

Review on Epidemiological Features of *Mycobacterium Bovis* at the Human, Cattle and Wildlife Interface in Ethiopia

Summary

Mycobacterium bovis is an intracellular, non-motile, facultative, weakly Gram-positive acid-fast bacillus which belongs to the Mycobacterium tuberculosis complex. The pathogen affects all age groups of susceptible hosts of domestic, wild animals and human. In cattle, Bovine tuberculosis is one of the endemic chronic diseases of cattle that have long been recorded in Ethiopia. The disease has been reported from several parts of the country mainly based on tuberculin tests and abattoir inspections. Studies undertaken in several parts of the country have indicated that, the individual animal and the herd level prevalence rate of Bovine tuberculosis is ranging from 0.8% to 42.5% and from 7.02% to 79.3% respectively. Whereas the prevalence of the disease reported from different slaughterhouses of the country varies from 1.5% to 24.7%. *Mycobacterium Bovis* was also confirmed to be a cause of human infections in the country. However, very little information on the extent of *Mycobacterium Bovis* either as an animal or human health problem are available and the current actual prevalence rate of Bovine tuberculosis at a national level is yet unknown. No infection due to *Mycobacterium Bovis* was reported in Ethiopia wildlife population so far. In Ethiopia, cattle breeds, age, sex, body condition score and herd size, management condition, geographical origin, consumption of raw milk and close contact to livestock are most commonly identified risk factors for spread of *Mycobacterium Bovis*. Although, the disease represents a potential health hazard to all susceptible hosts, the economic effects of the disease are not well studied. With the exception of few attempts like condemnation of carcass and organs during meat inspection, culling of infected animals in some government owned farms and pasteurization of milk, effective disease control strategies do not yet established in our country.

Keywords: Bovine; Tuberculosis; *Mycobacterium Bovis*; Susceptible Hosts; Risk Factors; Ethiopia

Introduction

Mycobacterium bovis is among a pathogenic species which belongs to the Mycobacterium tuberculosis complex (MTBC), a group of genetically closely related mycobacteria [1]. *Mycobacterium bovis* (*M. bovis*) is an intracellular, non-motile, facultative, weakly Gram-positive acid-fast bacillus [2]. The MTBC sub-group also comprises *M. tuberculosis*, *M. africanum*, *M. canettii*, *M. pinnipedii*, *M. microti* and *M. caprae* that are generally regarded as host adapted but with the ability to spill over into other species. *Mycobacterium bovis* is the primary cause of bovine tuberculosis (BTB). *M. tuberculosis*, *M. africanum*, *M. caprae* and *M. canettii* are human pathogens. *M. caprae* which causes infection in goats has been initially classified as subspecies of *M. bovis* but was recently recognized as a species on its own. *M. microti* affects rodents and *M. pinnipedii* have been isolated from seals [2]. *Mycobacterium bovis* has an exceptionally wide range of mammalian hosts and affects all age groups of susceptible hosts of domestic, wild animals and human [2]. Cattle are the most common maintenance host for *M. bovis* infection from which transmission can occur to wildlife, or people animals [3]. Opossums, badgers and bison are known

maintenance hosts in different European countries and African buffalo, Kudu, deer, lechwe and wild boar have been classified as maintenance hosts for *M. bovis* in Africa [4]. Many susceptible animals and wildlife species, including man are spillover hosts in which infection is not self-maintaining [5]. Bovine tuberculosis is one of the chronic bacterial diseases of animals that can take a variable amount of time (from a few weeks to a life time) to develop from infection to clinical disease and to become infectious to other animals [2,6]. The disease mostly affects cattle and rarely other species of domestic animals [7]. The name "Tuberculosis" comes from the nodules, called 'tubercles', which form in the lymph nodes of affected animals and the disease is characterized by the progressive development of specific granulomatous lesions of tubercles in affected tissues and organs [2].

In addition to domestic animals, wild mammals can also be infected with BTB. The list of wildlife species around the world from which *M. bovis* has been isolated is estimated to be more than 40 free-ranging wild animal species [8,9]. Among African countries, the most detailed data has been collected in Southern Africa, Uganda and Tanzania. However, the status of BTB in

Book Review

Volume 1 Issue 1 - 2017

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Received: September 03, 2017 | **Published:** December 15, 2017

wildlife is still lacking and need further studies in most African countries [10,11]. *Mycobacterium bovis* is also the most frequent cause of zoonotic tuberculosis (TB) in humans [5]. Tuberculosis, which is primarily a respiratory disease, is responsible for the death of more people each year than any other infectious disease. The World Health Organization (WHO) reported 9.2 million new cases of human TB and 2 million deaths in 2006, with Sub-Saharan Africa having the highest annual risk of infection with tuberculosis, probably aggravated by the expanding Human Immunodeficiency Virus (HIV) epidemic and increasing drug resistance [10]. Global prevalence of human TB due to *M. bovis* has been estimated at 3.1% of all human TB cases accounting for 2.1% of pulmonary and 9.4% of extra pulmonary TB cases [12]. The WHO also reported in 2004 that 0.4-10% of sputum isolates from patients in African countries could be *M. bovis* [13]. Bovine tuberculosis is an endemic disease of cattle in Ethiopia and the disease has been reported from several regions of the country based on tuberculin tests [7,14] and abattoir inspections [15-17]. In Ethiopia, *M. bovis* was also isolated from sputum and fine needle aspirate of human and confirmed to be a cause of human TB cases [18-20]. On the other hand, no infection due to *M. bovis* was reported in Ethiopian wildlife populations so far and the status of the disease in wildlife populations is yet unknown [21]. On other side there is knowledge gap concerning indication of Epidemiological Features of *Mycobacterium Bovis* at the Human, Cattle and Wildlife Interface in Ethiopia which will play important role in controlling of the disease. So this review aims to elaborate the status of *M. bovis* in cattle, wildlife and human populations, to identify risk factors considered in studies conducted so far and to identify the knowledge gaps in the epidemiology of *M. bovis* in Ethiopia.

Prevalence of *Mycobacterium Bovis* in Ethiopia

In Ethiopia, isolation of *M. bovis* was done mainly from domestic animal species and humans. In cattle, most of the studies conducted on Bovine TB so far have been focusing on the highlands of Central Ethiopia while a lot of areas especially the pastoral lowlands are not covered by adequate studies [15,22]. The distribution of the disease varies from place to place based on the production systems under which livestock are managed [22].

Several studies undertaken in different parts of the country have confirmed the endemic nature of the disease in Ethiopian cattle populations. The individual animal and herd level prevalence rate of Bovine TB is ranging from 0.8% to 42.5% and from 7.02% to 79.3% respectively [23-25]. Studies reports have shown that, both animal and herd level prevalence rate of Bovine TB is higher in intensive production system than in animal managed under traditional husbandry system [22-26]. Moreover; in Ethiopia, exotic and cross breeds were found to be more susceptible than local breeds to *M. bovis* with manifestation of high prevalence rates of the disease [22-27]. *Mycobacterium bovis* also infects other species of domestic animals which are considered as spillover hosts such as: sheep, goats, equines, camels, pigs, dogs and cats. Equines and sheep are rarely infected by the disease and pigs can also acquire the infection when fed with infected milk or milk by-products [3]. Studies reports from

few parts of the country have also indicated the infection of small ruminants due to *M. bovis*. Tschopp et al. [28] and Mamo et al. [29] were reported the prevalence of *M. bovis* at 0.74%, and 5.29% in small ruminants based on tuberculin test. International Livestock Research Institute (ILRI) and Deresa et al. [30] also found 3.5% and 4.2% prevalence of *M. bovis* in Ethiopian goats and in caprine respectively. In addition, Gumi et al. [31] reported the infection of *M. bovis* in camel prevalence rate of 0.2%. The role of Bovine TB causing tuberculosis in humans has not been studied adequately. However, very few studies have indicated the isolation of the causal agent of Bovine TB from humans in Ethiopia. Teshome [32], Kiros [18], Asseged et al. [33], Kidane et al. [19], Regassa [14] reported that *M. bovis* and other group of microbacteria were found to be a cause for tuberculous lymphadenitis in humans. Thus, the correlation between the prevalence of *M. bovis* infection in humans and that of cattle populations highlights the potential threat of this disease for humans, most notably in developing countries like Ethiopia, where there is a habit of drinking raw milk and close contact with animal are a common practices [35,34]. Besides being a potential zoonotic threat through consumption of raw animal products and close animal-human contact, the disease can have major economic impacts on national livestock sectors [36]. Despite the isolation of *M. bovis* from domestic animal and human, no infection due to *M. bovis* was reported in Ethiopian wildlife populations so far and the status of the disease in wildlife populations is yet unknown [15,21]. Moreover; the information on the epidemiology of the disease is scarce and the current actual prevalence rate of the disease is not well established at a national level. This is mainly due to the absence of disease surveillance, insufficient laboratory capacity and the lack of veterinary expertise [7,15].

Bovine Tuberculosis in Cattle

Bovine tuberculosis has long been reported in Ethiopian cattle populations [7]. Transmission of Bovine TB can be either direct, through close contact between infected and susceptible individuals, or indirect from exposure to viable bacteria in a contaminated environment [37]. Respiratory and alimentary or oral routes are routes of infection where transmission between cattle is mostly thought to occur by inhalation of contaminated aerosol [38]. Infection can also occur via the gastro-intestinal tract when animals ingest contaminated food, water, soil or milk [6]. Cutaneous, genital, and vertical (congenital) transmissions have been seen but are rare [37]. The disease can also transmitted indirectly through infected flightless vectors, winged vectors or mechanical vectors [6]. Nowadays there are a number of diagnostic tests available to detect *M. bovis* in cattle. In Ethiopia, detection of Bovine TB is carried out most commonly based on the tuberculin skin testing, abattoir meat inspection and very rarely on bacteriological techniques [7]. *Mycobacterium bovis* multiplies quite slowly and also there are usually low in number. These make *M. bovis* hard to detect either directly in clinical sample from live animals or by growing it in the laboratory organisms in clinical sample. Therefore techniques looking directly for the organisms or its DNA, such as culture or polymerase chain reaction (PCR), are insensitive. Hence, primary diagnostic tests for *M. bovis* rely on detecting the immune response of the host to the organism using

skin tests and gamma interferon [2]. Single intradermal tuberculin skin test (SIDT) and comparative skin test (CIDT) remain the international field diagnosis methods of Bovine TB. The skin test is the central ante mortem diagnostic test applied to the diagnosis of tuberculosis in cattle. Pivotal for the intradermal skin test are the purified protein derivative (PPD) tuberculins. Tuberculin skin test is based upon the measurement of a delayed type hypersensitivity response to intradermally injected tuberculins [3]. The cellular response, the pathology and clinical signs seen with the disease on cattle are associated with the body's immune response to the bacteria and not solely with the pathogenicity of the bacteria itself [2]. Both SIDT and CIDT are typically performed either in the neck or caudal tail fold. The decision which test to apply is influenced by a variety of considerations which include the prevalence of disease and the exposure of cattle to other mycobacteria. Although CIDT has more specificity and sensitivity than SIDT, these tests seem to lack sensitivity [3]. Sensitivity depends on the potency and dose of tuberculin administered, the post infection interval, desensitization, postpartum immune suppression and observer variation and the estimates of the sensitivity of tuberculin tests ranged from 68 to 95% [39].

Detection of Bovine TB prevalence in different production systems based on tuberculin skin tests

The production systems under which livestock are managed may have a significant influence on distribution of animal tuberculosis. The prevalence of Bovine TB is different in various production systems due to environmental and management factors (malnutrition, pregnancy and concurrent infection) that may suppress the immune responsiveness [18,41]. Livestock production systems are identified on the basis of contribution of the livestock sector to the total household revenue (income and food), type and level of crop agriculture practiced, types of livestock species kept and mobility and duration of movement [42]. Mode of livestock production is basically classified into three categories. These production systems include: pastoral and agro-pastoral, smallholder and intensive production systems [7]. The prevalence of Bovine TB in Ethiopia studied based on the different production systems are stated herein.

Pastoral and agro pastoral production systems: In pastoral areas, livelihoods of the people entirely depend on extensive livestock production with little or no cropping [43]. In Ethiopia, the pastoral production systems are practiced in the arid and semi-arid lowland areas. The numbers of livestock in pastoral areas account for 42% of the country's livestock in the lowland arid and semi-arid regions [42]. Agro pastoral production systems are mainly practiced in the highland agro - ecology of the country, where there is mixed crop - livestock production (integrated extensive production system) [44]. This production system holds about 85% of the total livestock population of the country. In this production systems, crop and livestock production are both important activities. However, most notably crop production is the primary target. Here a small number of herds are reared for seasonal milk and meat productions under traditional animal husbandry practice with low hygienic standards [42]. In both production systems drinking raw milk is a common practice,

in rural areas in particular, which may expose the community to contagious diseases most notably Bovine TB. Despite the presence of a huge livestock population in this production system, the actual prevalence of BTB is not yet known. The remoteness of sites, the difficult logistics combined with inadequate veterinary infrastructures and poor security in these areas are contributing factors to the scarcity of research studies [7,42]. In Ethiopia, few prevalence studies were conducted in cattle kept under traditional husbandry system. According to these study results, the animal level prevalence of Bovine TB in pastoral and agro pastoral production systems varies from 0.8% in Hamer pastoral areas [21] to 15.8% in Bokoji and Tiyo (Arsi Zone) of highlands agro pastoral districts [45]. Whereas the herd level prevalence rates varies from 7.02% in Boji (West Wellega) [46] to 54.1% Amibara districts of Afar pastoral region [29]. Among very few studies undertaken in the pastoral and agro pastoral production system (based on tuberculin skin test), the individual animal and herd level prevalence rates of Bovine TB are summarized in (Table 1 & 2).

Table 1: Individual animal level prevalence of BTB in traditional managed husbandry system.

| Study Area | Prevalence (%) | Reference |
|-----------------------------|----------------|-------------------------|
| Afambo* | 6.6 | Mamo et al., 2013 |
| Ambo and Toke Kutaye * | 1 | Tamiru et al., 2013 |
| Amibara | 14.1 | Mamo et al., 2013 |
| Arsi Negele and Shashamane* | 8.9 | Dinka and Asmamaw, 2011 |
| Boji* | 1.6 | Laval and Ameni, 2004 |
| Bokoji and Tiyo* | 15.8 | Dinka and Asmamaw, 2011 |
| Chifra | 1.9 | Mamo et al., 2013 |
| Dubti | 6.6 | Mamo et al., 2013 |
| Filtu | 2 | Gumi et al., 2011 |
| Hamer | 0.8 | Tschoop et al., 2011 |
| Liben and Goro-Dola | 5.5 | Gumi et al., 2011 |

Comparative intradermal skin test was used in all studies and result was interpreted at > 4 mm cut-off. * Agro pastoral production system.

Smallholder production systems: Smallholder production systems is dominantly in highland areas near towns where dairy animals are reared for subsistence and/or commercial milk production purposes through the introduction of exotic breeds [22,42]. However, in contrast, this introduction of exotic and cross-bred cattle, into the central highlands of Ethiopia in particular has created conducive environment for the spread of Bovine TB [7]. Although there is some cross - sectional studies, prevalence studies on Bovine TB have not been conducted adequately under this production system. In smallholder production system, the individual animal prevalence of the Bovine TB ranging from 4.3% in Dilla [47] to 13.5% in Central highlands of Ethiopia [22] (Table 3 & 4).

Table 2: Herd level prevalence of Bovine TB in pastoral and agro - pastoral production system.

| Study Area | Prevalence (%) | Reference |
|----------------------|----------------|-----------------------|
| Afambo | 46.2 | Mamo et al., 2013 |
| Ambo and Toke Kutaye | 7.02 | Tamiru et al., 2013 |
| Amibara | 54.1 | Mamo et al., 2013 |
| Boji | 19 | Laval and Ameni, 2004 |
| Chifra | 11.8 | Mamo et al., 2013 |
| Dubti | 25 | Mamo et al., 2013 |
| Hamer | 33.3 | Tschoop et al., 2011 |
| Liben and Goro-Dola | 41.9 | Gumi et al., 2011 |

Table 3: Individual animal prevalence of BTB in smallholder production.

| Study Area | Prevalence (%) | Reference |
|-------------------------------|----------------|-------------------------|
| Adama | 11 | Ameni and Erkihun, 2007 |
| Central highlands of Ethiopia | 13.5 | Ameni et al., 2007 |
| Dilla | 4.3 | Romha et al., 2014 |
| Mekelle | 11.3 | Zeru et al., 2014 |
| North Gondar | 7.1 | Mohammed et al., 2012 |
| Sululta | 11.4 | Biru et al., 2014 |
| Wuchale Jida | 7.9 | Ameni et al., 2003 |

Comparative intradermal skin test was used in all studies and result was interpreted at > 4 mm cut-off.

Table 4: Herd level prevalence of BTB in smallholder dairy farms.

| Study Area | Prevalence (%) | Reference |
|--------------|----------------|-------------------------|
| Adama | 15 | Ameni and Erkihun, 2007 |
| Dilla | 15.3 | Romha et al., 2014 |
| Mekelle | 20 | Zeru et al., 2014 |
| North Gondar | 21 | Mohammed et al., 2012 |
| Sululta | 20 | Biru et al., 2014 |

Intensive production system: Although some few intensive feed lots exist, dairy production is the major practice of this system, which is targeted for the production of milk and milk products. The total number of the cattle population under this production system is insignificant compared to the national livestock population [26,33]. Intensive farming systems are usually performed in peri-urban and/or urban areas and they are the main source of milk for the city dwellers [22]. As compared to both extensive and smallholder production system, higher prevalence rates have been reported from intensive farming systems which are characterized by high numbers of dairy farms, exotic breeds and their crosses [22-27]. In intensive dairy farms, animal level prevalence of Bovine TB is ranging from 10.1% to 42.5% [14]. Individual and herd level prevalence rates of Bovine TB reported from different intensive farms are summarized in (Table 5 & 6).

Table 5: Individual animal level prevalence of BTB in intensive dairy farms.

| Study Area | Prevalence (%) | Reference |
|-------------|----------------|-----------------------|
| Addis Ababa | 18.7 | Shitaye et al., 2006 |
| Addis Ababa | 23.7 | Elias et al., 2008 |
| Addis Ababa | 34.1 | Tsegaye et al., 2010 |
| Addis Ababa | 12.2 | Firdessa et al., 2012 |
| Debre Zeit | 20.07 | Firdessa et al., 2012 |
| Holeta | 10.1 | Firdessa et al., 2012 |
| Sebeta | 42.5 | Firdessa et al., 2012 |
| Sendafa | 31.2 | Firdessa et al., 2012 |
| Sululta | 37.7 | Firdessa et al., 2012 |

In all studies, comparative intradermal skin test was used and the result was interpreted at > 4 mm cut-off.

Table 6: Herd level prevalence of BTB in intensive dairy farms.

| Study Area | Prevalence (%) |
|-------------|----------------|
| Addis Ababa | 33.3 |
| Debre Zeit | 77.7 |
| Holeta | 61.2 |
| Sebeta | 70.3 |
| Sendafa | 79.3 |
| Sululta | 41.3 |

Meat inspection and detection of tuberculous lesions at slaughterhouses

Abattoir surveillance can be a cost effective method for surveying TB in animals. In addition to tuberculin skin testing, detection of *M. bovis* also carried out on the basis of abattoir meat inspection. However this diagnostic method can also lack sensitivity [48]. In Ethiopia, the routine abattoir inspection was conducted according to the method developed by the meat inspector and quarantine division of the ministry of agriculture [49]. Abattoir meat inspection at the moment remains economically affordable and valuable technique to detect Bovine TB in carcasses of slaughtered animals in most of African countries [50,51]. *Mycobacterium bovis* has a wide range of target organs (lungs, gastrointestinal tract, mammary gland, kidney and reproductive organs) to infect [52]. Routine abattoir inspection therefore involves visual examination and palpation of organs these organs as well as pleural lymph nodes and palpation and incision of the bronchial, mediastinal and prescapular lymph nodes [53]. According to literature, in areas where disease control program is absent, up to 40% prevalence of TB can be detected in public abattoirs during meat inspection [54]. However, due to the manner of examination, there is a failure in correctly detect tuberculosis infection during meat inspection. It was noticed that in standard meat inspection procedure only few sites (organs) are often inspected at a glance and smaller lesion could be missed due to heavy duty of inspecting large number of animals each day and limited time available for the examination of each

tissue [10]. Furthermore, a lack of competence in meat inspection training could be another reason for inefficiency of the service as most of the personnel lack adequate training in the area of meat inspection [55,56]. Studies conducted so far have confirmed the presence of the disease based on abattoir meat inspection. The prevalence rate of *M. bovis* in cattle has been found to differ from place to place [56]. The highest and lowest prevalence of *M. bovis* was recorded in Adama (24.7%) [17] and Addis Abeba (1.5 %) [14] respectively. The prevalence of *M. bovis* reported from several city abattoirs are summarized in (Table 7). Several reports have shown that, tuberculous lesions were predominantly detected in mediastinal lymph nodes and bronchial lymph nodes in the thoracic cavity [17,27,55,]. However, the lesions were also detected from abdomen (Mesenteric lymph node) region, lymph nodes of head region and from the carcass.

Table 7: Prevalence of bovine tuberculosis detected by abattoir meat inspection.

| City Abattoirs | Prevalence (%) | Reference |
|----------------|----------------|------------------------------------|
| Adama | 24.7 | Demelash <i>et al.</i> , 2008 |
| Adama | 6.79 | Terefe, 2012 |
| Addis Ababa | 1.5 | Asseged <i>et al.</i> , 2004 |
| Addis Ababa | 15.2 | Demelash <i>et al.</i> , 2008 |
| Akaki | 5.83 | Ewnetu <i>et al.</i> , 2012 |
| Awassa | 8.8 | Demelash <i>et al.</i> , 2008 |
| Butajira | 9 | Namomsa <i>et al.</i> , 2014 |
| Dilla | 2.6 | Gebrezgabiher <i>et al.</i> , 2014 |
| Melge-Wondo | 4.5 | Demelash <i>et al.</i> , 2008 |
| Nekemte | 5.9 | Mezene <i>et al.</i> , 2014 |
| Sululta | 3.5 | Biru <i>et al.</i> , 2014 |
| Yabello | 4.2 | Demelash <i>et al.</i> , 2008 |

***Mycobacterium Bovis* Infection in Wildlife**

The emergence of newly recognized diseases in wildlife is the result of complex, and sometimes unintended, interactions between wildlife, domestic animals and humans, in terms of host ecology, pathogen and environment [57]. These interactions include factors such as translocation or introduction of wildlife to new ecosystems, encroachment of human populations on traditional wildlife habitat, supplemental feeding of wildlife and contact with infected livestock can infect wildlife [10]. Infection of wild animals by *M. bovis*, is raising concern worldwide [58]. Wild animals are susceptible to infection with many of the same disease agents that afflict domestic animals [55]. Transmission of *M. bovis* from domestic animals to wildlife (spillover) and subsequent transmission from wildlife back to domestic animals (spillback) is common in several regions of the world. This transmission between domestic and wild animals requires either direct contact or indirectly through shared environment. They can also get infection from other wild animals. In carnivores and scavenging wildlife species (which is a characteristic of spill over

hosts) infection per os is an important route of infection [56]. *Mycobacterium bovis* has been isolated from different maintenance and spillover hosts of wildlife species in many African countries. Extensive studies conducted in the Kruger National Park of South Africa have shown the infection of 38% of the buffaloes with strains of *M. bovis*. Within the same area, BTB has been diagnosed in lions (*Panthera leo*), whose main prey are buffaloes [60,61]. In addition, a recent study conducted in Zambia has shown a prevalence of 27.7% of Bovine TB in the lechwe [62].

Ethiopia is a home to 255 wild mammal species, of which 31 are endemic and 38 are listed on the International Union for Conservation of Nature's Red List of Threatened Species [62]. The rapid intensification of the human-livestock-wildlife interaction in Ethiopia is fueled by rapid human population growth, massive land degradation, and recurrent drought and presents a potential risk of disease transmission [24]. Recently, studies conducted in some parts of our country (Welega, Awash, Babille, Bale Mountains, and South Omo) have identified a high prevalence of the non-tuberculous mycobacteria in wildlife. [24] reported that 20 out of 87 tested animals (23%) were serologically positive for Bovine TB and acid-fast bacilli were cultured from 29 of 89 animals (32.5%). However, none of the cultured acid-fast bacilli yielded mycobacteria from the MTBC. Moreover; the status of the *M. bovis* infection in Ethiopian wildlife populations has not yet confirmed from the study conducted so far [25]. This is may be due to problem in diagnostic facilities, number of animals tested and geographical condition where they are localized.

Lesser kudu (60%), mountain nyalas (40%), buffaloes (33%), bushbucks (25%) and elephants (25%) were among the wildlife species from which acid fast positive rates were mainly isolated. *Mycobacterium terrae*, *Nocardia testacea*, *M. avium* *M. paratuberculosis*, *M. vaccae* were some of the isolated species of environmental mycobacteria, where *M. terrae* was the most frequently identified one [24]. In Africa, *M. terrae* and *M. avium* was isolated from wildlife in Tanzania [63] and *M. vaccae* in the Republic of South Africa [56]. On the other hand, in Tanzania and Ethiopia, *M. terra* was shown to be a pathogen, associated with granulomatous lesions in cattle and in humans [64].

***Mycobacterium Bovis* Infection in Human**

Zoonotic diseases are responsible for most (60.3%) emergent diseases of humans. Moreover, 71.8% of emerging pathogens are of wildlife origin or have an epidemiologically important wildlife host [64]. Zoonotic tuberculosis is one of the many sequels of the adaptability of *Mycobacterium* species in different hosts. *Mycobacterium bovis* infections may be maintained within livestock populations and within wildlife populations, whereas human infections result from pathogen spillover from animals and very rarely from human-to-human transmission [66]. Transmissions of TB from cattle to humans mostly occur through the consumption of unpasteurized milk, eating infected raw meat and close contact to infected animals [67]. Exposure to aerosol-borne infection with *M. bovis* from cattle remains highest in farmers, veterinary staff and slaughterhouse workers [68]. Transmission of *M. bovis* from humans back to cattle was also reported in Switzerland in 1998 [69]. Wildlife is also increasingly described as a source for *M. bovis*

in humans that have close contact with infected animals, such as hunters (in North America) and game farmers [70,71]. However, no cases of Bovine TB spillback from wildlife to livestock has been confirmed [72]. Tuberculosis is among the most devastating human infectious diseases throughout the world. The public health importance of animal TB was recognized by WHO early in its 1950 report of the Expert Committee on Tuberculosis [73]. Cases of TB can be classified as pulmonary and extra pulmonary (EPTB). Pulmonary TB accounts for 85 % of all TB cases whereas EPTB represents 15% of all TB cases in the world and 12% of all TB in high burden cases. Human TB occurs in the EPTB form in particular are suggestive of infections due to *M. bovis* [65]. Tuberculous lymphadenitis (most common), TB of the spine or joints and TB of the serous membranes are the most common forms of EPTB [74]. Tuberculosis caused by *M. bovis* is clinically indistinguishable from TB caused by *M. tuberculosis* [11,75]. In developed countries, eradication programs have reduced or eliminated animal tuberculosis in cattle, and human disease is now rare. However, the disease is still common in developing countries [76]. In developing countries, the human population has a greater vulnerability due to poverty, HIV and reduced access to health care [38]. The proportion of which *M. bovis* contributes to the total of TB cases in humans depends on the prevalence of the disease in cattle, socioeconomic conditions, consumer habits, practiced food hygiene and medical prophylaxis measures [55]. In addition, identifying the burden of *M. bovis* infection requires accurate diagnosis. Even though it is the primary tool for diagnosing of TB nowadays, determining the exact percentage of *M. bovis* in human TB cases based on the sputum smears is difficult [38]. In general, the role of *M. bovis* in causing TB in humans has not been studied adequately [74]. Ethiopia is the country with the highest TB cases and has a yearly incidence of 341 of all forms TB cases/100,000 population [74]. The prevalence and mortality of Tuberculosis of all forms is estimated to be 546 and 73 per 100,000 populations respectively. According to latest estimates, among the 22 high TB burden countries that account for 81% of estimated cases, Ethiopia ranks 7th [20,74]. However, very few studies have been conducted on isolation of *M. bovis* from humans TB cases in Ethiopia so far. In Ethiopia particularly in rural areas, most people have lack awareness about the disease, drink raw milk and do have extremely close attachment with cattle (such as sharing shelter) that intensifies the transmission and spread of the disease [38]. In addition, most people of the rural areas drink raw milk [38]. Even in urban areas, 82% milk is supplied unpasteurised to consumers [11]. Tigre et al. [76], Mohammed et al. [77], Biru et al. [78], and Namomsa et al. [79] were reported that 85.7%, 81.8%, 79.3% and 89.5% of people consume raw milk respectively. In countries where BTB in cattle is still highly prevalent, pasteurisation is not widely practiced and/or milk hygiene is insufficient, usually estimated to be about 10% to 15% of human tuberculosis is considered to be caused by *M. bovis* [80]. Human TB cases due to *M. bovis* mainly takes place through drinking raw milk and the infections occur in the extra-pulmonary form in the cervical lymphadenitis form in particular [74]. With respect to this, *World Health Organization* [20] reported that TB lymphadenitis in cervical lymph nodes accounts for approximately 33% of all new cases in Ethiopia, which is greater than the global average of ≈15%. Kiros [20] also demonstrated that out of 7138 human

patients with tuberculosis, 38.4% were found with EPTB and the proportion of patients with EPTB was significant in patients who have close contact with cattle and in those who frequently used to drink raw milk in particular. Similarly Asseged et al. [24] have also demonstrated that, more than 30% of TB patients have EPTB and the majority of them were directly or indirectly in contact with cattle, which suggests the possible association that may exist between EPTB and *M. bovis*. The prevalence of EPTB identified in Ethiopia in the year 1999-2007 G.C is summarized in (Table 8). In Ethiopia, Teshome [32], Kiros [18], Ameni and Erkihun [22], Elias et al. [26], and Biru et al. [78] detect *M. bovis* from raw milk. The isolation rate of *M. bovis* from symptomatic human patients in specific studies was 6.9% in Uganda [81], 5% in Nigeria [82] and between 0 and 2.5% in Latin American countries [83]. Few studies undertaken in Ethiopia also isolated *M. bovis* from human sputum and fine needle-aspirate samples. This isolation has shown that, the role of *M. bovis* in causing human TB cases seemed to be significantly important [74]. In addition, Ameni and Erkihun [21] and Elias et al. [26] were isolated *M. tuberculosis* from milk of reactor cows. The presence of both a human TB patient and reactor cattle in a household could indicate that either the human TB patient was a source of infection for the cattle or vice versa [84]. It is well established that cattle infected with *M. bovis* can excrete the bacillus in their milk. However, it is not likely that cattle infected with *M. tuberculosis* would excrete the bacillus in their milk since they rarely develop TB due to *M. tuberculosis*. The other possible source of *M. tuberculosis* in milk is contamination by the cough spray from infected farmers during milking [84].

On the other hand, assessment of the knowledge of cattle owners about the disease and its zoonotic potential was conducted in different parts of the country. Ameni et al. [7] showed that 30.8% of the cattle owners knew that Bovine TB is zoonotic. Study conducted by Ameni & Erkihun [22] demonstrated that 35 % of the respondents knew about bovine TB while only 32% (121/378) were aware it could be transmitted from cattle to humans. Biru et al. [78] also found that only 6.9% of farm attendants had awareness about the existence of Bovine TB and 10.3% knew that milk and meat could be a source of Bovine TB infection. Although milk borne infection is the main cause of non-pulmonary tuberculosis in human, contaminated meat can also play its own role for the transmission of *M. bovis* [35].

Risk Factors Conducive to the Spreading of *Mycobacterium Bovis*

Several risk factors have been suggested for the spread of *M. bovis* so far [85]. Risk factors will vary across regions due to factors such as differing farm structures and management practices, *M. bovis* infection control and eradication programmes, regional TB incidences, wildlife densities and the relative importance of specific risk factors within individual areas [86]. They can broadly be separated into genetic and non-genetic (environmental), which act jointly to influence susceptibility of the hosts [87,88]. Risk factors can vary based on the susceptibility hosts involved.

Risk factor for cattle

In cattle, risk factors for bovine TB can be classified as animal level and herd level [88]. Among these, some of the animal level

and herd level risk factors identified in our country are discussed as follows.

Animal level: Animal level risk factors are cattle breeds, genetic resistance, physiological state of the animal, age, sex, stress, concurrent infection, immune status and body condition score (BCS) [26,32,89]. Several past and recent studies have shown that susceptibility to bovine TB can vary between cattle breeds with suggestions that indigenous zebu cattle are more resistant to BTB than exotic breeds [90]. This fact is substantiated by the lower prevalence recorded in several studies and it is evident where European breeds of cattle have been used to establish a dairy industry. Genetically improved cattle may suffer more severely from deficient housing and malnutrition and thus be more prone to infection [91]. Studies conducted in different areas of our country also confirm variation in susceptibility to bovine TB among cattle breeds. Ameni et al. [22], Elias et al. [26], Dinka and Asmamaw [44], Romha et al. [92] & Zeru et al. [91] have reported that, there is statistically significant difference ($P < 0.05$) prevalence of bovine TB among exotic, cross and zebu breed where exotic and cross breeds were observed with high prevalence of BTB as compared to zebu cattle breed. One of the main animal risk factor identified by numerous studies in both developed and developing countries is the age of animals. The duration of exposure increases with age. Several studies carried out in Tanzania, Zambia and Chad have shown that older animals are more likely to have been exposed than younger ones [60,65,82]. Animals might get infected at a young age, but only express the disease clinically when they are adults. Mycobacteria have the ability to remain in a latent state for a long period before reactivation at an older age. In contrast to this, Demelash et al. [17]. reported high disease prevalence young animals as compared to middle age group. Ameni and Erkihu [21] also found fewer reactor animals were recorded in the younger age groups. This may be related to the development of infection mainly through ingestion of infected milk, in addition to aerosol exposure. Furthermore; as animals become older (above 5 years), immune response also get depression; as a result animals commonly show lower reaction to tuberculin tests [93]. In Ethiopia, Elias et al. [26], Tsegaye et al. [27], Gumi et al. [31], Firdessa et al. [14], Mamo et al. [29], Gebrezgabihier et al. [80] and Namomsa et al. [80] found that, statistically significant difference prevalence among age groups where higher prevalence of BTB was observed in older animals than younger ones. Gender mostly appears as a risk factor in published African studies [85]. Gender-linked factors are probably related to management practices or behavioral habits; males and females are managed differently, both in developed and developing countries [94]. Males have potentially more contact with other herds during breeding, which may increase their risk [85]. Study conducted in Tanzania revealed that male cattle were significantly more affected by bovine TB than female animals; because they are mostly used as oxen and kept longer in the herd than females [89,95] reported high prevalence of BTB in male cattle than female. In developed countries, dairy cows usually reach an older age than males because of their role in calving and milk production. Female cattle are usually confined in a barn and kept long for production purpose which may facilitate infection and acquisition of the disease. Moreover, dairy cows experience greater production stress and gathering of

cattle during milking increases the risk of transmission as shown by bovine TB transmission modeling in New Zealand [94]. Study conducted in Uganda revealed significantly more females positive to the skin test than males [96]. In Ethiopia, Elias et al. [26], Mamo et al. [29], Biru et al. [79] and Zeru et al. [91] found statistically significant difference ($P < 0.05$) prevalence of bovine TB, which was higher in female than male animals. In addition to management practices or behavioral habits, variation in disease prevalence between sexes of the animal can also be related with sample size problem [79]. Factors associated with bovine TB also differed statistically according to body condition categories. Low BCS was associated with increased risk of tuberculin reactivity in a cross sectional study in Zambia [97]. Study carried out in Tanzania also suggested that, skin test reactors animals might have a poor BCS as a consequence of an advanced stage of bovine TB [89]. Elias et al. [26], Mohammed et al. [78], Biru et al. [79], Namomsa et al. [80] and Zeru et al. [91] were found statistically significant difference ($P < 0.05$) prevalence of *M. bovis* in Ethiopia. According to the study reports, higher bovine tuberculin reactivity was observed in animals with poor body condition as compared to those with good BCS. However, in cross-sectional studies, it is difficult to know the initial status of animals and this challenge to decide whether BTB has caused poor body condition in animals or animals with poor BCS are more susceptible to the disease. The real impact of BCS should be the subject of directed studies dealing with diet restriction [89,79]. Animal's resistance to tuberculosis is reduced by a shortage of feed and/or unbalanced diet, attributable to a deficiency of proteins, minerals and vitamins in the diet [52]. In contrast to the above results, Ameni and Erkuhin [22] and Regassa et al. [96] were found higher prevalence of the disease in animals with good body condition than poor body conditioned animals. On the other hand, during abattoir meat inspection animals, Demelash et al. [17], [95], Gebrezgabihier et al. [80], Namomsa et al. [81] and Zeru et al. [92] were found that animals with medium and good body condition were less likely to have tuberculous lesions than those with poor body conditions. Although it is not commonly reported in our country, physiological state of the animal is also considered as one of the animal risk factor [26]. The physiological and immunological state of an animal, including the degree of environmental stress being experienced at the time, could strongly influence the course of tuberculosis [98]. Cosivi et al. [75] reported that, the longer productive situations such as frequent pregnancies and high milk yields expose dairy cows to erogenous infection. Similarly, Wood et al. (1991) have also indicated that pregnant animals show lower reactivity as a result of stress induced immune suppression. This could be because animals lose sensitivity to tuberculin shortly before and after calving [96]. In Ethiopia, Ameni & Erkuhin [22] were found significant variation in prevalence ($P < 0.05$) in relation to reproductive status.

Herd level: Risk factors at herd level are herd size, types of farming practice and housing of cattle, geographical origin, history of bovine TB in the herd and human antecedent of tuberculosis in the household, contact between animals and with wildlife reservoirs, introduction of cattle in a herd, herd movements and trading, lack of performance of diagnostic tests, the use of hired/shared bulls, manure and environmental persistence of *M. bovis*

[64,24,86,88]. Studies carried out in several parts of the world, both in developed and developing countries, identified herd size as one of the major BTB herd-level risk factors [64]. O'Reilly and Daborn [37] also suggested that, the transmission of BTB from cattle to cattle is largely influenced by herd size; the larger the herd size the greater the chance of transmission. When larger proportion of the study animals was grazing in the field, the level of confinement is reduced to a certain degree, which in turn minimizes the rate of infection in the herd [37]. On the other hand, since skin test specificity is not perfect, if herd size increases, the probability of a false positive reactor will be greater [3]. In Ethiopia, Ameni and Erkuhin [22], Elias et al. [26], Tsegaye et al. [27], Firdessa et al. [14], Biru et al. [79], Romha et al. [46] and Zeru et al. [91] were observed statistically significant difference ($P < 0.05$) prevalence of *M. bovis* where both individual animal and herd prevalence were found higher in large and medium herd size as compared to small herds. According to literature, in some intensive dairy farms of our country, particularly in those having large herd size, the prevalence of the disease in individual animal and herd level could be rises up to (89.9%) and (100%) respectively [14]. Animal husbandry conditions are also a major influence on the prevalence of BTB [89]. Exotic dairy cows are usually kept under intensive conditions. Intensive farming systems promote close contact between animals, overcrowding and stress in animals, thereby favouring the spread of *M. bovis* [3-22]. Cosivi et al. [75] reported that, the highest incidence of BTB is generally found in areas where intensive dairy systems are practiced. Studies conducted in different parts of our country have also shown that, there is statistically significant difference ($P < 0.05$) prevalence of BTB between farming systems. According to these study results, higher skin-test prevalence was observed in cattle kept under intensive conditions than those kept under extensive conditions [22,26,14,91]. This would make extensive farming systems safer than zero grazing and more effective in preventing transmission of BTB [38]. Moreover; Radostits et al. [3] were found a significant association between respiratory pathology and reactivity to tuberculin test, which could indicate that inhalation is the most common route of infection into housed cattle. In addition, some study results of postmortem conducted in different abattoirs can also support this [14]. The localisation of lesions in infected animals can determine the route of infection (De Lisle et al., 2001). Ewnetu et al. [56], Gebrezgabiher et al. [80] and Namomsa et al. [80] were found tuberculous lesions in the lung and associated lymph nodes at the proportion of 67.7%, 69.8, 75% and 62.5% respectively. O'Reilly and Daborn [37] and Corner [53] were also reported tuberculous in the lung and associated lymph nodes at the proportion of that 68.5% and 90% respectively, suggesting that TB in cattle primarily involves the pulmonary system. Contrary to this finding, Tsegaye et al. [27] found 94.5% of the lesions in mesenteric lymph nodes in animals that kept on pasture. Ameni et al. [22] also reported that, mesenteric lymph node lesions were more often found in grazing animals compared to animals kept indoors.

Under the nomadic conditions, the risk of exposure to *M. bovis* also increased significantly by creating multiple herd contacts and increasing the total herd size [7]. Nomadic transhumance relies on the movement of livestock to follow grazing and water over

considerable distances following seasonal changes. Gumi et al. [30] were observed significant difference in prevalence between herds' drinking water from river to stagnant water sources during the main dry season, which may be due to aggregation of large number of different livestock from different pastoral households around limited watering points facilitating BTB transmission either directly between animals or by contaminated pastures and water sources. However, in the most cases of the traditional animal husbandry system of Ethiopia, animals are kept in open-air even in the night, which is expected to minimise the rate of transmission of *M. bovis* and this is one evidence for low prevalence of the disease in these areas [78,91]. The herd prevalence of BTB also varied significantly based on the management conditions and many study reports have shown higher infection rates in farms under poor management conditions [74]. Elias et al. [26], Romha et al. [46] and Zeru et al. [91] were observed statistically significant difference ($P < 0.05$) prevalence, where cattle under poor management condition were more likely to be infected with BTB as compared to cattle under good management condition. Geographical location is also one of the herd level risk factor that determines the prevalence of the disease. Demelash et al. [53], Tsegaye et al. [27], Dinka and Asmamaw [46], Gumi et al. [31] and Mamo et al. [29] were found significant difference prevalence of the disease in cattle from different geographical origin.

Mixing or introduction of new cattle from different herds is common in Africa, increasing contact between animals. Purchase of animal in a BTB free herd is one of the major risk factors for introducing the disease, as suggested by studies carried out in the UK, Michigan, Italy and Tanzania [89]. In Ethiopia, Tschopp et al. [21] found statistically significant difference prevalence between purchase of cattle and presence of other livestock in the herd, where high prevalence was observed in purchased cattle. Furthermore, the risk factor related with history of BTB outbreak in the herd and human antecedent of TB in the household is probably primordial in dairy herds, where animals often remain in the same herd for several years [63]. Study conducted by Ameni and Erkuhin [22] have demonstrated a significant ($P < 0.01$) association between the presence of reactor cattle and human TB cases in a household. Similarly, Regassa [34] and Tamiru et al. [25] were reported that cattle owned by tuberculous patients had a higher prevalence (24.3%) and (1.36%) than cattle owned by non-tuberculous owners with (8.6%) and (0.56%) respectively.

Risk factor for wildlife

Although no *M. bovis* infections have been reported in Ethiopian wildlife population so far, reports from different parts of the world have demonstrated several risk factors for the presence of the disease in wildlife. Direct contact or sharing of environment with domestic cattle, the extent of the disease prevalence within the region/country or within domestic animal reservoir host, herd size (wildlife densities) and previous history of *M. bovis* in the wildlife populations are among the potential risk factors [26-63]. The presence of the aforementioned animals in different wildlife reserves may have an epidemiological role in the spread of the disease among other wild and domestic animal [99]. On the other hand, in Ethiopia, as wildlife habitats are not fenced, there is intensive interaction between a fast-growing human population

and livestock and wildlife competing for scarce grazing land. Wildlife and, in particular, herbivores sharing pastures with cattle might therefore be at risk for bovine TB transmission [100]. With respect to this, Mamo et al. [29] have reported that, in Amibara district of Afar pastoral region, domestic animal were sharing grazing land in close proximity with wildlife in the area where wild animals lives (in and around Awash National Park). This suggests that there is a possible exposure for potential risk of disease transmission to wildlife populations in Ethiopia.

Risk factor for human

The main risk factors which contribute to the acquisition *M. bovis* infections in both urban and rural human populations are poverty, malnutrition, HIV infection, illiteracy, the consumption of raw milk (unpasteurised milk), uncooked or poorly cooked meat, work condition and close contact to livestock and using cow dung for plastering wall or floor [74,89]. The habit and tradition of consumption raw milk and meat in Ethiopian societies is the main risk factors for *M. bovis* infection in human [34,38]. Teshome [32], Kiros [18], Ameni and Erkuhin [22], Elias et al. [26], and Biru et al. [79] detect *M. bovis* from raw milk and confirm the existing problem and the potential risk of the infection in humans. Cases of human TB of animal origin will continue to pose a serious public health problem, especially in areas where raw milk or its products are commonly consumed [74]. Nowadays many developing countries have intensified their livestock production to meet the growing demand for food security. This intensification promotes close physical contact between the owner and his or her cattle, especially at night and thus facilitates the transmission of bovine TB as zoonosis. In addition, there is a habit of chewing and spitting tobacco to their cattle among Ethiopian farmers. This led to a higher risk of transmission for *M. tuberculosis* as well as for *M. bovis* at the human–livestock interface through inhalation of the cough spray from infected animals or transmission of *M. tuberculosis* from human to cattle as the organism can spread to the animal [21,101]. Tuberculosis and other mycobacterial infections are major opportunistic infections in the HIV/AIDS infected individuals, while HIV/AIDS is a major predisposing factor for TB through accelerating the progression from primary infection to disease, increasing the reactivation rate of TB and the re-infection rate [75]. It is estimated that 50 to 60% of HIV infected people will develop TB disease in their lifetime in contrast with HIV negative persons, whose lifetime risk is only 10% [73]. In addition, poverty, malnutrition also play own role in inducing infection. Families with low income often face malnutrition which, when associated with the burden of HIV/AIDS infection, increases susceptibility to various infectious diseases [75]. 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 [67].

Economic Importance of *Mycobacterium Bovis*: *Mycobacterium bovis* has been widely distributed throughout the world and it represents a very significant economic and public health problem in numerous countries in both developed and the developing world [5]. Consequently, most developed nations have embarked on campaigns to eradicate *M. bovis* from the cattle

population or at least to control the spread of the infection [82]. In developed countries, although tuberculosis is eliminated in cattle, the disease still has a major economic impact, mainly due to the existence of a permanent wildlife reservoir that reduces the efficiency of control strategies. For instance, in the United Kingdom, where badger and other wildlife such as deer remain an important source of infection for livestock, approximately £100 million is spent annually in efforts to control the disease. Republic of Ireland and New Zealand also spent approximately 35 and 13 million US \$ annually for disease control [102]. In Argentina, the annual loss due to bovine TB is approximately US\$63 million [74]. Although the disease has zoonotic threat, economical and financial burden to society, its cost has rarely been assessed and is largely unknown for Africa [103]. Animal tuberculosis is a disease of high economic relevance within the context of livestock farming as it directly affects animal productivity. The disease considerably reduces milk and meat production of infected animal and affect animal reproduction as well as it reduce pulling power in traditional farming system [35]. Infected animal loses 10 to 25% of their productive efficiency. Direct losses due to the infection become evident by decrease in 10 to 18% milk and 15% reduction in meat production [97]. The culling loss is estimated to be 30–50 % of the difference between the values of a dairy or beef breeding cow and its value at slaughter [22]. Moreover, national and international trade (market restrictions) and other economic sectors may be indirectly affected by the disease [36]. Tuberculosis has also an economical and financial burden to society human health costs. The disease become is an obstacle to socio-economic development; 75% of people affected by TB are within the economically productive age group of 15-54 years. This may have a negative influence on the national economy [33,73]. Although the economic importance and public health significance of tuberculosis has been established in many countries, the economic impact of *M. bovis* on cattle productivity, bovine TB control programmes and other related economic effects of the disease are not yet well documented or studied in Ethiopia [36]. Only few abattoir meat inspection surveillances have shown the economic loss due to condemnation of total or partial carcass and organs. According to Gezahegne [102], a report from eight export abattoirs showed a prevalence of 0.8% (978/144 487) of slaughtered animals, in which the whole carcasses of the infected animals were condemned. Asseged et al. [15] also demonstrated that, based on the ten years retrospective analysis of the detection of tuberculous lesions in the Addis Ababa abattoir, there was a cause of 0.028% for whole carcass condemnation. Furthermore, study results of Shitaye et al. [16], conducted in Addis Ababa and Debre-Zeit abattoirs [35] indicated that, causes condemnation of carcasses and/or organs due to tuberculous lesions found to be highly significant economically. According to the study reports, a prevalence of 0.052% (695) and 0.001% (11) was observed in cattle and shoats respectively, and causes the whole animal's carcass condemnation. *Mycobacterium bovis* infections in wildlife can affect the ecosystem; moreover, the disease constitutes a threat to endangered species and can hamper BTB eradication and control schemes in domestic cattle [11].

Control of Tuberculosis: The effective control and eradication of *M. bovis* depend on identifying and isolating potential sources

of infection [104]. Limiting the number of receptive individuals using Bacillus Calmette-Guérin (BCG) vaccination and decreasing the number of infected animals through test-and-slaughter policy are commonly used methods for control and eradication of TB [105]. Although test-and-slaughter policy is guaranteed to eradicate tuberculosis from domesticated animals, the policy has a negative economic impact [71,16]. As a result, control of bovine TB in cattle through the test-and-slaughter policy is not yet established in Ethiopia [21]. Control strategies are mostly limited to the inspection of carcasses at slaughterhouses [51]. Certain few attempts have been also undertaken in government state farms in particular. For example, culling and slaughtering of the positive reacted cattle based on tuberculin skin testing results [106]. Most commonly culling of infected animals (especially in government owned farms) and improving sanitary and hygienic standards in other dairy farms is the actual undergoing control measure of BTB infection. Vaccination of cattle using BCG vaccine is another possible strategy for control of bovine TB. Although BCG vaccination confers poor protection in animal and interferes with tuberculin test, cattle TB vaccination has some of the qualities required for a veterinary vaccine (excellent safety profile and cost-effective control strategy) in developing countries where other control strategies are difficult and expensive to implement [22,52]. Treating animals with anti-tuberculosis drugs can also reduce the number of infected animals. However, this is generally considered impracticable as it is highly uneconomic, limited drugs for treatment, prolonged drug course, hazards to humans and potential for drug resistance make treatment controversial [105]. Although no *M. bovis* infections have been reported in Ethiopian wildlife population so far, proper management strategies at the domestic cattle and wildlife interface are very important. Animal husbandry practices, particularly grazing lands, should be properly managed in order to reduce/prevent transmission of *M. bovis* between domestic cattle and wildlife [107]. In small size parks, fences can also keep wildlife and domestic cattle separated, which efficiently reduces the risks of disease spillover [70]. Bacillus Calmette-Guérin vaccination has also shown to give protection many wildlife species [108]. Practical elimination of human *M. bovis* infection can be achieved with a control programme targeting only domestic animals and through BCG vaccination and employment of chemotherapy [109-129]. In 1994, WHO launched the Directly Observed Treatment, Short course (DOTS) Strategy, which is the brand name of the internationally recommended strategy for TB control in human. The DOTS strategy ensures that infectious TB patients are identified and cured using standardized drug combination [72]. The conventional anti-tuberculosis drugs (isoniazid, rifampicin, pyrazinamide, thiacentazone and ethambutol) are used to control and prevent the spread of the disease [14]. In order to reduce the risk associated with consumption of contaminated milk and meat, performing routine pasteurisation of milk and milk products and abattoir meat inspection procedures is important. Farmers and other occupationally at-risk individuals should be required to adopt appropriate measures to minimise exposure of employees [58]. In general, health education is one of the pivotal means to control through sensitization and increasing awareness of the community about the epidemiological characters of the disease and other effective measures are being made to ensure better access throughout the country [73].

Conclusion and Recommendations

In Ethiopia, the endemic nature of infection due to *M. bovis* has long been confirmed. The prevalence rate of tuberculosis in livestock varies among different production system and is much higher intensive dairy farms. Most of the studies conducted on bovine TB so far have been focusing on the urban and/or peri-urban parts of the county. However, a lot of rural areas, where over 80% of the Ethiopian population is directly dependent on livestock for their daily livelihood, are not covered by adequate studies and bovine TB prevalence in these areas is largely unknown. There is no legislation on restricting cattle movements and reducing the size of herd particularly in traditional extensive production systems. The information on the disease epidemiology in general, is scarce and the current actual prevalence rate of the disease is not well established at a national level. Although bovine TB is known to be endemic in Ethiopian cattle, the status of the disease in wildlife populations, that often share the same habitat with livestock, is unknown. On the other hand, very limited studies have been conducted to identify the status of *M. bovis* in free ranging wildlife populations so far. There are no proper management strategies, which help to prevent transmission of the disease at the domestic cattle and wildlife interface. The role of *M. bovis* causing TB in humans has not been studied adequately. Currently, diagnosis of TB relies on minimal culture methods such as sputum smears. Most people particularly in rural areas have lack awareness about the existence and zoonotic potential of the disease. Collaboration between human and animal health sectors on reducing/preventing the burden of the disease is weak. The disease represents a very significant economic and public health problem; however the magnitude of economic impact of bovine TB is not yet well studied in Ethiopia. Condemnation of carcasses at slaughterhouses, test and slaughtering of tuberculin positive cattle in some government farms and pasteurisation of milk are among few attempts performed to control bovine TB. However, these measures, as compared to the cattle population of the country, are found to be insignificant.

Based on the above conclusions the following recommendations are forwarded.

1. Future researches should be focused on further investigating tuberculosis in all animal production systems especially in cattle populations managed under traditional husbandry systems.
2. Restriction of cattle movements and reducing the size of herd particularly in traditional extensive production systems
3. Strict control and quarantine measures during the importation of animals and animal products
4. Extensive disease surveillances should be needed to assess the magnitude and importance of *M. bovis* infections in Ethiopian wildlife populations and every effort should be made to protect wildlife populations from being infected
5. Animal husbandry practices, particularly grazing lands, should be properly managed in order to reduce/prevent transmission of *M. bovis* between domestic cattle and wildlife

6. More sensitive and specific Rapid Test is needed to screen wildlife and test validation should probably focus on possible maintenance species or highly endangered wildlife species.
7. There should be strong sectoral collaboration in reducing or preventing the burden of *M. bovis* infection. Institutions have stressed on the need to prevent and control tuberculosis in both humans and animals.
8. Awareness should be created among the people in order to meet the standard hygienic requirement and to improve husbandry practices.
9. Pasteurisation of milk and milk products should be done as routine practice most notably in rural communities.
10. The economical and public health impact of the disease should be studied adequately at national level.
11. Legislation that makes it obligatory to register dairy farms for enabling enforcement of control measures about any animal purchase, sales or transfer of farms should be established. These measures can be gradually expanded to the traditional integrated extensive farm systems.
12. Dairy farms insurance that may encourage owners to cull their infected cattle after testing for bovine TB should be established within the country and disease free areas should be established and maintained.
13. Routine abattoir meat inspection procedures have to be made for the detection of tuberculous lesions and with the qualified veterinary staff at the slaughterhouses.
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