



REVIEW ARTICLE

Recent advances and challenges in the management of bovine tuberculosis

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ABSTRACT

Introduction: bovine tuberculosis, caused by *Mycobacterium bovis*, persists as a global health and economic problem, with zoonotic implications that affect public health and livestock sustainability.

Objective: to analyze recent advances in the diagnosis, epidemiology, prevention, and control of bovine tuberculosis, identifying current challenges and future perspectives.

Methods: a systematic review of the scientific literature was conducted across various databases. The search was performed using an algorithm with keywords and Boolean operators, allowing the identification of relevant sources. The selected studies, after applying inclusion and exclusion criteria, were critically analyzed considering timeliness, methodological quality, and thematic relevance, and integrated into the final synthesis of the review.

Development: the literature shows the persistence of the disease in multiple regions, with variable prevalence and diagnostic limitations associated with the tuberculin test. Vaccination with BCG and attenuated variants shows promising results, although still insufficient for eradication. Risk factors such as age, pregnancy, and coexistence with wildlife, which act as reservoirs, are highlighted. Control strategies include biosecurity programs, quarantine, and culling, though they face economic and social barriers. WHO and international organizations promote integrated approaches under the One Health paradigm, emphasizing the need for diagnostic innovation and greater investment in research.

Conclusions: bovine tuberculosis remains a complex challenge that requires integrated strategies of control, surveillance, and vaccination. International cooperation and the One Health approach are essential to mitigate its zoonotic and economic impact, strengthening livestock sustainability and public health.

Keywords: One Health; Diagnostic Techniques and Procedures; Tuberculosis, Bovine; Zoonosis Surveillance; Zoonoses.

INTRODUCTION

Bovine tuberculosis (bTB), primarily caused by *Mycobacterium bovis* (*M. bovis*), continues to be an endemic disease affecting livestock worldwide. Despite control efforts, it remains a significant concern for animal health, public health, and the livestock economy. Transmission of bTB from animals to humans, although less common than human tuberculosis, poses a risk—particularly in regions where the disease is endemic in cattle. In recent years, significant advances have been made in understanding the epidemiology, diagnosis, and treatment of bTB. However, challenges persist, including the need for more sensitive and specific diagnostic methods and more effective control strategies.⁽¹⁾

The disease affects both domestic and wild animals globally. It became one of the first pathological entities in which the role of a bacterium as the cause of disease was demonstrated, thereby making a substantial contribution to the consolidation of the microbial theory of disease.⁽²⁾ Scientist Robert Koch isolated the tubercle bacillus and presented this major finding to the Physiological Society of Berlin on March 24, 1882. This advance in understanding tuberculosis etiology, combined with empirical observation that individuals who recovered from the disease did not suffer from it again, laid the groundwork for the scientific design of vaccines. This milestone represented a revolution in human medicine and significantly altered human population history.⁽³⁾

Mycobacterial pathogenicity is a multifactorial process dependent on several virulence factors, primarily complex lipids in the cell wall, as well as proteins and protein complexes. Mycobacteria possess a very thick cell wall containing complex hydrophobic lipids. The core of the cell wall consists of three linked molecules: peptidoglycan, arabinogalactan, and mycolic acid—known as the mycolyl-arabinogalactan-peptidoglycan complex. This complex lies beneath a superficial sheet-like layer of glycolipids composed of surface lipids such as mycosides, cord factor, wax D, sulfolipids, and sulfatides.⁽⁴⁾

Globalization and modernization have increased the complexity of the global tuberculosis disease burden. Therefore, a fundamental understanding of disease ecology and transmission becomes mandatory. The interdependence among humans, animals, and the environment plays a key role in disease transmission. Among the various elements impacting transmission, basic variables include the natural attributes of the bacterium and potential host, as well as bacterial persistence.⁽⁵⁾ In light of this, the present review aimed to analyze recent advances in diagnosis, epidemiology, prevention, and control of bovine tuberculosis, identifying current challenges and future perspectives.

METHODS

The study was structured as a systematic literature review following PRISMA recommendations. The search covered publications from January 2010 to December 2024, aiming to identify recent advances and challenges in bovine tuberculosis management.

Information sources included Web of Science, Scopus, PubMed, Redalyc, EBSCO, and Google Scholar, as well as gray literature in the form of technical reports from international organizations (WHO, FAO, OIE). Secondary references from relevant articles were also reviewed to broaden thematic coverage. The search strategy employed keywords and Boolean operators: "bovine tuberculosis" OR "Mycobacterium bovis" AND ("diagnosis" OR "epidemiology" OR "control" OR

“biosecurity”). Publications in English and Spanish were considered, prioritizing peer-reviewed articles.

Inclusion criteria were: articles published within the defined timeframe, clinical studies, narrative or systematic reviews, and documents addressing epidemiological, diagnostic, therapeutic, or preventive aspects of bovine tuberculosis. Duplicates, articles without full-text access, irrelevant publications, and documents outside the temporal range were excluded.

The selection process involved title and abstract screening followed by full-text analysis. Initially, 74 records were identified; 49 were excluded for failing to meet inclusion criteria. Ultimately, 25 articles were incorporated into the review.

Data extraction included variables such as author, year, study design, analyzed population, main findings, and conclusions. Analysis was performed through qualitative synthesis, grouping results into categories related to epidemiology, diagnosis, treatment, and prevention. No meta-analysis was conducted due to study heterogeneity, but narrative integration allowed identification of recent advances and persistent challenges in bovine tuberculosis control.

DEVELOPMENT

A recent study indicated that zoonotic tuberculosis is re-emerging as an infectious disease in high-income countries and remains a neglected disease in low- and middle-income countries. Moreover, because the burden of *M. bovis*-associated zoonotic tuberculosis is unknown, it is likely underestimated. Estimates of zoonotic tuberculosis prevalence are also inaccurate, as current laboratory tests cannot distinguish between *Mycobacterium tuberculosis* complex species infecting humans or animals.⁽⁶⁾

Since 2016, WHO has estimated the burden of zoonotic tuberculosis based on scientific studies and has proposed strengthening surveillance to more accurately determine disease burden. Of the 10 million people in 2019 with new cases of active tuberculosis, an estimated 140,000 (range: 69,800–235,000) had zoonotic tuberculosis (1,4 %), and approximately 11,400 (range: 4,470–21,600) ultimately died (8,1 %). For zoonotic tuberculosis in cattle, studies have reported a confirmed *M. bovis* prevalence ranging from 0 % to 28 %; however, some of the culture methods and molecular techniques currently used in laboratories are inadequate for tuberculosis diagnosis.⁽⁶⁾

Achieving a tuberculosis-free world is a desirable goal concerning human, animal, and environmental health, in accordance with the One Health principles. Given the cross-species transmission of *Mycobacterium tuberculosis* through close human-animal interaction, human tuberculosis cannot be eradicated without addressing zoonotic tuberculosis. The 2020 UN Secretary-General’s progress report recommended ten priority actions to accelerate progress toward global tuberculosis targets. Additionally, the roadmap developed by WHO, FAO, and OIE outlines ten priorities for tackling zoonotic tuberculosis. Both call for high-level leadership, multisectoral and collaborative action, increased investment in high-quality scientific research and innovation, and universal health coverage for all tuberculosis patients.⁽⁷⁾

WHO, civil society, and the Stop TB Partnership have issued a strong call to action for greater access to tuberculosis preventive treatment, urging governments to support research and innovation—particularly in vaccine development—to better combat tuberculosis and ensure that at least 30 million people receive tuberculosis preventive treatment by 2022.⁽⁸⁾

It is important to note that, beyond cattle, tuberculosis affects a wide variety of domestic and wild animal species, both free-ranging and captive—including goats, sheep, pigs, deer, wild boar, badgers, opossums, and ferrets—many of which are recognized as potential reservoir hosts. Indeed, experimental and field trials studying the BCG vaccination response in some of these species suggest that, while vaccination provides incomplete protection, its use in domestic, captive, or free-living wildlife species should be seriously considered to reduce cross-species transmission risk.⁽⁸⁾

Alternative approaches to tuberculosis control have also been explored, such as test-and-segregation and treatment with antimycobacterial agents, including isoniazid. Isoniazid treatment is not cost-effective and is not recommended due to the long duration required and the necessity to withdraw milk, along with reports that bacterial shedding may resume shortly after discontinuation. Furthermore, the use of a first-line antimycobacterial agent in animals intended for human consumption raises serious concerns regarding its potential contribution to the spread of drug-resistant tuberculosis.⁽⁹⁾

Over the past decade, research in this field has also focused on alternative therapeutic strategies against tuberculosis, including heterologous prime-boost approaches, genetic modifications of BCG strains to enhance immunogenicity, and complete replacement of BCG with attenuated *M. bovis* strains.⁽¹⁰⁾

According to Yuta S, et al.,⁽¹¹⁾ an increase in bTB prevalence was observed in a cattle herd, suggesting an urgent need for enhanced control interventions. Conversely, Kelly RF, et al.,⁽¹²⁾ reported a significant decrease in tuberculin test efficacy for detecting bTB in certain cattle populations. These findings highlight the complexity of bTB epidemiology and the need for multifaceted, adaptive control approaches.

Heat-inactivated *M. bovis* vaccines have also shown promise recently in wild boar, pigs, deer, badgers, and goats. However, despite significant efforts and promising preclinical results, there is limited evidence from clinical and field trials demonstrating substantial gains in efficacy for these next-generation modified BCG vaccines.⁽¹³⁾

Interestingly, both heat-inactivated and attenuated vaccines for another major mycobacterial disease—paratuberculosis (Johne's disease)—have been licensed and widely tested for use in cattle and small ruminants, but their use is restricted in many countries due to potential interference with tuberculin tests and diagnostic tools currently employed in bTB control and eradication programs.⁽¹⁴⁾ In some countries, vaccination has been used to manage reservoir wildlife and domestic species and may thus serve as a valuable complementary tool for bovine tuberculosis control.⁽¹⁵⁾

Although many animals are susceptible, relatively little is known about the status and potential of other wild animals—as illustrated by a UK study on badger proximity and farm surveillance in Northern Ireland, where cats were frequent visitors. Farm and feral cats could be considered potential sentinel hosts for bovine tuberculosis in cattle, but culture-confirmed *M. bovis* reports in cats are relatively rare and mainly occur in endemic areas. There are some publications on bovine tuberculosis in farm cats, but apparently none on feral cats.⁽¹⁶⁾

Complete eradication of bovine tuberculosis has not been achieved in any country due to major obstacles, including failures in detecting infected animals or confirming infection at slaughterhouses via bacteriological culture. These failures stem from anergic carriers, breaches in herd biosecurity, or infection introduced by newly added animals into previously free herds. Undetected reactors create administrative and public relations difficulties. Wildlife reservoirs

further complicate eradication. Large herds—as found in North and South America—where cattle are raised extensively on vast ranches or stations, pose additional challenges.⁽¹⁷⁾

As a respiratory infection, infectious particles may originate from sputum (respiratory tract) or contaminated fine dust particles, representing a potential environmental route. Subsequent transmission appears to require lung lesions and associated lymph nodes. Contrary to established dogma, most (40–73 %) confirmed bTB reactors exhibit pulmonary lesions, although many are too small to be routinely detected during meat inspection at slaughterhouses—posing a zoonotic risk.⁽¹⁸⁾

Notably, in 2022, the World Organisation for Animal Health (WOAH) replaced the bovine tuberculosis chapter in its *Terrestrial Animal Health Code* with a new chapter on mammalian tuberculosis, recognizing that the original definition—limited to tuberculosis in cattle caused by *Mycobacterium bovis*—was no longer adequate. It has been demonstrated that tuberculosis in cattle is also caused by other newly characterized members of the complex, while simultaneously *M. bovis* has been shown to cause tuberculosis in a wide variety of other mammalian hosts.⁽¹⁹⁾

At the individual animal level, age and pregnancy were identified as potential risk factors for bovine tuberculosis in Bangladesh. Pregnancy-related immunosuppression may predispose animals to *M. bovis* infection, with higher prevalence observed in crossbred cattle in peri-urban and urban areas. The study underscores the urgent need to develop a comprehensive national strategy for bovine tuberculosis control in high-risk cattle groups to minimize animal-to-human and inter-animal transmission risks.⁽²⁰⁾

Currently, the recognized bovine tuberculosis control strategy in South Africa is based on “test-and-slaughter,” using the intradermal tuberculin test followed by culling of positive animals. Affected herds are placed under veterinary quarantine with movement restrictions until the outbreak is eradicated—a process that may take several years or continue indefinitely if eradication proves unattainable.⁽²¹⁾

The same measures apply to infected buffalo populations, often with no prospect of eventual eradication. In contrast, many European livestock farms have adopted alternatives to avoid business closures, such as promoting biosecurity interventions to reduce tuberculosis risk and developing integrated disease control plans designed to manage infection in appropriate reservoir hosts (wild and domestic) and thereby interrupt primary transmission chains.⁽²²⁾

Wildlife often shares pasture with livestock, and research indicates this contributes to mycobacterial spread, clearly posing a risk of disease transmission to domestic animals and presenting a zoonotic threat. Cases have been observed in breeding centers—such as zoos or bison facilities—and infected animals in Poland may represent a potential risk to tourists, caretakers, or veterinarians.⁽²³⁾ More effective disease control strategies could be implemented if we better understood how risk factors influence this disease with complex epidemiology, which likely varies between herds and regions.⁽²⁰⁾

Major consequences of this disease include adverse impacts on: animal welfare; trade in animals and animal products; farmers’ livelihoods; natural resources, such as the conservation of endangered wildlife species; and public health. Livestock tuberculosis control strategies largely rely on ante-mortem testing and post-slaughter inspection to identify infected animals, followed by epidemiological traceback investigations to identify herds at risk of infection.⁽²¹⁾

No symptoms appear in the early, asymptomatic stage of the disease. In advanced cases, lymph node enlargement may obstruct airways, the digestive tract, and blood vessels. Ante-mortem examination based on clinical signs may be used for tentative and presumptive diagnosis. Although *M. bovis* is not the primary cause of human tuberculosis, it can infect humans through consumption of infected animal products, inhalation of infectious droplets, or direct exposure to infected animals. Advanced tuberculosis can lead to death in both animals and humans. Therefore, disease control and prevention are essential to save lives and reduce illicit trade.⁽²²⁾

A review study estimating bovine tuberculosis prevalence in South America found that Ecuador has a relatively high prevalence of over 1 %. This finding is supported by other reports from Ecuador recording a prevalence range of 0,71–8,63 %, depending on geographic region or methodology used—such as tuberculin skin test surveys or slaughterhouse inspection. Regarding the zoonotic aspect of bovine tuberculosis, *M. bovis* is estimated to account for 2 % of all human TB cases in South America.⁽²³⁾

In a cross-sectional study conducted at the Municipal Slaughterhouse of Mejía Canton, apparent bovine tuberculosis prevalence was estimated based on macroscopic post-mortem inspection and *M. bovis* isolation. A total of 395 bovine carcasses were examined during the study period; 4 animals were diagnosed with pulmonary lesions compatible with tuberculosis, yielding an apparent prevalence of 1.01 % (95 % CI: 0,28 %–2,57 %). Bacteriological culture identified *M. bovis*-compatible isolates in six animals, resulting in an apparent prevalence of 1,52 % (95 % CI: 0,56 %–3,28 %).⁽²⁴⁾

Risk factors such as age, breed, sex, and origin of the animals were not significantly associated with apparent disease prevalence. Significant prevalence of macroscopic lesions and *M. bovis* was observed without significant association with predisposing factors for visible lesions or pathogen presence, preventing redirection of control strategies toward specific at-risk populations.⁽²⁵⁾

CONCLUSIONS

It is essential to develop an integrated strategy for bovine tuberculosis control to minimize the risk of animal-to-human and inter-animal transmission through disease prevention and control. Wildlife contributes to mycobacterial spread, clearly posing a risk of disease transmission to domestic animals and representing a zoonotic threat to public health.

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