

Systematic Review on *Mycobacterium Bovis* as Potential Cause of Tuberculosis to Humans in Ethiopia

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Abstract *Mycobacterium bovis* is a zoonotic pathogen; widely distributed throughout the world having a range of hosts imposing great risk to the public particularly for those who had direct contact with cattle. This manuscript was compiled by reviewing published literatures to know the magnitude/distribution of *M. bovis* and its public health significance in Ethiopia. Cross-sectional study designs were selected and studies done since 2002-2011 were reviewed. Lesions, milk, sputum, and fine needle aspirate were taken from animals and human, respectively. In this review, 309 and 21 *M. bovis* isolates were recorded from animal and human samples, respectively. The isolation of *M. bovis* from human cases in Ethiopia indicates how the agent is a potential risk to the public.

Keywords Animals, Bovine, Human, Infections, *Mycobacterium bovis*, Zoonoses

1. Introduction

Mycobacterium bovis (*M. bovis*) primarily the causative agent of bovine tuberculosis is in the *Mycobacterium tuberculosis* complex of the family Mycobacteriaceae. *Mycobacterium bovis*, which have a wide host range including humans, can survive for several months in the environment, particularly in cold, dark and moist conditions. Cattle shed *M. bovis* in respiratory secretions, feces and milk, and sometimes in the urine, vaginal secretions or semen and it can infect humans, primarily by the ingestion of unpasteurized dairy products, inhalation of aerosols and through breaks in the skin. 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. *M. bovis* caused as much as 25% of cases of human tuberculosis (TB) in developed countries in the late 19th and early 20th centuries. Today, only 1%–2% of human TB cases in developed countries are caused by *M. bovis* [1] which usually affects persons who acquired the infection locally before the implementation of control measures or in developing countries where control measures have not been implemented.

Mycobacterium bovis / bovine tuberculosis results with worldwide annual losses to agriculture of \$3 billion, but the human burden of tuberculosis caused by the agent is still unknown [2]. Some African countries like Cameroon, Djibouti, Egypt, Ghana, Nigeria, Tanzania and Uganda

collected 1475 (aggregate) sputum samples from human cases at different health institutes in their respective countries and were able to isolate 43 *Mycobacterium bovis* which accounts for about 2.9% [3-14]. In Ethiopia, the agent is isolated from human sputum and fine needle aspirates of cervical lymphadenitis samples, which is an indication of the contribution of this agent to human tuberculosis [15-17]. Moreover, the skin test positivity of cattle owned by tuberculosis patients is higher compared to non-tuberculosis household cattle [16]. In general, cattle harboring both *M. tuberculosis* and *M. bovis* at a time could put a challenge in the move of tuberculosis prevention/control program that currently runs in our country like the STOP-TB program agenda and the Millennium development goal achievements. This systematic review was aimed to show the magnitude/distribution of *M. bovis* and its public health importance in Ethiopia.

2. Methodology

For this review Endnote [18] and Google scholar engines were used to search relevant articles that are done in our country. The study design selected for this purpose was cross-sectional ones since most of the studies conducted so far are based on intradermal tuberculin skin test and meat inspections on animals. In a similar manner, human samples were collected once. In the articles reviewed, isolated *M. bovis* were identified by culturing and then using either biochemical tests or molecular techniques to confirm the agent. For this review key words; namely, *Mycobacterium bovis*, *M. bovis*, Bovine tuberculosis, Cattle tuberculosis, bovine tuberculosis in wildlife and *M. bovis* in humans were used to search articles using Endnote and Google. As

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inclusion criteria, culture positivity/biochemical tests, molecular positive results, cross-sectional study designs, human and cattle as well as wildlife samples and Articles written in English languages only were used for this purpose. The review covered research works from 2002-2011.

3. Results

From this review Fine needle aspirate and sputum from humans and milk and tubercle lesions from cattle were used as a sample for *M. bovis* isolation. Two, 3, 5 and 8 articles revealed the detection of *M. bovis* from sputum, fine needle aspirate, milk and tubercle lesions, respectively. In some circumstances, two or more samples were collected from a case. The details are presented hereunder.

M. bovis, the cause of bovine tuberculosis, was recorded in different parts of the country from human and animal samples. The result is presented in Table-1 based on years of publication. According to this review *M. bovis*, was reported in four regions of the country from FNA, sputum, milk, lesion samples collected and processed from humans and animal species, respectively. The number of *M. bovis* isolated from each samples vary and this is presented as a summary in Table-2. From human FNA samples collected and processed *M. bovis* accounted for about 2.42%, 17.14% and 50% from 165, 35 and 6 *Mycobacterium species* isolated, respectively.

The mean *M. bovis* isolation from the total FNA samples processed was 1.8% and it was 2.5% from the total *Mycobacterium species*. Eight point thirty three percent and 11.11% of *M. bovis* were isolated from 48 and 36 total *Mycobacterium species* detected from human sputum samples, respectively. The mean *M. bovis* isolation from the total sputum samples processed was 2.10% and it was 4.76% from the total *Mycobacterium species*. From cattle lesions and milk samples the contribution of *M. bovis* to the total *Mycobacterium species* detected ranged from 11.63%-100%. From the total milk samples and from the total *Mycobacterium species* isolated from the milk, *M. bovis* average percent detection was 1.12% and 7.10%, respectively. The average percentage isolation of *M. bovis* from the total cattle lesions processed was 0.83% and it was 5.83% of the total *Mycobacterium species*. From 31 *Mycobacterium species* detected *M. bovis* accounted for about 6.5% in camels. Eighteen *Mycobacterium bovis* were isolated from 20 *Mycobacterium species* detected in Goats, which accounted for about 90%. In this review there is no *M. bovis* recorded from wildlife samples.

M. bovis isolated in different parts of the country from human samples based on year of publication is presented in Table 3. Four hundred forty nine samples were collected from human cases and 21 *M. bovis* was isolated, which is about 4.7%. Of the total (290) positive *Mycobacteria species* isolated in human cases *M. bovis* accounted for about 7.2%. From 206 FNA and 84 sputum samples *Mycobacteria species* isolated, *M. bovis* accounted for about 6.3% and

9.52%, respectively.

M. bovis isolated from samples of different animal species from 2002-2011 is presented in Figure 1. From the Figure 1 it is possible to see that 4390 milk, tuberculous lesions were collected from cattle, and *M. bovis* was isolated from 289 cases, which accounted for about (6.6%). Of the total 625 positive findings for *Mycobacterium species* in cattle, *M. bovis* accounted for about 46.24%. From 65 Goats tuberculous lesions, *M. bovis* accounted for about 18 (27.7%). From the total 20 *Mycobacterium species* isolated in Goats 90% was *M. bovis*. From 91 total camel tuberculous lesions, *M. bovis* accounted for about 2 (2.2%). From the total 31 *Mycobacterium species* isolated in camels *M. bovis* accounted for about 6.5%. No *M. bovis* was isolated from samples of wildlife's. In total during these study periods (2002-2011) 4635 samples were collected from different animal species and of these 309 (6.7%) were *M. bovis*. From the total 705 *Mycobacterium species* isolated *M. bovis* accounted for about 43.3%.

4. Discussion

Mycobacterium bovis, which is a primary cause of bovine tuberculosis, is isolated in samples taken from animals as well as human tuberculosis patients in different parts of the world. Although the exact prevalence of bovine tuberculosis is not known in Ethiopia, different studies showed that the disease is endemic having a range of prevalence values from 10.1% in smallholder farms to 50% in peri-urban intensive dairy farms [19-21]. In our country, samples were collected from animals as well as humans. According to the studies conducted so far *M. bovis* isolated in 4 regions of the country namely; Amhara National Regional State (Gondar, Woldiya, Adet, Achefer, Bahir Dar zuria, and Kombolcha, Cheffa), Oromiya National Regional State (Central Ethiopia, Fiche, Adama, Methara abattoir, Modjo abattoir, Yabello, Gimbi, Ambo, Selalle, Debrezeit, and Holeta), Southern Nation and Nationalities Regional State (Hawassa, Hamer, Butajira, Hosenna and Melka Wonde) and Addis Ababa [16-40]. Even though the studies conducted are not exhaustive and wide in their scale the results obtained are indicative of the potential of the agent as a risk to the public. The agent was isolated from goats tuberculous lesions collected from Modjo export abattoir at a higher percentage that is, 18 out of 20 (90%) [38]. Nowadays small ruminates like Goat meat are exported to different countries from Ethiopia. The finding of *M. bovis* in these animals during meat inspection may result in trade embargo from importing countries. In addition to this the isolation of *M. bovis* from goats indicates that goats could be among the very susceptible host for the agent serving as a source of infection or maintenance host for the agent like badgers (*Meles meles*) in UK and African Buffalo in Africa [41]. This might need a special attention while considering/conducting any intervention program. In Nigeria out of 1387 screened goats, 62 (4.47%) had tuberculous lesions in their liver, lungs as well as mesenteric lymph

nodes and of these 4 goats were confirmed positive for *M. bovis* by molecular techniques and this figure is very low when compared to the findings in our country [42].

In this review from a total of 4390 milk and lesion samples collected from cattle 289 (6.6%) *M. bovis* was isolated shown that cattle are the main sources of infection with the agent. In total during these study periods (2002-2011) 4635 samples were collected from different animal species and of these 309 (6.7%) were *M. bovis*. From the total 705 *Mycobacterium species* isolated *M. bovis* accounted for about 43.3% signifying that it is the major isolate in animals [16, 23-31, 33, 35-40] Although the number of isolates was smaller that is 2 out of 31 (6.5%), *M. bovis* was also isolated from camel samples [40] indicating its importance in this animal species too as well as the agent epidemiology. Besides, eighty nine samples were collected and processed from different wild animal species in Hamar, Southern Ethiopia region. Although *M. bovis* is reported in wildlife by a number of articles in the literature, the *M. bovis* was not isolated from wildlife samples.

In the review out of 257 Fine Needle Aspirates processed [16, 26, 29]: 206 (80.2%) *Mycobacteria species* were isolated and 13 (6.3%) of them were *M. bovis*. From a total of 192 sputum samples processed from human TB cases [16, 29]: 84 (43.8%) *Mycobacterium species* were isolated and 8 (9.5%) of them were identified as *M. bovis*. Of the total (290) positive *Mycobacteria species* isolated in human cases from both samples ([16, 26, 29]) *M. bovis* accounted for about 7.24%. According to the review *M. bovis* in humans was isolated in central Ethiopia, Fitcha and three West Gojjam district. Isolation of *M. bovis* from these samples entails the contribution of the agent in pulmonary and extra-pulmonary tuberculosis. Infection of humans with *M. bovis* and becoming a tuberculosis patient is common in the world. In the United States and in other industrialized nations where few cattle are infected and milk is pasteurized, *M. bovis* causes less than 1% of tuberculosis cases in humans. From 2001 to 2004 there have been 35 identified cases of *M. bovis* tuberculosis in New York City [43]. In seven African countries between 2001-2008, from a total of 1475 positive *Mycobacterial tuberculosis* complexes isolated from suspected tuberculosis human samples 43 (~3.0%) isolate were *M. bovis* [3-14]. The figure obtained in these African countries is smaller than the findings obtained in Ethiopia, which is 7.24%. In another scenario in America, in Mercy Hospital, California, from 2000 through 2007, a total of 110 cases of adult HIV-TB co-infection were identified, of which 86 patients had culture-confirmed TB due to *M. tuberculosis* or *M. bovis*. Of the 86 TB cases 30 (34.9%) were identified as *M. bovis*, which is a larger figure compared to us and this might be related to the co-infection with HIV/AIDS in which one accelerates the other [44]. All these studies in general indicate that Bovine tuberculosis is becoming increasingly important due to the susceptibility of humans to the disease/disease causing agent, *M. bovis* and hence *M. bovis* infections may be much more significant than generally considered [45].

Out of the total 342 cow's milk samples processed [16, 23, 28-30, 33]; 54 (15.8%) samples revealed a positive result for *Mycobacterium species* and of which 23/54 (42.6%) were *M. bovis* with a mean percentage value of 1.12% and 7.10% from the total samples and total isolates, respectively. Similarly, out of the total 4048 different cattle lesion samples processed [24-27, 31, 35, 36, 38] 571 (14.12%) were positive for *Mycobacterium species* and of which 266/571 (46.60%) were identified as *M. bovis* with a mean percentage value of 0.83% and 5.83% of the total samples and total isolates, respectively. The isolation of *M. bovis* in both samples was high and this implies that milk and organs could serve as a good source/vehicle of infection for humans as well as animals. Milk should be seen as a vehicle for *M. bovis* infection to humans since one percent of skin test reactor cows will excrete tubercle bacilli in their milk [46] particularly in countries where bovine tuberculosis remain uncontrolled and ingestion of contaminated raw milk or other dairy products like cheese [47] with *M. bovis* is practiced. This in fact should be given attention since our community used cheese prepared from raw milk. In general it is possible to say that apart from acquiring *M. bovis* infections the chance of being a person developing the disease (human bovine tuberculosis) seems realistic and this is confirmed in countries like Egypt, Nigeria, Zaire and Tanzania [48-51].

In a nut shell isolation of *M. bovis* from these populations would have a great epidemiological importance. In countries like Ethiopia where most of the population lives in the rural community and their lives depend on agriculture, which is mainly, supported by participation of livestock activities the causative agent would have a dual effect to the community. For one thing, the agent may cause diseases to their animals and result in considerable morbidity and mortality thereby reducing labor, production as well as productivity. Secondly, animals would serve as a source of infection for humans to acquire human tuberculosis due to *M. bovis* and this is the most challenging effect. In countries like ours where animals and humans share the same shelter aerosol transmission could occur effectively. Besides, there is a tradition of taking raw milk in different parts of the country, which could expose individuals to acquire the infection easily and this is particularly true for children whose immunity is not well developed and HIV/AIDS patients whose immunity is compromised.

5. Conclusions and Recommendations

Although the studies conducted are limited, the current review gives brief evidence on the distribution of *M. bovis* in different animal species level including human beings and areas in the country. The isolation of the agent from humans indicates the possibility of the agent adaptation to humans having a chance of disease induction by its own stand and therefore it should be seen as a potential cause for human tuberculosis of bovine origin. The agent isolation from camels as well as goats in our country gives an alarming

situation as to the circulation of the agent in different animal species indicating the potential danger of the agent to humans, other domestic and wild animals. Even though the agent is not isolated in wild animals as per this review, particularly in areas where there is a communal grazing and

watering points for domestic and wild animal populations, the agent transmission would be simplified, thereby complicating its epidemiology. The isolation of *M. bovis* should be considered as a potential threat to humans in the country and various aspects of the disease should be studied.

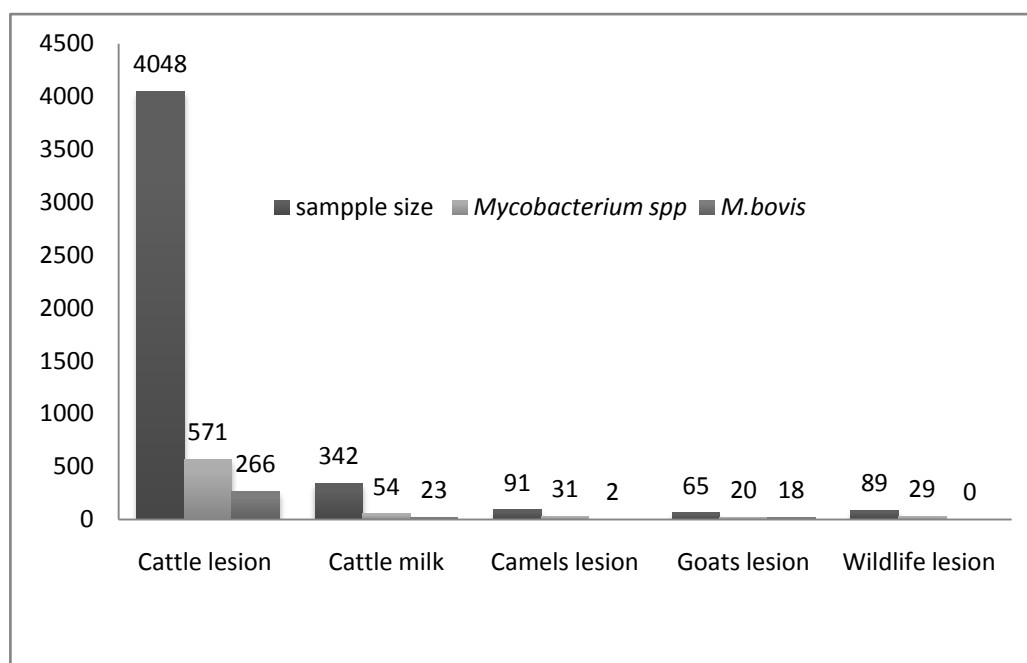


Figure 1. *M. bovis* isolated from samples of different animal species

Table 1. Distribution of *M. bovis* in different parts of Ethiopia based on laboratory findings from 2003-2011 G.C

Year	Areas where <i>M. bovis</i> recorded	Sample			<i>M. bovis</i>	References
		Species	Type	size		
2002	Sothern Ethiopia	Human	FNA ¹	40	6	[22]
2003	12 dairy farms in the country: Debrezeit, Zway, Holetta, Ambo, Cheffa(wollo), Sebeta and Selalle,	Cattle	Milk	30	4	[23]
2004	AA abattoir and Hosaena abattoir	Cattle	Lesion	893	62	[24, 26]
2006	AA abattoir	Cattle	Lesion	69	5	[26]
2007	Holeta farm and Adama town	Cattle	Lesion and milk	61	44	[27, 28]
2008	Central Ethiopia, Fiche and AA farms	Human	Sputum and FNA ¹	108	7	[29, 30]
		Cattle	Milk	201	10	
2009	Gondar, Jinka Woldiya, Gimbi, Butajira Abattoir, Butajira, Achefer, Adet bahirdar zuria	Cattle	Lesion and milk	1593	62	[16, 31]
		Human	FNA ¹ and sputum	299	8	
2010	Hawassa town and surrounding, AA, Adama, Hawasa, Yabello and Melkawondo abattoirs, Kombolcha/Wollo, Hamer area	Cattle	Lesion and Milk	1921	318	[33, 35-37]
		Wild life	Lesion	89	0	
2011	Central Ethiopia	Cattle	Lesion	52	31	[39]
	Modjo Export abattoir	Goats	Lesion	65	18	[38]
	Akaki and Methara abattoir	Camels	Lesion	91	2	[40]

FNA¹: Fine Needle Aspirates

Table 2. Isolation of *M. bovis* from different samples in percent from 2003-2011 G.C

Sample		<i>M. bovis</i>				References
Type	Size	<i>M. species</i>	Isolated in No	% from total samples	% from total isolates	
FNA ¹	257	206	13	80.2%	6.3%	[16, 22, 29, 32]
Sputum	192	84	8	4.20	9.52	[16, 29]
Milk	342	54	23	6.73	42.60	[16, 23, 28-30, 33]
Cattle lesion	4048	571	266	6.60	46.6	[24-27, 31, 35-37, 39]

FNA¹: Fine Needle Aspirates**Table 3.** *M. bovis* isolated in different parts of Ethiopia from human samples in 2002, 2008 and 2009 G.C

Year of publication	Sample		<i>M. Species</i> isolated in No	<i>M. bovis</i> Isolated in No	Area detected	References
	Type	Size				
2002	FNA ¹	40	35	6	Southern Ethiopia	[22]
2008	FNA ¹	21	6	3	Fiche	[29]
	Sputum	87	36	4		
2009	FNA	196	165	4	Achefer, Adeit and Bahir Dar Zuria weredas	[16, 32]
	Sputum	105	48	4		
Total		499	290	21		

FNA¹: Fine Needle Aspirate

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