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Epidemiology of *Mycobacterium bovis* and *Mycobacterium tuberculosis* in animals: Transmission dynamics and control challenges of zoonotic TB in Ethiopia

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ABSTRACT

Mycobacterium tuberculosis complex is the cause of tuberculosis (TB) in humans and other animals. Specifically, *Mycobacterium bovis* (*M. bovis*) and *Mycobacterium tuberculosis* (*M. tuberculosis*) are highly pathogenic mycobacteria that may infect different animal species and are the sources of TB in humans. The objective of this paper was to review the epidemiology of *M. bovis* and *M. tuberculosis* in animals. The review also highlighted the transmission dynamics of *M. bovis* and *M. tuberculosis* in humans and animals and control challenges of zoonotic TB in Ethiopia. The literature review focused on scientific peer-reviewed articles from studies exclusively conducted in Ethiopia that were published from 1998 to 2017. Husbandry system, breed and herd size have significant role in the epidemiology of bovine tuberculosis (BTB) in Ethiopia. The information presented reveals that 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. 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 human and animal which may have impact on the TB control program in human. In Ethiopia, a human TB control program has been widely implemented, however, 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. This warrants the need for incorporating animal TB control programs using "One Health" approach for effective TB control for both human and animal.

1. Introduction

M. tuberculosis complex cause TB in various mammalian hosts but exhibit specific host tropisms (Smith et al., 2006). *M. tuberculosis* and *M. bovis* are the major causes of TB. They are highly pathogenic mycobacteria that may infect many animal species and are the sources of TB in humans (Mathema et al., 2006). *M. bovis*, the main but not exclusive causative agent of bovine tuberculosis (BTB), is a member of the *M. tuberculosis* complex, which also comprises the important human pathogen, *M. tuberculosis*, as well as *Mycobacterium canettii*, *Mycobacterium africanum*, *Mycobacterium pinnipedii*, *Mycobacterium microti*, and *Mycobacterium caprae*. These species are phylogenetically closely related mycobacteria sharing more than 99.9% chromosomal identity and they cause TB with similar pathology in various mammalian hosts (Smith et al., 2006).

Human TB and BTB share key aspects such as the development of similar lesions and immune responses, which often result in colonization and spread to various organs, mainly to lungs and lymphatic tissues (O'Reilly and Daborn, 1995; Buddle et al., 2005; Cassidy, 2006; Van Rhijn et al., 2008). Recent studies showed that some reactor animals to bovine tuberculin skin test were found infected with *M. tuberculosis* isolates (Tschopp et al., 2011; Kassa et al., 2012; Ameni et al., 2013). In fact, tuberculin test cannot discriminate *M. bovis* from *M. tuberculosis* (De la Rua-Domenech, 2006).

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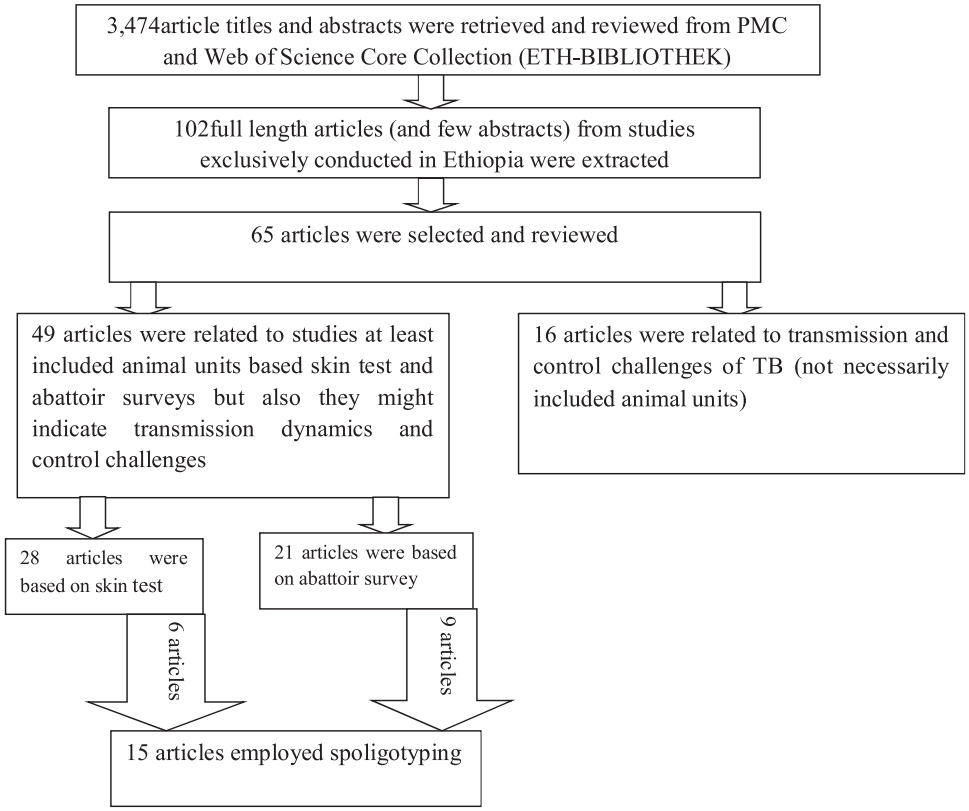

Fig. 1. Articles retrieval and screening method.

In Ethiopia, research on BTB began in the mid-1970s when slaughterhouse studies confirmed the presence of the disease (reviewed in Shitaye et al., 2007). Analysis of nine years of meat inspection records also revealed an increasing incidence of BTB over the years (Demelash et al., 2009). Currently, conventional and molecular epidemiological studies have provided evidence for the widespread distribution of BTB in cattle populations throughout the country (Ameni et al., 2007a; Elias et al., 2008; Berg et al., 2009; Demelash et al., 2009; Biffa et al., 2010a; Tsegaye et al., 2010; Gumi et al., 2012a; Firdessa et al., 2012; Tschopp et al., 2013). The widely spread distribution of TB in livestock, in turn, could be a major obstacle to the country's livestock export trade due to strict sanitary requirements by the importing countries (Elias et al., 2008; Demelash et al., 2009). It is also suggested that the disease may impact productivity of animals and this is likely linked to economic losses (Tigre et al., 2010; Tschopp et al., 2012). 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 (Berg et al., 2009; Gumi et al., 2012b) as well as due to meat-borne infections as a result of poor meat inspection practices (Biffa et al., 2010b) and consumption of unpasteurized dairy products (Firdessa et al., 2012).

On the other hand, studies have also indicated that cattle and other animals can acquire *M. tuberculosis* from humans (Ameni et al., 2011; Dawson et al., 2012; Kassa 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; Arega et al., 2013; Aylate et al., 2013; Deresa et al., 2013, Kassa 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; Kassa et al., 2012). On the other hand, *M. tuberculosis* plays a significant role in TB lymphadenitis (cervical lymph node TB) (Kidane et al., 2002; Firdessa et al., 2013; Berg et al., 2015), and contact with livestock has been suggested as a risk factor when compared to pulmonary TB (Berg et al., 2015).

The epidemiology of BTB has been widely explored in Ethiopia; however, the role of zoonotic TB has been overlooked. The molecular identification of *M. tuberculosis* and *M. bovis* in animals and animal products as well as demonstration of *M. tuberculosis* lymphadenitis TB (cervical lymph node TB) in humans in recent times have brought new insights about the epidemiology and transmission dynamics of *M. bovis* and *M. tuberculosis*. Therefore, the objectives of this paper were to review (1) the epidemiology of *M. bovis* and *M. tuberculosis* in animals, (2) the transmission dynamics of *M. bovis* and *M. tuberculosis* in humans and animals, and (3) control challenges of zoonotic TB in Ethiopia.

2. Methods

A systematic literature review was used to identify publications on the distribution of *M. bovis* and *M. tuberculosis* in animals, its (zoonotic) transmission dynamics and control challenges. The literature review focused on scientific peer-reviewed articles from studies exclusively conducted in Ethiopia that were published from 1998 to 2017 and found in PubMed central (PMC) and Web of Science Core Collection (ETH-BIBLIOTHEK). Broad search terms were used to capture the majority of the scientific publications under the scope of this review. Publications that are not from Ethiopia were excluded. Articles, both full length and abstracts, which are available online, were included. However, abstracts without adequate evidence, technical reports, book chapters and review articles were not considered.

The review depended on three steps. First, key words and search terms were identified for use in the search process. Second, searching for relevant publications using the search terms and key words was conducted. Third, once we retrieved all the sources, we reviewed and identified the pertinent publications. Publications were considered as eligible if they included at least one of the following three broad themes. (1) Articles that focused on the epidemiology of animal TB and