter based control strategies based on tuberculin skin testing were favored above BCG vaccination in many countries (Parlane and Buddle, 2015). It had been reported that bTB in cattle follows subclinical presentation and most TB infected cattle seem apparently healthy, but they show an immunological response to tuberculin skin test (Collin, 2006).

In human

Distinction of *M. bovis* from *M. tuberculosis* has significant relevance to patient management. In contrast to the other members of the *M. tuberculosis* complex, *M. bovis* is intrinsically resistant to pyrazinamide. Beyond its use for specific *M. bovis* identification, this natural resistance is particularly important to consider. Pyrazinamide is usually given in the classical first-line TB treatment, as it is an effective sterilising drug that helps to shorten TB therapy due to its synergistic effect with rifampicin .A major challenge in the case of effective treatment and recovery of a patient infected with zoonotic TB is the natural resistance of *M. bovis* to pyrazinamide, one of the four essential medications used in the standard first-line anti-TB treatment regimen (Cousins *et al.,* 1989).

Most of the health-care providers initiate the treatment without drug susceptibility testing due to which patients with zoonotic TB may receive inadequate treatment. This may lead to development of resistance to other anti-TB drugs. Resistance to additional drugs has also been reported in some *M. bovis* isolates, including rifampicin and isoniazid, and resistance to these two essential first-line drugs is defined as a multidrug-resistant TB, which is a major threat to human health globally. Such a shortcoming has significant implications for the treatment of zoonotic TB. Because most patients worldwide begin tuberculosis treatment without identification of the causative mycobacterium species, the risk of inadequate treatment of patients with undiagnosed *M. bovis* who do not have drug susceptibility testing is increased (Allix-Béguec *et al.,* 2010).

Diagnosis of active TB in people in many parts of the world is based on the sputum smear examination or some rapid assays like Xpert MTB/RIF. But these commonly used tests are not able to differentiate the *M. tuberculosis* complex into the distinct species of *M. tuberculosis* and *M. bovis* ; therefore, most cases of zoonotic TB are misclassified. The identification of *M. bovis* can be done by PCR and gene sequencing of culture isolates, but for these tests the proper collection of samples is very essential as zoonotic TB is extra-pulmonary. However, most of the countries lack the capacity to routinely conduct these tests(Allix-Béguec *et al.,* 2010).

Absence of specific identification of *M. bovis* may have adverse consequences for TB patient management and even in high-income countries, human TB due to *M. bovis* is underestimated, because of frequent use of identification techniques that do not specifically distinguish *M. bovis* from the rest of the *M. tuberculosis* complex, and because susceptibility to pyrazinamide is not systematically tested (Allix-Béguec *et al.,* 2010). Microbiologic methods (acid-fast smear and mycobacterial culture) must be used to discriminate latent from active TB. Unfortunately, acid-fast smears are relatively insensitive for TB diagnosis, and mycobacterial culture requires clinicians to wait up to several weeks to obtain a result as well as significant investments in equipment. Recently, Interferon-gamma Release Assays (IGRAs) have been developed which deal with some of the TST's limitations (Nahid *et al.,* 2006)

Therefore, clinical laboratories should routinely use molecular tests to differentiate *M. bovis* from *M. tuberculosis* and/or systematically check resistance to pyrazinamide and molecular-guided cooperation between human and veterinary health services can improve detection of zoonoses. Long standing risky feeding practices such as eating of raw meat and drinking of raw milk and very common close contact of animals with humans in most rural areas not, so far, been avoided in the rural areas. These conditions are considered as main potential risk factors that favor the spreading of zoonotic TB between human and cattle (Mamo *et al.,* 2012).

CONCUSION AND RECOMMENDATIONS

Bovine tuberculosis (bTB) is chronic bacterial disease, caused by *Mycobacterium bovis*, distributed globally. Although bTB mainly affects cattle, humans as well as domestic and wildlife animal species are also affected. The main route of transmission is through consumption of unpasteurized dairy products, and thus *M. bovis* usually presents as extra-pulmonary disease. Cattle kept under intensive and semi-intensive production systems had higher prevalence of bTB than those kept in extensive livestock production system. In humans TB due to *M. bovis* is clinically, radiologically and pathologically indistinguishable from disease caused by *M. tuberculosis*. Absence of specific identification of *M. bovis* may have adverse consequences for TB patient management and even in high-income countries, human TB due to *M. bovis* is underestimated, because of frequent use of identification techniques that do not specifically distinguish *M. bovis* from the rest of the *M. tuberculosis* complex, and because susceptibility to pyrazinamide is not systematically tested. The standard control measure applied to bTB is test and slaughter. The life styles of the Ethiopian communities, close contact with domestic animals and/or the habit of consuming raw animal products, are suggested as the main factors for transmission of *M. bovis* and *M. tuberculosis* between humans and animals, which may have impact on the TB control program in human. The role of animal in the transmission of the causative agent has been neglected which could be one of the challenges for an effective control program. Zoonotic TB cannot be controlled by the human or animal health sector alone. The increase of this disease in such areas calls for stronger intersectoral collaboration between the medical and veterinary professions to assess and evaluate the scale of the problem, mostly when zoonotic TB could represent a significant risk.

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

- Educating the people about the risk of bTB transmission through consumption of raw/under-cooked meat and unpasteurized milk are effective implementation of TB control measures.
- Molecular epidemiological studies, tuberculin test and slaughterhouse surveillance across the country so as to estimate the national prevalence of bTB as well as identification and characterization of the non-*tuberculosis Mycobacterium* complex and evaluation of their pathogenicity in bovine is essential.
- Mathematical modeling of bTB transmission dynamics from cattle to humans in order to estimate the disease cost and simulate potential interventions in cattle is essential
- Developing an effective, interactive, holistic and flexible decision tools for control of bovine tuberculosis to pave the way toward elimination of the disease in Ethiopia is required

Conflict of interest:
none to declare

REFERENCES

Alemu, J., Mamo, G., Ameni, G. and Pal, M., (2016a). Molecular epidemiology of bovine tuberculosis in cattle and its public health implications in gambella region molecular Ethiopia. *Microbiol. Res*., **6**:1–15.

Alemu, B., Nazir, S., Tintagu, T. and Teklu, A.(2016b).Diagnostic efficacy of abattoir meat inspection for detecting bovine tuberculosis at Adama municipal abattoir, Ethiopia. Comp. *Clin. Pathol*. **25**: 885–893.

Ali, M. (2006): The status of bovine tuberculosis in selected area of north Gondar administrative zone, MSc. Thesis, Ethiopia.

Agusto, F.B., Lenhart, S. and Gumel, A.B.(2011). Mathematical analysis of a model for the transmission dynamics of bovine tuberculosis. *Math. Meth. Appl. Sci.,* **34**: 1873–1887.

Akpabio,U.(2015) : Review on Bovine Tuberculosis. *J. Vet. Adv*. , **5**:841.

Allix-Béguec, C., Fauville-Dufaux, M., Stoffels, K., Ommeslag, D., Walravens, K., Saegerman, C. and Supply, P.(2010). Importance of identifying *Mycobacterium bovis* as a causative agent of human tuberculosis. *Eur. Respir. J*., **35:**692-694.

Amanfu, W. (2006). The situation of tuberculosis and tuberculosis control in animals of economic interest, *Tuberculosis,* **86** :330−335.

Ameni G., Aseffa A., Engers H., Young D., Hewinson G. and Vordermeier M.(2006). Cattle husbandry in Ethiopia is a predominant factor affecting the pathology of bovine tuberculosis and gamma interferon responses to mycobacterial antigens. *Cli n. Vaccine Immunol*. **13**:1030–1036.

Ameni, G. and Erkihun, A. (2007). Bovine tuberculosis on small-scale dairy farms in Adama town, central Ethiopia, and farmer awareness of the disease. *Rev. Sci. Tech*., **26:**711–719.

Ameni, G. and Regasa, A. (2001). Survey on bovine tuberculosis in cattle and its public health implications to cattle raising families in Wolaita Soddo, southern Ethiopia. *Ethiop. J. Anim. Prod*., **1**:55–62.

Ameni, G., Amenu, K. and Tibbo, M. (2003a). Bovine Tuberculosis: prevalence and risk factor assessment in cattle and cattle owners in Wuchale-Jida district, central Ethiopia. *Int. J. Appl. Res. Vet. Med.*, **1:**17–26.

Ameni, G., Aseffa, A., Engers, H., Young, D., Gordon, S., Hewinson, G. and Vordermeier, M. (2007a). High prevalence and increased severity of pathology of bovine tuberculosis in holsteins compared to zebu breeds under field cattle husbandry in central Ethiopia. *Clin. Vaccine Immunol.,* **14**:1356–1361.

Ameni G., Amenu K., Tibbo M. (2003a). Bovine tuberculosis: prevalence and risk factors assessment in cattle and cattle owners in Wuchale-Jida district, Central Ethiopia. *Int. J. Appl. Res. Vet. Med.*, **1**:17–25

Ameni, G., Aseffa, A., Sirak, A., Engers, H., Young, D.B.,Hewinson, G.R., Vordermeie, M.H. and Gordon, S.V.(2007b). Effect of skin testing and segregation on the incidence of bovine tuberculosis, and molecular typing of *Mycobacterium bovis* in Ethiopia. *Vet. Rec.* **161**:782–786.

Ameni, G., Bekele, S. and Tolosa, T. (2010a). Preliminary study on the impact of bovine tuberculosis on the reproductive efficiency and productivity of holstein dairy cows in central Ethiopia. *Bull. Anim. Health Prod. Afr*., **58:** 222–226.

Ameni, G., Belay, M. and Medhin, G. (2003c). A preliminary study on bovine tuberculosis in stallholder farms and its zoonotic implication to owners in fitche town, central Ethiopia. Sudan *J. Vet. Res*. **18**:37–46.

Ameni, G., Bonnet, P. and Tibbo, M.(2003b). A cross-sectional study of bovine tuberculosis in selected dairy farms in Ethiopia. *Int. J. Appl. Res. Vet. Med*., **1**:253–258.

Ameni, G., Desta, F. and Firdessa, R. (2010b). Molecular typing of *Mycobacterium bovis* isolated from tuberculosis lesions of cattle in north eastern Ethiopia. *Vet. Rec*. **167**:138–141.

Ameni, G., Tadesse, K., Hailu, E., Deresse, Y., Medhin, G., Aseffa, A., Hewinson, G., Vordermeier, M. and Berg, S.(2013). Transmission of Mycobacterium tuberculosis between Farmers and Cattle in Central Ethiopia. *PLoS One*, **8**:1–10.

Ameni, G., Vordermeier, M., Firdessa, R., Aseffa, A., Hewinson, G., Gordon, S. V.and Berg, S., (2011): Mycobacterium tuberculosis infection in grazing cattle in central Ethiopia. *Vet. J.,* **188:**359–361.

Ameni, G., Wudie, A.(2003): Preliminary study on bovine tuberculosis in Nazareth municipality abattoir of central Ethiopia. *Bull. Anim. Heal. Prod. Africa,* **51:**125–132.

Amenu, K., Thys, E., Regassa, A. and Marcotty, T. (2010). Brucellosis and tuberculosis in Arsi- Negele district, Ethiopia: prevalence in ruminants and people's behaviour towards zoonoses. *Tropicultura* , **28:** 205–210.

Areda, D.B., Muwonge, A. and Dibaba, A.B. (2019). Status of Bovine Tuberculosis in Ethiopia: Challenges and Opportunities for Future Control and Prevention. In: Dibaba A., Kriek N., Thoen C. (eds) Tuberculosis in Animals: An African Perspective. Springer, Cham

Ashford, D.A., Whitney, E., Raghunathan, P.and Cosivi, O.(2001). Epidemiology of selected mycobacteria that infect humans and other animals. *Rev. Sci. Tech*., **20:** 325–337.

Asseged, B., Woldesenbet, Z., Yimer, E.and Lemma, E.(2004). Evaluation of abattoir inspection for the diagnosis of *Mycobacterium bovis* infection in cattle at Addis Ababa abattoir. *Trop. Anim. Health Prod*., **36:** 537–546.

Asseged, B., Lübke-Becker, A., Lemma, E.,Taddele, K., Bayleyegn, M. and Britton, S.(2000). Bovine tuberculosis: cross-sectional and epidemiological study in and around Addis Ababa. *Bull. Anim. Health Prod. Afr*., **48:**71–80

Awada ,L., Tizzani ,P., Erlacher-Vindel ,E., Forcella, S. and Caceres P.(2018). Bovine Tuberculosis: Worldwide Picture.in ''Bovine Tuberculosis'', M.Chambers, S.,Gordon,F.,Oea-Popelka, P.Barrow(eds).CAB International. Pp.1-15

Ayana, T., Tafess, K., Mamo, G., Sisay, T.T. and Ameni, G.(2013). Isolation and molecular characterization of non-tuberculosis mycobacteria from skin positive reactors and pathological lesions of cattle at Bako, Western Ethiopia. *Afr. J. Microbiol. Res*., **7**:2190–2197.

Ayele, W.Y., Neill, S.D., Zinsstag, J., Weiss, M.G.and Pavlik, I.(2004). Bovine tuberculosis: an old disease but a new threat to Africa. *Int. J. Tuberc. Lung Dis.,* **8:** 924–937.

Aylate, A., Shah, S.N., Aleme, H.and Gizaw, T.T. (2013). Bovine tuberculosis: prevalence and diagnostic efficacy of routine meat inspection procedure in Woldiya municipality abattoir north Wollo zone, Ethiopia. *Trop. Anim. Health Prod*., **45**:855–864.

Bekele, M. and Belay, I. (2011). Evaluation of routine meat inspection procedure to detect bovine tuberculosis suggestive lesions in Jimma municipal abattoir, south west Ethiopia. *Glob. Vet*., **6:**172–179.

Bekele, M., Mamo, G., Mulat, S., Ameni, G., Beyene, G. and Tekeba, E. (2016). Epidemiology of bovine tuberculosis and its public health significance in debre- zeit intensive dairy farms, Ethiopia. *Biomed. Nurs*. **2**:8–18.

Berg, S., Firdessa, R., Habtamu, M., Gadisa, E., Mengistu, A., Yamuah, L., Ameni, G., Vordermeier, M., Robertson, B.D., Smith, N.H., Engers, H., Young, D., Hewinson, R.G., Aseffa, A. and Gordon, S.V. (2009). The burden of Mycobacterial disease in Ethiopian cattle: implications for public health, *PLOS one,* **4:**e5068. http://dx.doi.org/10. 1371/journal.pone.0005068.

Bezos, J., Álvarez, J., Romero, B., Aranaz, A.and de Juan, L. (2012). Tuberculosis in goats: assessment of current in vivo cell-mediated and antibody-based diagnostic assays. *Vet. J.* **191:** 161–165.

Bidart, R.(2011): Bovine tuberculosis. Bov. Tuberc. 1–2. https://doi.org/10.5962/bhl.title.26710

Biru, A., Ameni, G., Sori, T., Disassa, F., Teklu, A. and Tafess, K. (2014). Epidemiology and public health significance of bovine tuberculosis in and around Sululta District, Central Ethiopia. *Afr. J. Microbiol. Res*., **8:**2352–2358.

Buddle, B.M., Vordermeier, H.M. and Chambers, M.A. (2018). Efficacy and Safety of BCG Vaccine for Control of Tuberculosis in Domestic Livestock and Wildlife, *Front Vet Sci.,***5**:1–17.

Buddle MB, Wedlock ND, Parlane A.N, Corner LAL, Lisle WG and Skinner AM (2003). Reactivation of neonatal caves with *Mycobacterium bovis* BCG reduces the level of protection against bovine tuberculosis induced by single vaccination. *Infection and Immunity*, **71**:6411– 6419.

Bussa, M.W.(2014).Survey of bovine tuberculosis in guduru cattle breeding and research center, Western Ethiopia. *Agric. Healthcare,* **4**:215–219.

Centis, R., D'Ambrosio, L., Zumla, A., Migliori, G.B.(2017). Shifting from tuberculosis control to elimination: Where are we? What are the variables and limitations? Is it achievable? Int. J. Infect. Dis., 56, 30–33.

Chukwu, I.D., Chukwu, C.O.O., Kandakai-Olukemi, Y.T., Owolodun, O., Nwosuh, C., Agada, G.O., Audu, B.J.and Chollom, S.C.(2013). Detection of Mycobacterium tuberculosis complex in lung specimen of slaughtered cattle and goats by a DNA based multiplex polymerase chain reaction and Ziehl-Neelsen methods in Jos, Nigeria. *Microbiol. Res. J. Int.,* **3**:550–556.

Conlan, A.J.K., Pollock, E.B., Mckinley, T.J., Mitchell, P., Jones, G.J., Vordermeier, M. and Wood, J.L.N. (2015). Potential Benefits of Cattle Vaccination as a Supplementary Control for Bovine Tuberculosis 1–26. https://doi.org/10.1371/journal.pcbi.1004038

Constable, P.D., Hinchcliff, K.W., Done, S.H. and Grünberg, W. (2017). Bovine tuberculosis. Veterinary Medicine: A Textbook of the Diseases of Cattle, Horses, Sheep, Pigs, and Goats, 11th ed. Elsevier, St. Louis, Missouri, pp. 2015–2023.

Cousins, D. V.(2001). *Mycobacterium bovis* infection and control in domestic livestock. *Rev. Sci. Tech. Int. des Epizoot*., **20**: 71–85.

Cousins D.V., Francis, B.R. and Gow, B.L. (1989). Advantages of a new agar medium in the primary isolation of *Mycobacterium bovis*. *Veterinary Microbiology*. **20**:89-95

Dejene, S.W., Heitkönig, I.M., Prins, H.H., Lemma, F.A., Mekonnen, D.A., Alemu, Z.E., Kelkay, T.Z. and de Boer, W.F. (2016). Risk factors for bovine tuberculosis (bTB) in cattle in Ethiopia. PLoS One **11**:e0159083. http://dx.doi.org/10.1371/journal.pone. 0159083

Demelash, B., Inangolet, F., Oloya, J., Asseged, B., Badaso, M., Yilkal, A. and Skjerve, E.(2009). Prevalence of Bovine tuberculosis in Ethiopian slaughter cattle based on post-mortem examination. Trop Anim Heal. Prod., **41**:755–765.

De la Rua-Domenech, R., Goodchild, A.T., Vordermeier, H.M., Hewinson, R.G., Christiansen, K.H. and Clifton-Hadley, R.S.(2006). Ante mortem diagnosis of tuberculosis in cattle: a review of the tuberculin tests, γ-interferon assay and other ancillary diagnostic techniques. *Res. Vet. Sci*., **81:**190–210.

De la Rua-Domenech, R. (2006). Human *Mycobacterium bovis* infection in the United Kingdom: Incidence, risks, control measures and review of the zoonotic aspects of bovine tuberculosis, *Tuberculosis,* **86**:77–109.

Dharamdheeran, S., Nigam, P., Prasad, H.K.and Katoch, V.M.(2008). Isolation of *Mycobacterium bovis* and M. tuberculosis from cattle of some farms in north India-possible relevance in human health. Indian J. Med. Res., 128:26–31.

Dibaba, A.B., Kriek, N.P. and Thoen, C.O.(2019). Tuberculosis in Animals: An African Perspective. https://doi.org/10.1007/978-3-030-18690-6_2

Dinka, H. and Duressa, A. (2011). Prevalence of bovine tuberculosis in arsi zones of oromia, Ethiopia. *Afr. J. Agric. Res*., **6**:3853–3858

Domingo, M., Vidal, E. and Marco, A.(2014). Pathology of bovine tuberculosis. *Res. Vet. Sci*., **97:** 20–29.

Duguma, A., Abera, S., Zewdie, W., Belina, D. and Haro, G. (2016). Status of bovine tuberculosis and its zoonotic implications in Borana zone, Southern Ethiopia. Trop. *Anim Health Prod*., **49**: 445–450

Elias, K., Hussein, D., Asseged, B., Wondwossen, T. and Gebeyehu, M. (2008). Status of bovine tuberculosis in Addis Ababa dairy farms. *Rev. Sci. Tech*. **27**:915–923.

El-Sayed, A., El-Shannat, S., Kamel, M., Castañeda-Vazquez, M.A. and Castañeda-Vazquez, H.(2016). Molecular epidemiology of *Mycobacterium bovis* in humans and cattle. *Zoonoses Public Health,* **63:**251–264.

Endalew, M.A., Gelalcha, B.D. and GobenaAmeni, G. (2017). Bovine tuberculosis prevalence, potential risk factors and its public health implication in selected state dairy farms, Central Ethiopia. *World Vet. J.* **7**:21–29.

Ewnetu, L., Melaku, A. and Birhanu, A. (2012). Bovine tuberculosis prevalence in slaughtered cattle at Akaki municipal abattoir, based on meat inspection methods. *Glob Vet*., **9**:541–545.

Fetene, T. and Kebede, N. (2009). Bovine tuberculosis of cattle in three districts of northwestern Ethiopia. *Trop. Anim. Health Prod*. **41**:273–277

Fikru, R., Bonnet, P. and Moges, W. (2005). Prevalence of bovine tuberculosis in indigenous Zebu cattle under extensive farming system in Western Ethiopia. *Bull. Anim. Health Prod. Afr*., **53**:85–88.

Firdessa, R., Tschopp, R., Wubete, A., Sombo, M., Hailu, E., Erenso, G., Kiros, T., Yamuah, L., Vordermeier, M., Hewinson, R.G., Young, D., Gordon, S. V, Sahile, M., Aseffa, A.and Berg, S.(2012). High Prevalence of Bovine Tuberculosis in Dairy Cattle in Central Ethiopia : Implications for the Dairy Industry and Public Health. *PLOS Neglected Trop. Dis.,* **7:**1–12.

Finlay, E.K., Berry, D.P., Wickham, B., Gormley, E.P. and Bradley, D.G.(2012). A genome wide association scan of bovine tuberculosis susceptibility in Holstein-Friesian dairy cattle. *PLoS One*, 7: e30545.

Floyd, K., Glaziou, P., Houben, R.M.G.J., Sumner, T., White, R.G. and Raviglione, M.(2018). Global tuberculosis targets and milestones set for 2016–2035: definition and rationale. *Int. J. Tuberc. Lung Dis.,* **22**:723–730.

Forrellad, M.A., Klepp, L.I., Gioffré, A., Sabio y Garcia, J., Morbidoni, H.R., Santangelo, M.D.L.P., Cataldi, A.A. and Bigi, F.(2013). Virulence factors of the Mycobacterium tuberculosis complex. *Virulence,* **4** : 3–66.

Gebrezgabiher, G., Romha, G. and Ameni, G. (2014). Prevalence study of bovine tuberculosis and genus typing of its causative agents in cattle slaughtered at Dilla municipal abattoir, southern Ethiopia. *Afr. J. Basic Appl. Sci*. **6**:103–109.

Gelalcha, B.D., Zewude, A. and Ameni, G.(2019). Tuberculosis Caused by *Mycobacterium bovis* in a Sheep Flock Colocated with a Tuberculous Dairy Cattle Herd in Central Ethiopia. *J. ofVeterinary Med.*, **2019:**1–6.

Global Plan to End TB 2016 – 2020(2016). The Paradigm Shift. Geneva: Stop TB Partnership; 2016 (*http://www.stoptb.org/global/plan/plan2/).*

Global Plan to End TB (2014). Paradigm shift 2016-2020. Geneva, Switzerland: STOP TB Partnership. Available at: http://www.stoptb.org/assets/documents/ global/plan/plan2/ExecutiveSummary.pdf (accessed July 10, 2019).

Gumi, B., Schelling, E., Firdessa, R., Aseffa, A., Tschopp, R., Yamuah, L., Young, D. and Zinsstag, J. (2011). Prevalence of bovine tuberculosis in pastoral cattle herds in the Oromia region, southern Ethiopia. *Trop. Anim. Health Prod*., **43**:1081–1087

Gumi, B., Schelling, E., Firdessa, R., Erenso, G., Biffa, D., Aseffa, A., Tschopp, R., Yamuah, L., Young, D. and Zinsstag, J. (2012). Low prevalence of bovine tuberculosis in Somali pastoral livestock, Southeast Ethiopia. *Trop. Anim. Health Prod*., **44**:1445–1450

Gumi, B., Schelling, E., Berg, S., Firdessa, R., Erenso, G., Mekonnen, W., Hailu, E., Melese, E., Hussein, J., Aseffa, A. and Zinsstag, J. (2012). Zoonotic Transmission of Tuberculosis Between Pastoralists and Their Livestock in South-East Ethiopia. *EcoHealth.* **9:** 139–149

Humblet, M.F., Boschiroli, M.L. and Saegerman, C.(2009). Classification of worldwide bovine tuberculosis risk factors in cattle: a stratified approach. *Veterinary research*, **40:**1-24.

Kaneene, J.B. and Pfeiffer, D.(2006). Epidemiology of *Mycobacterium bovis*. In: Thoen, C.O., Steele, J.H., Gilsdorf, M.J. (Eds.), *Mycobacterium bovis* Infection in Animals and Humans, 2nd ed. Blackwell Publishing, Ames, Iowa, pp. 34–48.

Kazwala, R.R., Kambarage, D.M., Daborn, C.J., Nyange, J., Jiwa, S.F.H. and Sharp, J.M. (2001). Risk factors associated with the occurrence of bovine tuberculosis in cattle in the Southern Highlands of Tanzania. *Vet. Res. Commun*., **25**:609–614

Kelly, R.F., Hamman, S.M., Morgan, K.L., Nkongho, E.F., Ngwa, V.N., Tanya, V., Andu, W.N., Sander, M., Ndip, L. and Handel, I.G.(2016). Knowledge of bovine tuberculosis, cattle husbandry and dairy practices amongst pastoralists and small-scale dairy farmers in Cameroon. *PLoS One,* **11**: e0146538.

King, H.C., Murphy, A., James, P., Travis, E., Porter, D., Sawyer, J., Cork, J., Delahay, R.J., Gaze, W., Courtenay, O. and Wellington, E.M.(2015). Performance of a Noninvasive Test for Detecting *Mycobacterium bovis* Shedding in European Badger (Meles meles) Populations. *J. Clin. Microbiol*., **53:**2316–2323.

Krauss, H., Weber, A., Appel, M., Enders, B., Senberg, D., Schiefer, G., Slenczka, W. and von Graevenitz, A.(2003). Zahner Zoonoses: Infectious Diseases Transmissible From Animals to Humans (3rd Ed.), 2003: 213.

Kwaghe, A. (2015). Bovine tuberculosis: Effects and challenges faced by developed and developing countries in the eradication process, CAB Reviews: Perspectives in Agriculture, Veterinary Science, Nutrition and Natural Resources. https://doi.org/10.1079/PAVSNNR201510036

Langer, A.J. and LoBue, P.A.(2014). Public health significance of zoonotic tuberculosis caused by the Mycobacterium tuberculosis complex. Zoonotic Tuberc. *Mycobacterium bovis* Other Pathog. Mycobacteria. Third Ed. Ed, 2014, Pp.21–33.

Laval, G. and Ameni, G. (2004): Prevalence of bovine tuberculosis in zebu cattle under traditional animal husbandry in Boji district of Western Ethiopia. *Rev. Méd.Vét*. **155**:494–499.

Mahmud, M.A.A., Belal, S.M.S.H. and Shoshe, N.Z. (2014). Prevalence of bovine tuberculosis in cattle in the selected Upazila of Sirajganj district in Bangladesh. *Bangladesh Journal of Veterinary Medicine*, ***12*:**141-145.

Mamo, G., Abebe, F., Worku, Y., Getachew, T., Hussein, N., Legesse, M., Tilahun, G., Medhin, G., Bjune, G. and Ameni, G.(2013). Bovine tuberculosis and its associated risk factors in pastoral and agro-pastoral cattle herds of Afar Region , Northeast Ethiopia. *J. Vet. Med. Anim. Heal. Threat,* **5**:171–179.

Mamo G, Kassaye A, Sanni, M, Ameni G (2009). A cross sectional study of camel tuberculosis in Ethiopia. *Bull Anim Hlth Prod Afr,* **57**: 13-20.

Mamo, G., Abebe, F., Worku, Y., Legesse, M., Medhin, G., Bjune, G.and Ameni, G.(2012). Tuberculosis in goats and sheep in Afar Pastoral Region of Ethiopia and isolation of Mycobacterium tuberculosis from goat. *Vet. Med. Int*., **10**:1-8.

Mamo, G., Baylegn, G., Sisay Tessema, T., Legesse, M. and Medhin, G. (2011). Pathology of camel tuberculosis and molecular characterization of its causative agents in pastoral region of Ethiopia. *PLOS one,* **6:**158-162.

Mariam, S.(2014). Identification and survival studies of Mycobacterium tuberculosis within laboratory-fermented bovine milk. *BMC Res.,* **7:**175

Markos, T. and Tadesse, T.(2017). Review on the Epidemiology , Public Health and Economic Importance of Bovine Tuberculosis. *J. Biol. Agric. Healthc***.,** **7:**16–23.

Michel, A.L., Bengis, R.G., Keet, D.F., Hofmeyr, M., De Klerk, L.M., Cross, P.C., Jolles, A.E., Cooper, D., Whyte, I.J. and Buss, P.(2006). Wildlife tuberculosis in South African conservation areas: implications and challenges. *Vet. Microbiol*., **112**: 91–100.

Mekibeb, A., Fulasa, T.T., Firdessa, R. and Hailu, E. (2013). Prevalence study on bovine tuberculosis and molecular characterization of its causative agents in cattle slaughtered at Addis Ababa municipal abattoir, Central Ethiopia. *Trop. Anim. Health Prod*., **45**:763–769

Naugle, A., Schoenbaum, M., Hench, C.W., Henderson, O.L. and Shere, J. (2014). Bovine tuberculosis eradication in the United States. In: Thoen CO, Steele JH, Kaneene JB, eds. Zoonotic Tuberculosis: *Mycobacterium bovis* and Other Pathogenic Mycobacteria, 3rd Edition, Ames, IA: Wiley- Blackwell Publishing, 2014; Pp.235-52.

Nahid, P., Pai, M. and Hopewell, P.C. (2006). Advances in the Diagnosis and Treatment of Tuberculosis. *Proc Am Thorac Soc*., **3**:103–10

Neill, S.D., Bryson, D.G.and Pollock, J.M.(2001). Pathogenesis of tuberculosis in cattle. *Tuberculosis,* **81**:79–86.

Nishi, J.S., Shury, T. and Elkin, B.T.(2006).Wildlife reservoirs for bovine tuberculosis (*Mycobacterium bovis*) in Canada: strategies for management and research. *Vet. Microbiol.,* **112**:325–338.

Ntoumi, F., Kaleebu, P., Macete, E., Mfinanga, S., Chakaya, J., Yeboah-Manu, D., Bates, M., Mwaba, P., Maeurer, M., Petersen, E. and Zumla, A.(2016).Taking forward the World TB Day 2016 theme "Unite to End Tuberculosis" for the WHO Africa Region. *Int. J. Infect. Dis*., **46**:34–37.

Nuru, A., Zewdie, A., Mohammed, T., Wondale, B., Teshome, L., Getahun, M., Mamo, G., Medhin, G., Pieper, R. and Ameni, G.(2017). Nontuberculosis mycobacteria are the major causes of tuberculosis like lesions in cattle slaughtered at Bahir Dar Abattoir, northwestern Ethiopia. *BMC Vet. Res*. 13:237.

Nwanta, A., Onunkwo, J., Wilfred, E. and Umeononigwe, C.(2010). Zoonotic tuberculosis: A review of epidemiology, clinical presentation, prevention and control. *J. Public Heal. Epidemiol.,* **2** :118–124.

Olea-Popelka, F., Fujiwara, P.I.(2018). Building a Multi-Institutional and Interdisciplinary Team to Develop a Zoonotic Tuberculosis Roadmap. *Front. Public Heal*. **6**:1–5.

Olea-Popelka, F., Muwonge, A., Perera, A., Dean, A.S., Mumford, E., Erlacher-Vindel, E., Forcella, S., Silk, B.J., Ditiu, L., El Idrissi, A., Raviglione, M., Cosivi, O., LoBue, P., and Fujiwara, P.I.(2017). Zoonotic tuberculosis in human beings caused by *Mycobacterium bovis*—a call for action*. Lancet Infect. Dis*., **17**: e21–e25.

Oloya J., Muma J.B., Opuda-Asibo J., Djønne B., Kazwala R. and Skjerve E.(2007). Risk factors for herd-level bovine tuberculosis seropositivity in transhumant cattle in Uganda. *Prev. Vet. Med.,* **80**:318–329

Onozaki, I and Raviglione, M.(2010). Stopping tuberculosis in the 21st century: goals and strategies. *Respirology,* **15**:32–43.

Pal, M. and Boru, B. (2012). Zoonotic significance of *Mycobacterium bovis* infections. *J. Nat.Hist*., **8**:86-89

Palmer, M. V., Thacker, T.C., Waters, W.R., Gortázar, C. and Corner, L.A.L.(2012). *Mycobacterium bovis* : A Model Pathogen at the

Interface of Livestock, Wildlife, and Humans . *Vet. Med. Int*., **2012**:1–17.

Parlane, N.A. and Buddle, B.M. (2015). Immunity and vaccination against tuberculosis in cattle. *Current Clinical Microbiology Reports*, **2**:44-53

Phillips, C.J.C. and Foster, C.R.W., Morris P.A. and Teverson, R. (2002). Genetic and management factors that influence the susceptibility of cattle to *Mycobacterium bovis* infection. *Anim. Health Res. Rev*., **3**:3–13.

Prasad, R., Gupta, N. and Banka, A.(2017). 2025 too short time to eliminate tuberculosis from India. *Lung India Off. organ Indian Chest Soc*., **34:**409.

Quinn, P.J., Carter, M.E., Markey, B.K. and Carter, G.R. (2004). Clinical Veterinary Microbiology. 1st Edition, a John and Sons, Dublin. Pp. 157-169

Radostits, O.M., Gay, C.C., Blood, D.C., Hinchcliff, K.W. and Arundel, J.H.(2000). Mastitis. Vet. Med., **9**:603–700.

Ramos, D.F., Silva, P.E.A. and Dellagostin, O.A.(2015). Diagnosis of bovine tuberculosis : review of main techniques. *Braz. J. Biol.,* **75:** *830-837*

Raviglione, M.and Sulis, G.(2016). Tuberculosis 2015: Burden, challenges and strategy for control and elimination. *Infect. Dis. Rep*., **8**:33–37.

Regassa, A.(2005). Study on *Mycobacterium bovis* infection in humans and animals in Northwest Shoa Zone, Oromia National Regional State. *Msc. Thesis*, Ethiopia

Regassa, A., Tassew, A., Amenu, K., Megersa, B., Abunna, F., Mekibib, B., Marcotty, T. and Ameni, G. (2010). A cross-sectional study on bovine tuberculosis in Hawassa town and its surroundings: Southern Ethiopia. *Trop. Anim. Health Prod*., **42**: 915–920

Rodriguez-Campos, S., Smith, N.H., Boniotti, M.B. and Aranaz, A.(2014). Overview and phylogeny of Mycobacterium tuberculosis complex organisms: implications for diagnostics and legislation of bovine tuberculosis. *Res. Vet. Sci*., **97**: 5–19.

Romha, G., Ameni, G., Berhe, G. and Mamo, G. (2013). Epidemiology of mycobacterial infections in cattle in two districts of Western Tigray Zone, Northern Ethiopia. *Afr. J. Microbiol. Res.,* **7**:4031–4038.

Romha, G., Gebreegziabher, G. and Ameni, G. (2014): Assessment of bovine tuberculosis andits risk factors in cattle and humans, at and around Dilla town, Southern Ethiopia. *Anim. Vet. Sci.,* **2**:94–100

Romha, G., Gebru, G., Asefa, A. and Mamo, G.(2018). Epidemiology of *Mycobacterium bovis* and Mycobacterium tuberculosis in animals: Transmission dynamics and control challenges of zoonotic TB in Ethiopia. *Prev. Vet. Med*., **158**:1–17.

Rowe, M.T. and Donaghy, J.(2008). *Mycobacterium bovis*: The importance of milk and dairy products as a cause of human tuberculosis in the UK. A review of taxonomy and culture methods, with particular reference to artisanal cheeses. *Int. J. Dairy Technol*., **61**:317–326.

Schiller, I., Oesch, B., Vordermeier, H.M., Palmer, M. V, Harris, B.N., Orloski, K.A., Buddle, B.M., Thacker, T.C., Lyashchenko, K.P. and Waters, W.R.(2010). Bovine tuberculosis: a review of current and emerging diagnostic techniques in view of their relevance for disease control and eradication. *Transbound. Emerg. Dis*., **57**: 205–220.

Sibhat, B., Asmare, K., Demissie, K., Ayelet, G., Mamo, G. and Ameni, G.(2017). Bovine tuberculosis in Ethiopia: Systematic review and meta-analysis. *Prev.Vet.Med*.,**147:** 149–157.

Shitaye, J.E., Tsegaye, W. and Pavlik, I. (2007). Bovine tuberculosis infection in animal and human populations in Ethiopia: *Vet Med*., **8:** 317-332.

Shitaye, J.E., Getahun, B., Alemayehu, T., Skoric, M., Treml, F., Fictum, P., Vrbas, V. and Pavlik, I.(2006). A prevalence study of bovine tuberculosis by using abattoir meat inspection and tuberculin skin testing data, histopathological and IS6110 PCR examination of tissues with tuberculous lesions in cattle in Ethiopia. *Vet. Med (Praha.)* **51**:512–522.

Sihvonen, L.H. and Willeberg, P.(2017). Assessment of listing and categorisation of animal diseases within the framework of the Animal Health Law (Regulation (EU) No 2016/429): bovine tuberculosis. *EFSA J*., **15**:4959

Stop TB Strategy (2006). Building on and enhancing DOTS to meet th e TB-related MillenniumDevelopment Goals.Geneva, World Health Or ganization, 2006WHO/HTM/TB/2006.368)

Sulis, G., Roggi, A., Matteelli, A. and Raviglione, M.C.(2014). Tuberculosis: epidemiology and control. Mediterr. J. Hematol. Infect. Dis., **6**: e2014070

Tamiru, F., Hailemariam, M. and Terfa, W.(2013). Preliminary study on prevalence of bovine tuberculosis in cattle owned by tuberculosis positive and negative farmers and assessment of zoonotic awareness in Ambo and Toke Kutaye districts, Ethiopia. *J. Vet. Med. Anim. Heal*., **5**:288–295.

Tanimura, T., Jaramillo, E., Weil, D., Raviglione, M. and Lönnroth, K.(2014). Financial burden for tuberculosis patients in low-and middle-income countries: a systematic review. *Eur. Respir. J.,* **43**:1763–1775.

Teklu, A., Asseged, B., Yimer, E., Gebeyehu, M. and Woldesenbet, Z. (2004). Tuberculous lesions not detected by routine abattoir inspection: the experience of the Hossana municipal abattoir, Southern Ethiopia. *Rev. Sci. Tech*., **23**: 957–964

Teppawar, R.N., Chaudhari, S.P., Moon, S.L., Shinde, S. V, Khan, W.A., Patil, A.R.(2018). Zoonotic tuberculosis: a concern and strategies to combat, in: Basic Biology and Applications of Actinobacteria. IntechOpen.Pp.23-38

Terefe, D. (2014). Gross pathological lesions of bovine tuberculosis and efficiency of meat inspection procedure to detect-infected cattle in Adama municipal abattoir. *J. Vet. Med. Anim. Health,* **6:**48–55.

Tigre, W., Alemayehu, G., Abetu, T. and Ameni, G. (2012). Preliminary study on the epidemiology of bovine tuberculosis in Jimma and its surroundings, Southwestern Ethiopia. *Afr. J. Microbiol. Res*., **6**:2591–2597

Tschopp, R., Aseffa, A., Schelling, E., Berg, S., Hailu, E., Gadisa, E., Habtamu, M., Argaw, K., and Zinsstag, J. (2010a). Bovine tuberculosis at the wildlife-livestock-human interface in Hamer Woreda, South Omo, and southern Ethiopia. *PLoS One* **5**:e12205. http://dx.doi.org/10.1371/journal.pone.0012205.

Tschopp, R., Schelling, E., Hattendorf, J., Young, D., Aseffa, A. and Zinsstag, J. (2010b). Repeated cross-sectional skin testing for bovine tuberculosis in cattle kept in a traditional husbandry system in Ethiopia. Vet. Rec., **167**: 250–256.

Tschopp, R., Schelling, E., Hattendorf, J., Aseffa, A. and Zinsstag, J.(2009). Risk factors of bovine tuberculosis in cattle in rural livestock production systems of Ethiopia. *Prev. Vet. Med*. **89:** 205–211.

Tschopp, R.,Bobosha, K., Aseffa, A., Schelling, E., Habtamu, M., Iwnetu, R., Hailu, E., Firdessa, R., Hussein, J., Young, D. and Zinsstag, J.(2011). Bovine tuberculosis at a cattlesmall ruminant-human interface in Meskan, Gurage region, Central Ethiopia. *BMC Infect. Dis.*, **11**:318.

Tschopp, R., Abera, B., Sourou, S.Y., Guerne-Bleich, E., Aseffa, A., Wubete, A., Zinsstag, J. and Young, D.(2013). Bovine tuberculosis and brucellosis prevalence in cattle from selected milk cooperatives in Arsi zone, Oromia region, Ethiopia. *BMC Vet. Res*., **9**:163.

Tschopp, R., Bekele, S., Moti, T., Young, D. and Aseffa, A. (2015). Brucellosis and bovine tuberculosis prevalence in livestock from pastoralist communities adjacent to Awash National Park, Ethiopia. *Prev. Vet. Med*., **120**:187–194.

Tschopp, R., Hattendorf, J., Roth, F., Choudhoury, A., Shaw, A., Aseffa, A. and Zinsstag, J.(2012). Cost estimate of bovine tuberculosis to Ethiopia. In *One Health: The Human-Animal-Environment Interfaces in Emerging Infectious Diseases* (pp. 249-268). Springer, Berlin, Heidelberg

Tschopp, R., Berg, S., Argaw, K., Gadisa, E., Habtamu, M., Schelling, E.D., Young, Aseffa, A. and Zinsstag, J. (2010). Bovine Tuberculosis in Ethiopian Wildlife. *JWD*. **3**: 753–762

Tsegaye, W., Aseffa, A., Mache, A., Mengistu, Y., Berg, S. and Ameni, G.(2010). Conventional and molecular epidemiology of bovine tuberculosis in dairy farms in addis ababa city, the capital of Ethiopia. *Int. J. Appl. Res. Vet. Med*., **8**:143–151.

Thoen, C.O., LoBue,P., Enarson,D.A., Kaneene, J.B. and de Kantor, I.N.(2009). Tuberculosis: a re-emerging disease of animals and humans. *Veterinaria Italiana*, **45**:135–81.

Une, Y.and Mori, T.(2007). Tuberculosis as a zoonosis from a veterinary perspective. *Comp Immunol Microbiol Infect Dis*., **30**:415–25.

Unger, F., Münstermann, S., Goumou, A., Apia, C.N.and Konte, M.(2003). Risk associated with *Mycobacterium bovis* infections detected in selected study herds and slaughter cattle in 4 countries of West Africa. Banjul ITC (International Trypanotolerance Centre), Pp.1–25.

Uplekar, M.(2015). Implementing the End TB Strategy: Well begun will be half done. *Indian J. Tuberc*., **62**:61–63.

Uplekar, M. and Raviglione, M.(2015). WHO's End TB Strategy: From stopping to ending the global TB epidemic. *Indian J. Tuberc.,* **62**:196–199.

Usman, A., Ballah,F.M., Kudi, A.C, K., Loveth, L. Abdulrazak, H. and Abdulkadir**,** I.A(2016). Molecular Identification of Mycobacterium tuberculosis Transmission between Cattle and Man : A Case Report. *J.Microbiol Exp*., **3**:1-3

Waters, W.R., Maggioli, M.F., McGill, J.L., Lyashchenko, K.P.and Palmer, M. V(2014). Relevance of bovine tuberculosis research to the understanding of human disease: historical perspectives, approaches, and immunologic mechanisms. *Vet. Immunol. Immunopathol*., **159**: 113–132.

Whelan, A.O., Hope, J.C., Howard, C.J., Clifford, D. and Hewinson, R.G. (2003). Modulation of the bovine delayed-type hypersensitivity responses to defined mycobacterial antigens by a synthetic bacterial lipopeptide*. Infect Immun.,* **71**:6420-6425.

Wirth, T., Hildebrand, F., Allix-Béguec, C., Wölbeling, F., Kubica, T., Kremer, K., van Soolingen, D., Rüsch-Gerdes, S., Locht, C. and Brisse, S.(2008). Origin, spread and demography of the Mycobacterium tuberculosis complex. *PLoS Pathog*. 4, e1000160.

Woldemariam, T., Mamo, G., Mohammed, T. and Ameni, G. (2016). Prevalence of bovine tuberculosis in beef feedlot of Borena cattle by using comparative intradermal skin test, Adama, Ethiopia. *Ethiop. Vet. J*., **20**:17–29.

World Organisation for Animal Health (OIE). (2014). Report of the meeting of the OIE scientific commission for animal diseases, Paris, Pp.15-19 ,September 2014

World Organisation for Animal Health (OIE) (2012). WAHIS Portal: Animal Health Data. Available at http://www.oie.int/en/animal-health-in-theworld/wahis-portal-animal-health-data/ (accessed Jully 20, 2019).

World Health Organization (2014). Resolution WHA67/11: Global strategy and targets for tuberculosis prevention, care and control after 2015.available from http://apps.who.int/gb/ebwha/pdf_files/WHA67/A67_11-en.pdf.

World Health Organization (WHO). (2016). *Global tuberculosis report 2016,* Geneva

World Health Organization (WHO). (2006). The Stop TB Strategy: building on and enhancing DOTS to meet the TB-related Millennium Development Goals. Geneva: World Health Organization.

World Health Organization (WHO)(2018). Global tuberculosis report 2018. World Health Organization,Geneva

World Health Organization (WHO) (2014): End TB Strategy: global strategy and targets for tuberculosis prevention, care, and control after 2015. Geneva available on http://www.who.int/tb/post2015_strategy/en

World Health Organization (2018a). *The End TB Strategy*. Available on lineat: http://www.who.int/tb/post2015_strategy/en/ (Accessed July, 2019).

World Health Organization (WHO), Food and Agriculture Organization of the United Nations (FAO) and World Organisation for Animal Health (OIE). (2017). Road map for zoonotic Tuberculosis.https://www.visavet.es/bovinetuberculosis/data/Roadmap_zoonotic_TB_OIE.pdf

World health organization (WHO) (2014). Global tuberculosis report. Geneva, Switzerland.WHO press. Pp. 1-147.

World Organisation for Animal Health (OIE). (2014). Report of the meeting of the OIE Scientific Commission for Animal Diseases. Paris, sept, 2014

Woyessa, M., Jibril, Y., Ameni, G. and Duguma, R. (2014). Molecular epidemiology of mycobacterium tuberculosis complex at Nekemte municipality abattoir, Western Ethiopia. *Sci. Technol. Arts Res. J*., **3**:167–173.

Wubit, T., (2017). Study on epidemiology of bovine tuberculosis and its public health significance in jimma town and its surroundings, south west Ethiopia,MSc thesiss,Addis Ababa University College of Veterinary medicine and agriculture,Bishoftu,Ethiopia

Yacob, H.T., Basu, A.K. and Guesh, N. (2008). Bovine pulmonary tuberclosis at Bahirdar municipality abattoir, Ethiopia. *Bull. Anim. Health Prod. Afr*., **56:**223–229.

Zeru, F., Romha, G.and Ameni, G. (2013). Gross and Molecular Characterization of Mycobacterium tuberculosis Complex in Mekelle Town Municipal Abattoir, Northern Ethiopia. *Glob Vet*., **5:** 541-546.

Zeru, F., Romha, G., Berhe, G., Mamo, G., Sisay, T. and Ameni, G.(2014). Prevalence of bovine tuberculosis and assessment of Cattle owners' awareness on its public health implication in and around Mekelle, Northern Ethiopia. *J. Vet. Med. Anim. Health*, **6**:159–167.

Zeweld, S.W., Reta, D.H., Abay, A.G. and Zelelew, Y.B.(2013). Detection of human and bovine tuberculosis using an existing diagnostic practice in residential districts of tigray region, Northern Ethiopia. *J. Environ. Occup. Sci*., **2**:77–88.

Zinsstag, J., Schelling, E., Wyss, K., Bechir Mahamat, and M. (2005). Potential of cooperation between human and animal health to strengthen health systems. *The Lancet.,* **366**:2142-45.