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Bovine Tuberculosis and the Multidrug Resistance of *Mycobacterium*

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Bovine tuberculosis (bTB) caused *Mycobacterium bovis,* is a chronic infectious disease that primarily affects cattle and can affect other animals also. This zoonotic disease spread around the world, with the exception of Antarctica. Around fifty million cattle are suffering from bTB worldwide.

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This disease is highly significant to public health, leading to economic losses, especially in countries where livestock are the main source of livelihood. Aerosol mode of transmission is the most common way of infection in cattle and infection also can spread through contaminated material. bTB affected animals will show fluctuating low-grade temperature, weakness, gradual emaciation, decreased appetite and breathing difficulty, wet cough, or tachypnoea. The caseo-necrotic granuloma is the hallmark of TB and which is a process by the host to localize the disease and to allow immune and inflammatory mechanisms to act on bacilli. Treatment is not recommended for bTB due to its infectious nature. Due to its infectious nature, culling is often recommended as part of control strategies in many regions. The drug for treating bTB is Rifampin and Isoniazid. *Mycobacterium bovis*–BCG vaccination is used for bTB control in India.

Keywords: BCG vaccine; cattle; control; multi-drug resistance; Mycobacterium bovis; public health; risk factors; worldwide; zoonosis.

1. HISTORY

Borham et al. (2022) reported that in ancient times, many mammals were affected by tuberculosis. In 1832 J. L. Schonlein first published the name “tuberculosis” (German: Tuberkulose). *Mycobacterium tuberculosis* was discovered by Koch in 1882 (Mitermite et al., 2023) and in cattle *Mycobacterium bovis* from *Mycobacterium tuberculosis* found by Smith in the year of 1898. For 200 years, this disease was a leading cause of mortality in livestock mainly in cattle. bTB is occur by *M. bovis*, which is considered as a zoonotic disease and a financial concern that affects the productivity of cattle leading to death. Cattle farming in the UK are significantly facing challenges because of the presence of bTB (Fielding et al., 2021).

2. INTRODUCTION

Bovine tuberculosis (bTB) is a zoonotic as well as chronic disease caused by *M. bovis,* mostly affects cattle but it can affect other animals also. Kouengoua et al*.* (2024) reported that bTB is a notifiable disease by the World Organisation for Animal Health (WOAH) previously *Office International des Epizooties* (OIE). This disease is highly significant to public health, leading to economic losses, especially in countries where livestock are the main source for livelihoods. bTB is the persistent problem which needs to be controlled and eradicated mainly in middle-income and low-income countries. bTB is recognized as an important zoonotic disease by the World Health Organization, and bTB needs coordinated efforts for control and prevention (Robi et al., 2024).

In India, cattle population comprises more than 16% of world cattle population. Cattle are the natural host of *M. bovis*. The major source of spreading to the public is by the ingestion of beef from infected cattle. Aerosol exposure is the most common way of infection in cattle and infection can occur through contaminated material also. Barua et al*.* (2016) investigated the infection of bTB in abattoirs in Ri-Bhoi district of Meghalaya. Cattle are mainly reared as a source of income in Meghalaya. In Ri-Bhoi district local indigenous cattle (70%) are more than others like Jersey crossbred.

bTB is referred to as a zoonotic disease which can lead to economic losses in cattle production. In developed and developing countries this zoonotic disease directly affects public health. *M. bovis* is a member of the *M. tuberculosis* complex, and cattle acts as a host. In cattle, *M. bovis* infections are sometimes asymptomatic so it is very difficult to control. Clinical signs vary from dyspnoea, coughing and low-grade fever in respiratory form to constipation, and diarrhoea when it involves the digestive system (Dametto et al*.* 2020).

3. ETIOLOGY

bTB is caused by obligate pathogen *M. bovis* subsp. *bovis* but sometimes infections also caused by *M. bovis* subsp. *caprae*, *M. tuberculosis* and *M. africanum*. In the central part of Europe, *M. bovis* subsp. *capra*e are the leading cause of tuberculosis in cattle and commonly considered as bovine or zoonotic tuberculosis (Kuria, 2019).

Only genus *Mycobacterium* is included in the family *Mycobacteriaceae* in the order Actinomycetales*.* In the current study *Mycobacterium* genus has over 150 species and 13 subspecies and *Mycobacterium* genus is classified based on pathogenicity and growth rate. The two groups- tuberculous and non-tuberculous mycobacteria (mycobacteria other than tuberculosis (MOTTs) classification is based on pathogenicity. The genus is classified into obligatory pathogens, saprophytic or ubiquitous microorganisms and potentially pathogenic. *Mycobacterium tuberculosis* complex (MTBC) are obligatory pathogens belonging to groups which include *M. bovis* subsp. *bovis, M. bovis* subsp. *caprae, M. bovis BCG, M. tuberculosis, M. africanum, M. canetti, M. microti, M. leprae,* and *M. pinnipedii*. Identical 16S rRNA sequences are present in all species which are 99.9% similar with nucleotide level. This may also be considered as subspecies, depending on their host range (King et al., 2017).

M. bovis is facultative intracellular, non-motile, obligate aerobic, and non-spore forming. Its dimensions are 0.2–0.6 µm in breadth and 1–10 µm in length (Nava-Vargas et al., 2021). The microbes grow best in frozen tissue and incubation period is 3 weeks, the *M. bovis* can survive for long days in the chilly, damp and gloomy environment (Kasir et al., 2023). Survival period of *M. bovis* microbes differs from 18-332 days at 12°C to 24°C depending on sunlight exposure.

4. EPIDEMIOLOGY

bTB are spread around the world, except in Antarctica. Around fifty million cattle are suffering from bTB (Ramos et al*.,* 2020) worldwide. Ramanujam and Palaniyandi, (2023) said that worldwide, India has the largest bTB infected herds with a prevalence of 7.3%.

Mohamed, (2020) said that according to recent statistics, some countries are free from bTB like Australia, Jamaica, Sweden, the Czech Republic, Norway, Switzerland, Denmark, Luxembourg, Latvia, Slovakia, Austria, Iceland, Estonia, Canada, Lithuania, Finland, Barbados, and Singapore. The United States reported that New Zealand, Japan, and several European nations are taking initiatives to eradicate bTB. bTB are still a serious issue for cattle and other livestock including sheep, goats, camels and wild animals like deer, civets, and possum.

The underdeveloped countries have insufficient facilities to control this malady and day by day the disease spreads to public health. bTB is the most challenging infection for the livestock industry that causes considerable financial losses (Little, 2019). In Africa, 85% of cattle are reared in places where bTB reported. Variations in the production of strategies in the African continent, such as pastoralism, mixed farming, agro-pastoralism and intensive dairy cattle farming may have a major impact on the transmission of bTB (Ghebremariam et al., 2016; Pokam et al*.,* 2019).

Regional variations in bTB prevalence reported within a nation. Reports from South America show that locations near the towns with high concentrated milk production are hot spots of bTB (Avila et al*.,* 2018). India (7.3%) stands first in bTB prevalence followed by Brazil (2.5 %), and China (2.4 %) (Rodrigues et al., 2020).

5. RISK FACTORS

1. Risk factors: Animal level (Broughan et al., 2016);
2. Risk Factors: Herd-Level (Wright et al., 2015);
3. Environmental Risk Factors (Allen et al., 2021)

5.1 Risk factors- Animal level

i. **Genetics**: Significantly differs with heritability of susceptible cattle to bTB, especially pure-bred Holstein Friesian or crosses in Great Britain and Ireland.

ii. **Breed**: Jersey cattle showed higher bTB prevalence in some studies in India compared to Holstein Friesian. Reports from Africa showed that the native breeds like zebu cattle found in pastoral environments is more resistant to tuberculosis than European cattle.

iii. **Sex**: Most of the studies showed that female cattle have a higher prevalence of bTB compared to male. In dairy cows, which are aged ≥ 2 years are more susceptible than beef cattle, but very young cattle of 0-1 years are also affected by bTB.

iv. **Milk yield and reproductive status**: The reproductive status influence on the susceptibility of bTB infection may be difficult to ascertain since gestation and lactation period are inseparable. During the reproduction stage there will be large hormonal shifts and stress occurs in dairy cows which influence the development of infection. Infection in calves may be contracted through consumption of milk from infected cows. It is observed that lactating cows had higher prevalence of bTB than pregnant cows.

v. **Age:** It is observed that as the age increases prevalence of bTB infection also increases. bTB infection and age are related. It is found that 12 to 36 months aged cattle are at highest risk of infection.

vi. **Body condition of the animal and nutritional status:** Malnutrition reduces the immunity and infections are highly related to body score in HF dairy cows.

vii. **Concurrent infection:** bTB spread in two farms along with bovine viral diarrhoea infection. It is reported that bovine viral diarrhoea infected calves when infected with bTB has increased *M. bovis* shedding in nasal secretions.

5.2 Herd-Level Risk Factors

i. **Herd size:** Herd size is linked to development of bTB in cattle. Dynamic modelling showed that infection rate is higher in larger herds due to increased animal contacts which increase the herd transmission rate of infection.

ii. **Total farm area, neighboring herds and fragmentation:** Common boundary, fragmentation holdings with nearby cattle farms increases the contact. Increases in farm size are related to high susceptibility to infections. Although even after controlling the herd size the risk of infection may remain high due to the nearby premises or from increased wildlife contact.

iii. **Movements of Cattle:** In Ireland, bTB spreading is due to cattle movements (6% to 15%). In Great Britain, this disease is present in West and South-West Wales.

iv. **Farm management:** The poor dairy herd management practices like the one in farm buildings, and feed stores, and intensive management practices increase bTB transmission in a herd.

5.3 Environmental Risk Factors

Survival of Tubercle bacilli is good in moist, cool, and in areas protected from sunlight. The persistence of bacilli is based on the temperature, relative humidity and sunlight. Prolonged survival period observed in winter rather than summer. *M. bovis* remain alive more in shady conditions than sunny conditions. Bacilli can survive in a favourable environment for a few days to 2 years.

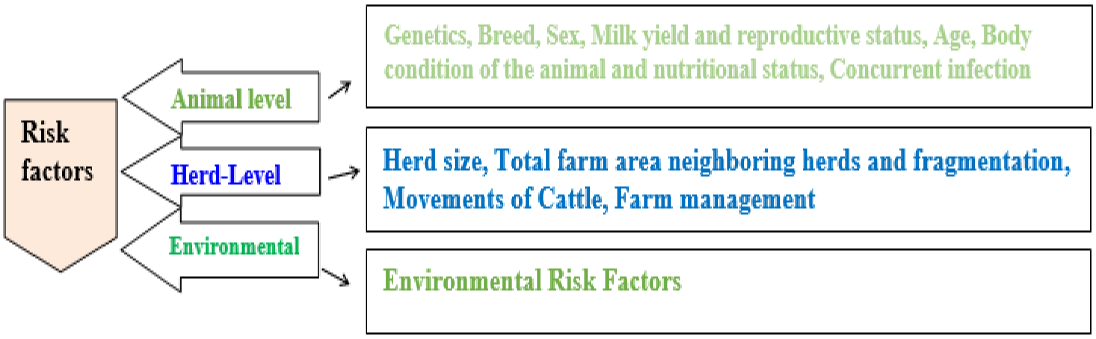

Fig 1. Risk factors

6. TRANSMISSION

Since first part of the 20th century in Europe, Denmark, the UK, Germany recorded a large number of humans to cattle transmission of TB cases. Recently many documented reports of association between cattle and humans' tuberculosis are reported in Africa (Sichewo et al., 2020).

The World Health Organisation referred to the TB caused by *M. bovis* as an ignored zoonotic disease in humans. *M. bovis* can get transmitted to humans through improperly cooked meat, soured milk, contaminated animal products, unpasteurized dairy products and animal to animal, animal to human or human to human direct contact. Infection with *M. bovis* in people is seen in sub-Saharan countries including South Africa (Sichewo et al*.,* 2019).

In Tanzania, *M. bovis* infection is reported in different hosts including cattle, wildlife species and humans. Livestock movements can increase the cross-species transmission of infections between wild and domestic animals. Transmission of bTB infection from domestic animals to wildlife and *vice versa* transmission is dependent on environmental conditions, and human behaviour (Katale et al., 2017).

Infected animals secrete *Mycobacterium* pathogens through saliva, aerosols, urine, feces, milk, and discharging lesions. Mainly transmission occurs through infective aerosols. Tuberculous lesions can be found in the airways and associated lymph nodes. Close contact among animals has a major role in transmission (Good et al*.,* 2018).

In intensive livestock practices such as zero-grazing enhances close contact among animals. Feed and water are less important sources of transmission in comparison to untreated manure. Oral route of transmission reported in calves during suckling. In extensive farming practices, contact can be seen in night shelters and other places (Yadav and Prakash, 2017).

Aerosols from infected cattle frequently infect others in close contact, and ingestion-based transmission is rare, with a possible exception of suckling calves from infected cows. In cattle congenital transmission also reported (Phipps et al., 2018).

7. PATHOPHYSIOLOGY

After inhalation the bacilli are present in the upper airways. Presence of cell wall lipids helps tubercle bacilli to resist phagocytosis and they can proliferate in macrophages. Cell-mediated immunity reactions occur due to *Mycobacterium* accumulation. The caseo-necrotic granuloma (tubercle) is the hallmark of TB which is an effort by the host to restrict the disease process and to destroy bacilli. In tubercle the peripheral zone is of fibroblasts and lymphocytes and the central area contains giant cells (Datta et al., 2016). If phagosome-lysosome combination is disturbed, the bacilli will multiply at the infection site (Zhai et al*.,* 2019).

Tubercles are hard, yellow, and spherical, with a diameter of 1–3 cm and core is of dried cellular debris. Tubercles, of 2–3 mm in diameter can also be caused by infection, and spread haematogenously to other organs which gave rise to the term known as “miliary tuberculosis” (Carrisoza-Urbina et al., 2019).

8. CLINICAL SIGNS

The clinical signs in cattle are developed according to the organ systems involved. During the initial stages of infection clinical signs are not appreciable. The gradual onset of signs characterized by mild fluctuating fever, debility, chronic moist cough, dyspnea, reduced exercise tolerance (Thoen et al*.,* 2016). Lymph nodes of the head and other may enlarge due to obstruction. Diarrhea or constipation may be seen because of gastrointestinal tract involvement.

Infected animals can remain bright and alert and maintain a good appetite despite weakness and sluggishness. Miliary tuberculosis may lead to acute or subacute death by rapid widespread from primary or secondary lesions through the haematogenous route (Krajewska-Wędzina et al., 2020).

The granulomatous bronchopneumonia can be detected by auscultation and percussion. Draining abscesses and superficial lymph node enlargement may also be seen. Deeply affected lymph nodes always cannot be palpated, although may cause obstruction of the airways, pharynx, and gut, and may lead to dyspnoea and ruminal tympany (Khairullah et al., 2024).

In advanced stages of bTB infection there will be weakness, a fluctuating low-grade temperature, decreased appetite, and gradual emaciation (Ramos et al*.,* 2015). Breathing difficulty, wet cough, or tachypnoea may be seen. The lesions are mainly observed in the upper airways, tonsils and lungs in affected animals (Pal et al*.,* 2022). Infected animals with a good appetite are seen in cows with progressive emaciation, temperature swings, erratic appetite and hair on the exterior may become abrasive (Krajewska-Wedzina et al*.,* 2022).

9. ECONOMIC IMPACT

bTB is a concern in the economic status of the farmer and animal health. *M. bovis* are incriminated as a reason for approximately 25% of TB cases in children. In the top 14 principal diseases, the bTB is listed that affect livestock production in South Asia and Africa. The loss due to bTB in these countries is approximately estimated to be US$300 million annually and globally around US$3 billion annually. The cost is attributed to culling and less productivity, trade restrictions and movement controls (Pereira et al., 2020; Pérez-Morote et al., 2020). Reduced milk and meat production and reproductive difficulties, and the stock replacement are the major things in livestock losses (Borja et al., 2018). bTB has an impact on global markets, with the bad effects significantly extending to various sectors related to livestock economics. Countries with enzootic bTB will become economically inefficient due to decrease in export of animal products (Gong et al., 2021). bTB can potentially disrupt entire ecosystems, and the efforts will become more costly and challenging to eliminate the negative impacts like those in tourism and land for agriculture (Kemal et al., 2019).

10. DIAGNOSIS

Tuberculin skin test is the ideal detection test for bTB when the cattle is alive. Procedure is injecting the tuberculin intradermally and then measuring the difference in skin thickness 72 hours of inoculation. Apart from this, blood-based tests like gamma interferon assay that measures cell mediated immunity (CMI) is also used. This test is detecting the gamma interferon levels in previously sensitized bovine blood cells with *M. bovis* (Shaltout, 2024).

Caudal Fold Tuberculin test (CFT) is readable at 72 h ± 6 h and if the animal is sensitive then it can be followed by the Comparative Cervical Tuberculin test (CCT) which is also readable in the same timeframe. Follow-up CCT testing can be done in 10 days of the first CFT in cattle, or 60 days later can be done to avoid desensitization (Picasso-Risso et al*.,* 2021).

M. bovis is contains Lipoarabinomannan (LAM), and for diagnosis LAM detection in the urine and milk of cattle can be done to diagnose bTB (Bulterys et al., 2019). The Lionex Animal TB Rapid Tuberculosis Test (Lionex-test, Braunschweig, Germany) is a rapid TB test that utilises serum, plasma, or even whole blood, to detect *M. tuberculosis* complex antigens (Kelley et al., 2020; Zewude et al*.,* 2019).

10.1 Field Diagnosis of bTB

i. **Tuberculin Test:** Diagnosis of bTB is Tuberculin skin test (TST) that considers a standard method of injecting purified protein derivative (PPD) intradermally and measuring the difference in skin thickness after 72 hours. The PPD injection stimulates CMI and sensitizes T cells at the injected site and release lymphokines which causes edema, local vasodilatation, fibrin and other inflammatory cells deposition, leading to swelling which can be seen in injected sites (Vordermeier et al., 2016).

ii. **Ante-Mortem Examination (Clinical Signs) of bTB:** In bTB the clinical signs are depending on many factors like sites of infection, virulence, infectious dose, host immune competence and outer influences. The incubation time for bTB is between 2 months to several years. Mostly infected cattle do not show clinical signs, but when clinical signs present then they are very variable and nonspecific due to the fact that the disease is always progressive and there will be debility, toxemia, weakness, and eventual death of the affected animal (Byrne et al*.*, 2022).

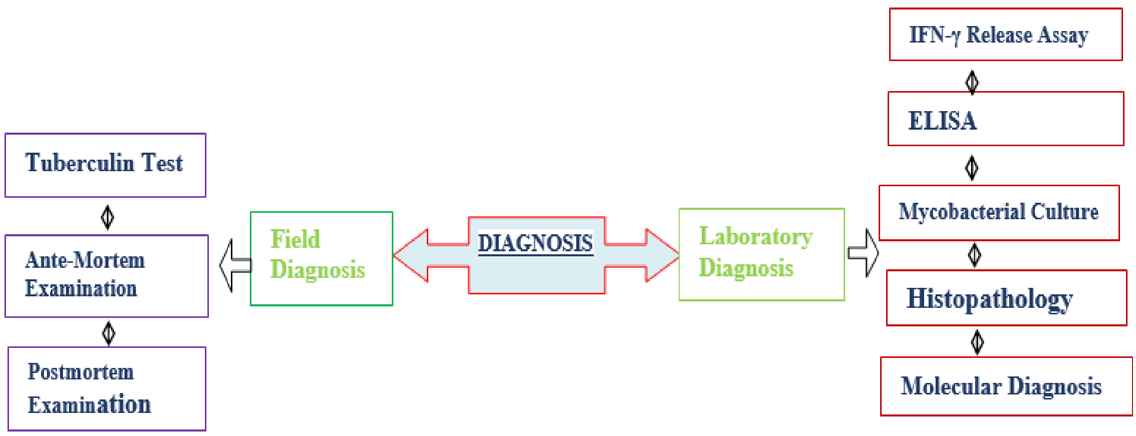

Fig. 2. Diagnosis of bTB

iii. **Postmortem Examination of bTB:** In endemic areas, postmortem examination aids in detection of bTB cases especially in slaughtered animals or in tuberculin reactors. Scarcity of diagnostic tests hinders the identification of bTB cases in the field. It is a concern that 20-30% of bTB cases are diagnosed during postmortem examination. Detection of characteristic tubercles of 2-20 mm in diameter with connective tissue and having necrosis in lymph nodes like retropharyngeal, bronchial and mediastinal are helpful in diagnosis (Pascual-Linaza et al*.,* 2017).

10.2 Laboratory Diagnosis

i. **IFN-γ Release Assay (IGRA):** The main ancillary test in bTB diagnosis is IFN-γ release assay and this is used as a parallel with TST. IFN-γ release assay (IGRA) can detect infection within 14 days after infection. No limitation of retesting through IGRA due to in contrast to TST and it is an in vitro test (Sinclair et al., 2016).

ii. **ELISA:** The specificity and sensitivity of tests for detection of bTB depend on many factors like stage of the disease, immune status of the animal, previous exposure to bovine tuberculin and type of antigen used. The sensitivity of ELISA which is antibodies-based is higher, when evaluated at an advanced stage of disease by gross lesions (van Der Heijden et al., 2020).

iii. **Mycobacterial Culture:** The international gold standard test for bTB is Isolation and identification of mycobacteria, due to the slow growth rate of MBTC it can go up to three months. On Lowenstein–Jensen slants can see moist growth, flat, white and friable colonies that indicate the primary cultures of *M. bovis*. For confirmation of the presence of acid-fast bacilli by Zihel–Neelsen stain (Soares Filho et al., 2019).

iv. **Histopathology as a Diagnostic Method of bTB:** Histopathological confirmation can be done with encapsulation of granuloma, with epithelioid cells, presence of Langhans cells, lymphocytes, or neutrophils in tuberculous-like lesions (Canal et al*.,* 2017).

v. **Molecular Diagnosis:** One of the widely used molecular techniques is PCR since it helps in rapid diagnosis (sensitivity is 85%) and further contributes in controlling the infection. Further PCR is far better than conventional histopathology or any other similar techniques. Many researchers are using PCR in conjunction with other techniques like ELISA as it is safer, quick and less expensive (Algammal et al., 2019).

Development of a loop-mediated isothermal amplification (LAMP) by Kapalamula et al. (2021) marked as a specific identification method of *M. bovis*. LAMP can detect *M. bovis* in 40 min of incubation and can be read with the naked eye. It is a low-cost and rapid method for regular surveillance of *M*. *bovis* infection in cattle in endemic areas.

10.3 *In silico* Analysis

In Egypt, Abdelaal et al. (2019) used in silico analysis to detect spoligotypes and lineages of *M. bovis* isolates. Such type of analysis on bTB is very limited worldwide. Bioinformatics tools can be used for nucleotide polymorphisms, prediction of mutations, drug resistance, protein–protein interactions (PPI) and lineages of ten *Mycobacterium* strains.

11. DRUGS FOR TREATMENT AND DEVELOPMENT OF RESISTANCE

Singh and Chibale, (2021) reported that tuberculosis caused by *M. tuberculosis* is a chronic necrotizing infection and considered as incurable until the introduction of Streptomycin (STM) for treatment. First clinical trial using STM was done by the British Medical Research Council (BMRC) in 1946. Treatment with STM showed reduction in mortality but unfortunately resistance started developing to this drug. In the 1960s, Isoniazid (INH)-Para-aminosalicylic acid (PAS) was discovered, which found that care in the home was also effective and comparable to treatment in a hospital. Modern-day chemotherapy against TB is effective to treat drug-susceptible disease which includes a therapy with a combination of drugs *viz*. INH, ethambutol (EMB), rifampicin (RIF), pyrazinamide (PZA) for six months. Tuberculosis was declared a global public health emergency by the World Health Organization (WHO) in 1993. Tuberculosis was commonly treated by INH, PZA, RIF, and EMB, followed by streptomycin and Kanamycin (KAN).

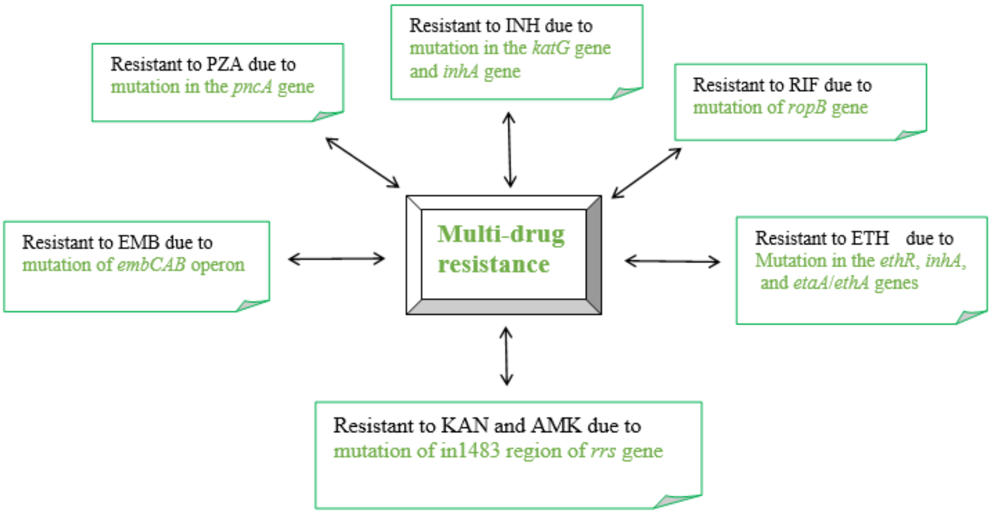

Fig. 3. Multi- drug resistance

12. MULTI-DRUG RESISTANCE (MDR)

Development of multi drug resistance to any organism is a challenge in treatment of cattle (Debbarma et al., 2025). Rajesh et al*.* (2025) reported that in another study at Mizoram, it was observed that antibiotics were inadvertently used for treating different ailments in canine patients which raise concerns. Similarly, *Mycobacterium* also developed resistance to different antibiotics which pose difficulty in its treatment.

i. Presence of C→G point mutation in the *pncA* gene, at nucleotide 169 makes *M. bovis* resistant to PZA and is considered as natural resistance to PZA.

ii. From different reports it is evident that there is an increase in INH resistance to *M. bovis* in Ireland (Anne et al., 2019). The resistance of *Mycobacterium* to INH is reported to be due to mutation in *katG* gene and *inhA* gene (Nono et al*.,* 2025).

iii. Sometimes *Mycobacterium* shows resistance to RIF due to mutation of *ropB* gene (Khan et al*.,* 2021).

iv. EMB resistance is attributed to *embCAB* operon mutations (Wu et al., 2022).

v. Loss of virulence factor synthesis and prevention of Coenzyme A depletion is the reason for resistance of *Mycobacterium* to PZA (Gopal et al., 2016).

vi. Abdelsadek et al. (2020) reported MDR with high resistance for both INH (59.3%) and PZA (78.5%).

vii. In addition, *Mycobacterium tuberculosis* complex (MBTC) isolates were resistant to the KAN (82.3%) and Amikacin (AMK) (80.7%). Research shows that resistance of *Mycobacterium* to KAN and AMK develop as a consequence to mutations in1483 region of *rrs* gene (Sheikh et al*.,* 2021).

viii. Islam et al. (2020) opined that *Mycobacterium* develops resistance to AMK when there is mutation in the *rrs* gene. Further they reported that seven *M. bovis* strains were resistant to EMB and ethionamide (ETH). It is reported that *Mycobacterium* may develop resistance to ETH due to mutations in the *ethR*, *inhA*, and *etaA*/*ethA* genes (Dookie et al., 2018). Resistance profile will provide useful empirical data for better treatment and management of tuberculosis and make the epidemiological surveys simpler.

Sterling (2020) pointed out that tuberculosis was treated with combination therapy for over 50 years. Common first line drugs are RIF, INH, PZA, EMB, and STM and second line of drugs are aminoglycosides and the new class of fluoroquinolones. Antimycobacterial drugs are not used singly. Treatment regimens that use only a single drug may result in rapid development of resistance and subsequent treatment failure. Extensively drug-resistant TB (XDR TB) is mostly rare and involves resistance to INH and rifampicin and resistance to any fluoroquinolone second-line drugs, AMK, KAN, or capreomycin (CAP). Extensively drug-resistant TB is resistant to both the first-line and second-line drugs, and hence less effective treatment (Maitre et al*.,* 2017; Krajewska-Wędzina et al., 2022). In a recent study in Iran, Shafipour et al. (2025) reported that the *relJ* gene may be associated with antibiotic resistance in *M. bovis*.

12.1 Treatment

Currently, treatment is not recommended for bTB due to its infectious nature. Culling is often recommended in many parts of the world if the animal is found infected by bTB. The anti-tuberculosis drug PZA is not effective for bTB. RIF and INH can be used effectively. INH @ 5 mg/kg body weight has been found beneficial against tuberculosis in cattle, but treatment requires 45 days. Administration of INH is @ 10 mg/kg body weight for 6-12 months period will give excellent prevention of tubercle bacilli excretion through cow milk. Oral administration of 300mg of RIF and 300mg INH along with 500mg STM intramuscular can be used for treatment (Admassu et al., 2015).

Domestic livestock are rarely treated except in cases of valuable animals. First line of anti-tuberculous chemotherapy has the greatest activity such as RIF, STM, EMB, INH and PZA. CAP, thioacetazone, ETH and cycloserine are the second line drugs. Primary control of bTB depends on testing of affected animals, tested by Tuberculin skin test (TST), isolation of affected animals from herds, routine slaughter, surveillance, culling of the infected animals and restriction of the movement in the affected herds. Border testing policies through epidemiological investigation of reported cases and certification of a negative TB test animal for entering into other countries can be implemented (McKinley et al*.,* 2018).

12.2 Control and Prevention

In India, prevalence of bTB was estimated at 7.3%, affecting approximately 21.8 million cattle and buffalo. Zoonotic tuberculosis is associated with extrapulmonary and pediatric infections that are very challenging to diagnose, and difficult to get appropriate samples. Control strategies for India's National TB Elimination Program and the global End TB programme goals 2035 as target (Ramanujam et al*.,* 2025). *M. bovis*–BCG vaccination strategies are examined for bTB control in India. New diagnostic tests can differentiate infected cattle and vaccinated animals (Srinivasan et al*.,* 2021). Study conducted in Ethiopia, showed that BCG vaccination can reduce bTB transmission by up to 74% and can prevent 50%–95% of cases (Fromsa et al*.,* 2024). This emphasizes the requirement for safe, efficient, and accessible vaccines to control bTB in endemic regions like India, and the importance to evaluate vaccine efficacy against *M. tuberculosis.*

Chandran et al., (2019) reported that novel BCG vaccine to protect animals against bTB, and novel skin test for differentiating infected from vaccinated animals (DIVA) will detect bTB. Many studies have been conducted in animal models with formalin-killed and heat-inactivated vaccines which give variable results. Production of effective, safe, and easily-implemented vaccines in domestic animals still remains a challenge. Since bTB is zoonotic and can cause many public health hazards, many organizations like OIE, WHO, FAO adopted the One Health approaches to curtail challenges due to tuberculosis (Olea-Popelka et al., 2017).

For the successful control and eradication of bTB in developed countries they have implemented national programs with regular testing and disposal of infected animals. Many countries have achieved TB free status. Tuberculosis control by targeting the whole host for successful control, evidence of close interactions among all forms of possible hosts needs to be addressed simultaneously (Gortázar et al., 2023; Krajewska-Wędzina et al., 2020).

Vaccination program was successful in many European Union member states as well as seven countries in central Europe between 1953 and 1980 (Jemal, 2016). Provision of specific hygiene for animal originated foods to stop diseased animals from the food chain and lower the hazards from consuming tainted milk and meat (Tora et al*.,* 2022). Inspecting the meat needs to be improved for preventing the disease. Examination of both pre and post-mortem on any animal which are used for consumption is also recommended (Clausi et al., 2021).

Standard bTB control strategy includes testing the animals and standard slaughterhouse inspection. The early detection of infected animals can help in removing it from the herd and this will prevent further infection. Tuberculin testing is helpful in the control of bTB. It is recommended that at least 12 months before slaughtering an animal tuberculin test needs to be done. Combined efforts involving veterinary and medical specialists are critical during outbreak of disease (Abbate et al., 2020; Picasso-Risso et al., 2021).

13. CONCLUSION

Bovine tuberculosis (bTB) is still a major zoonotic disease that affects public health and the economy globally. Its prolonged clinical history, production of distinctive granulomatous lesions, and aerosol inhalation provide major challenges to disease control in cattle. For the detection of infected animals, early diagnosis using skin testing, post-mortem inspection and molecular approaches is essential. Strict control measures, including isolation, monitoring, mobility limitations, and culling of positive animals, are essential for efficient management. Developed nations have shown that successful eradication and TB-free status may be achieved through extensive national programs that include regular testing and the disposal of affected animals. Strengthening control measures in endemic regions is essential to reduce disease prevalence, safeguard livestock productivity, and minimize zoonotic transmission to humans.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

Abbate, J. M., Arfuso, F., Iaria, C., Arestia, G., & Lanteri, G. (2020). Prevalence of bovine tuberculosis in slaughtered cattle in Sicily, Southern Italy. *Animals, 10*(9), 1473. https://doi.org/10.3390/ani10091473

Abdelaal, H. F., Spalink, D., Amer, A., Steinberg, H., Hashish, E. A., Nasr, E. A., & Talaat, A. M. (2019). Genomic polymorphism associated with the emergence of virulent isolates of *Mycobacterium bovis* in the Nile Delta. *Scientific Reports, 9*(1), 11657. https://www.nature.com/articles/s41598-019-48106-3

Abdelsadek, H. A., Sobhy, H. M., Mohamed, K. F., Hekal, S. H., Dapgh, A. N., & Hakim, A. S. (2020). Multidrug-resistant strains of *Mycobacterium* complex species in Egyptian farm animals, veterinarians, and farm and abattoir workers. *Veterinary World, 13*(10), 2150–2155. https://doi.org/10.14202/vetworld.2020.2150-2155

Admassu, B., Kebede, E., & Shite, A. (2015). Review on bovine tuberculosis. *European Journal of Biological Sciences, 7*(4), 169–185. https://doi.org/10.5829/idosi.ejbs.2015.7.04.96114

Algammal, A. M., Wahdan, A., & Elhaig, M. M. (2019). Potential efficiency of conventional and advanced approaches used to detect *Mycobacterium bovis* in cattle. *Microbial Pathogenesis, 134*, 103574. https://doi.org/10.1016/j.micpath.2019.103574

Allen, A. R., Ford, T., & Skuce, R. A. (2021). Does *Mycobacterium tuberculosis* var. *bovis* survival in the environment confound bovine tuberculosis control and eradication? A literature review. *Veterinary Medicine International, 2021*, 8812898. https://doi.org/10.1155/2021/8812898

Anne, N. S., Ronald, B. S. M., Kumar, T. S., & Thangavelu, A. (2019). Conventional and molecular determination of drug resistance in *Mycobacterium tuberculosis* and *Mycobacterium bovis* isolates in cattle. *Tuberculosis, 114*, 113–118. https://doi.org/10.1016/j.tube.2018.12.005

Baru, A. G., & HR, C. G. (2016). Slaughterhouse surveillance for tuberculosis among cattle in Ri-Bhoi district of Meghalaya. *Culture, 18*, 15–20. https://www.veterinarypaper.com/archives/2016/1/1/A/1-1-11

Borham, M., Oreiby, A., El-Gedawy, A., Hegazy, Y., Khalifa, H. O., Al-Gaabary, M., & Matsumoto, T. (2022). Review on bovine tuberculosis: An emerging disease associated with multidrug-resistant *Mycobacterium* species. *Pathogens, 11*(7), 715. https://doi.org/10.3390/pathogens11070715

Borja, E., Borja, L. F., Prasad, R., Tunabuna, T., & Toribio, J. A. L. (2018). A retrospective study on bovine tuberculosis in cattle on

Fiji: Study findings and stakeholder responses. *Frontiers in Veterinary Science, 5*, 270. https://doi.org/10.3389/fvets.2018.00270

Broughan, J. M., Judge, J., Ely, E., Delahay, R. J., Wilson, G., Clifton-Hadley, R. S., & Downs, S. H. (2016). A review of risk factors for bovine tuberculosis infection in cattle in the UK and Ireland. *Epidemiology & Infection, 144*(14), 2899–2926. https://doi.org/10.1017/S09502688160013 1X

Bulterys, M. A., Wagner, B., Redard-Jacot, M., Suresh, A., Pollock, N. R., Moreau, E., & Broger, T. (2019). Point-of-care urine LAM tests for tuberculosis diagnosis: A status update. *Journal of Clinical Medicine, 9*(1), 111. https://doi.org/10.3390/jcm9010111

Byrne, A. W., Barrett, D., Breslin, P., Fanning, J., Casey, M., Madden, J. M., & Gormley, E. (2022). Bovine tuberculosis in young stock cattle: A narrative review. *Frontiers in Veterinary Science, 9*, 1000124. https://doi.org/10.3389/fvets.2022.1000124

Canal, A. M., Pezzone, N., Cataldi, A., Zumarraga, M., Larzabal, M., Garbaccio, S., & Rodriguez-Bertos, A. (2017). Immunohistochemical detection of pro-inflammatory and anti-inflammatory cytokines in granulomas in cattle with natural *Mycobacterium bovis* infection. *Research in Veterinary Science, 110*, 34–39. https://doi.org/10.1016/j.rvsc.2016.10.006

Carrisoza-Urbina, J., Morales-Salinas, E., Bedolla-Alva, M. A., Hernández-Pando, R., & Gutiérrez-Pabello, J. A. (2019). Atypical granuloma formation in *Mycobacterium bovis*-infected calves. *PLOS ONE, 14*(7), e0218547. https://doi.org/10.1371/journal.pone.02185 47

Chandran, A., Williams, K., Mendum, T., Stewart, G., Clark, S., Zadi, S., & McFadden, J. (2019). Development of a diagnostic compatible BCG vaccine against bovine tuberculosis. *Scientific Reports, 9*(1), 17791. https://doi.org/10.1038/s41598-019-54108-y

Clausi, M. T., Ciambrone, L., Zanoni, M., Costanzo, N., Pacciarini, M., & Casalinuovo, F. (2021). Evaluation of the presence and viability of *Mycobacterium bovis* in wild boar meat and meat-based preparations. *Foods, 10*(10), 2410. https://doi.org/10.3390/foods10102410

Dametto, L. L., Santos, E. D. D., Santos, L. R., & Dickel, E. L. (2020). Bovine tuberculosis: Diagnosis in dairy cattle through the association of analyzes. *Pesquisa Veterinária Brasileira, 40*, 12–16. https://doi.org/10.1590/1678-5150-PVB-6294

Datta, M., Via, L. E., Chen, W., Baish, J. W., Xu, L., Barry, C. E., & Jain, R. K. (2016). Mathematical model of oxygen transport in tuberculosis granulomas. *Annals of Biomedical Engineering, 44*, 863–872. https://doi.org/10.1007/s10439-015-1415-3

Debbarma, B., Rajesh, J. B., Ralte, L., Debnath, A., Lucy, E., & Kar, P. (2025). Isolation of multi-drug resistant MRSA from cattle in Mizoram. *International Journal of Bio-Resource & Stress Management, 16*(4), 1–6. https://doi.org/10.23910/1.2025.5931

Dookie, N., Rambaran, S., Padayatchi, N., Mahomed, S., & Naidoo, K. (2018). Evolution of drug resistance in *Mycobacterium tuberculosis*: A review on the molecular determinants of resistance and implications for personalized care. *Journal of Antimicrobial Chemotherapy, 73*(5), 1138–1151. https://doi.org/10.1093/jac/dkx506

Fielding, H. R., McKinley, T. J., Delahay, R. J., Silk, M. J., & McDonald, R. A. (2021). Characterization of potential super spreader farms for bovine tuberculosis: A review. *Veterinary Medicine and Science, 7*(2), 310–321. https://doi.org/10.1002/vms3.358

Fromsa, A., Willgert, K., Srinivasan, S., Mekonnen, G., Bedada, W., Gumi, B., & Kapur, V. (2024). BCG vaccination reduces bovine tuberculosis transmission, improving prospects for elimination. *Science, 383*(6690), eadl3962. https://doi.org/10.1126/science.adl3962

Ghebremariam, M. K., Rutten, V. P. M. G., Vernooij, J. C. M., Uqbazghi, K., Tesfaalem, T., Butsuamlak, T., & Michel, A. L. (2016). Prevalence and risk factors of bovine tuberculosis in dairy cattle in Eritrea. *BMC Veterinary Research, 12*, 1–7. https://doi.org/10.1186/s12917-016-0705-9

Gong, Q. L., Chen, Y., Tian, T., Wen, X., Li, D., Song, Y. H., & Zhang, X. X. (2021). Prevalence of bovine tuberculosis in dairy cattle in China during 2010–2019: A systematic review and meta-analysis. *PLOS Neglected Tropical Diseases, 15*(6), e0009502.

https://doi.org/10.1371/journal.pntd.0009502

Good, M., Bakker, D., Duignan, A., & Collins, D. M. (2018). The history of *in vivo* tuberculin testing in bovines: Tuberculosis, a "One Health" issue. *Frontiers in Veterinary Science, 5*, 59. https://doi.org/10.3389/fvets.2018.00059

Gopal, P., Yee, M., Sarathy, J., Low, J. L., Sarathy, J. P., Kaya, F., & Dick, T. (2016). Pyrazinamide resistance is caused by two distinct mechanisms: Prevention of coenzyme A depletion and loss of virulence factor synthesis. *ACS Infectious Diseases, 2*(9), 616–626. https://doi.org/10.1021/acsinfecdis.6b00070

Gortázar, C., De la Fuente, J., Perelló, A., & Domínguez, L. (2023). Will we ever eradicate animal tuberculosis? *Irish Veterinary Journal, 76*(Suppl 1), 24. https://doi.org/10.1186/s13620-023-00254-9

Islam, M. M., Tan, Y., Hameed, H. A., Liu, Y., Chhotaray, C., Cai, X., & Zhang. (2020). Prevalence and molecular characterization of amikacin resistance among *Mycobacterium tuberculosis* clinical isolates from southern China. *Journal of Global Antimicrobial Resistance, 22*, 290–295. https://doi.org/10.1016/j.jgar.2020.02.019

Jemal, A. M. (2016). Review on zoonotic importance of bovine tuberculosis and its control. *Open Access Library Journal, 3*(3), 1–13. http://dx.doi.org/10.4236/oalib.1102504

Kapalamula, T. F., Thapa, J., Akapelwa, M. L., Hayashida, K., Gordon, S. V., Hang'Ombe, B. M., & Nakajima, C. (2021). Development of a loop-mediated isothermal amplification (LAMP) method for specific detection of *Mycobacterium bovis*. *PLoS Neglected Tropical Diseases, 15*(1), e0008996. https://doi.org/10.1371/journal.pntd.0008996

Kasir, D., Osman, N., Awik, A., El Ratel, I., Rafei, R., Al Kassaa, I., & Osman, M. (2023). Zoonotic tuberculosis: A neglected disease in the Middle East and North Africa (MENA) region. *Diseases, 11*(1), 39. https://doi.org/10.3390/diseases11010039

Katale, B. Z., Mbugi, E. V., Siame, K. K., Keyyu, J. D., Kendall, S., Kazwala, R. R., & Matee, M. I. (2017). Isolation and potential for transmission of *Mycobacterium bovis* at human–livestock–wildlife interface of the Serengeti ecosystem, Northern Tanzania. *Transboundary and Emerging Diseases, 64*(3), 815–825. https://doi.org/10.1111/tbed.12445

Kelley, H. V., Waibel, S. M., Sidiki, S., Tomatis-Souverbielle, C., Scordo, J. M., Hunt, W. G., & Torrelles, J. B. (2020). Accuracy of two point-of-care tests for rapid diagnosis of bovine tuberculosis at animal level using non-invasive specimens. *Scientific Reports, 10*(1), 5441. https://doi.org/10.1038/s41598-020-62314-2

Kemal, J., Sibhat, B., Abraham, A., Terefe, Y., Tulu, K. T., Welay, K., & Getahun, N. (2019). Bovine tuberculosis in eastern Ethiopia: Prevalence, risk factors and its public health importance. *BMC Infectious Diseases, 19*, Article 39. https://doi.org/10.1186/s12879-018-3628-1

Khairullah, A. R., Moses, I. B., Kusala, M. K. J., Tyasningsih, W., Ayuti, S. R., Rantam, F. A., & Nurhidayah, N. (2024). Unveiling insights into bovine tuberculosis: A comprehensive review. *Open Veterinary Journal, 14*(6), 1330. https://doi.org/10.5455/OVJ.2024.v14.i6.2

Khan, A. S., Phelan, J. E., Khan, M. T., Ali, S., Qasim, M., Napier, G., & Khan, T. A. (2021). Characterization of rifampicin-resistant *Mycobacterium tuberculosis* in Khyber Pakhtunkhwa, Pakistan. *Scientific Reports, 11*(1), 14194. https://doi.org/10.1038/s41598-021-93501-4

King, H. C., Khera-Butler, T., James, P., Oakley, B. B., Erenso, G., Aseffa, A., & Courtenay, O. (2017). Environmental reservoirs of pathogenic mycobacteria across the Ethiopian biogeographical landscape. *PLoS One, 12*(3), e0173811. https://doi.org/10.1371/journal.pone.0173811

Kouengoua, A. P. K., Tsissa, Y. L., Noudeke, N. D., Chimi, R. N., Njayou, A., Youssao, A. K. I., & Souaibou, F. (2024). Prevalence and zoonotic risk factors of *Mycobacterium bovis* tuberculosis in cattle at the cattle-wildlife-human interface in South and East Cameroon. *Veterinary World, 17*(1), 8–16. https://doi.org/10.14202/vetworld.2024.8-16

Krajewska-Wędzina, M., Didkowska, A., Sridhara, A. A., Elahi, R., Johnathan-Lee, A., Radulski, Ł., & Waters, W. R. (2020). Transboundary tuberculosis: Importation of alpacas infected with *Mycobacterium bovis* from the United Kingdom to Poland and potential for serodiagnostic assays in detecting tuberculin skin test false-negative animals. *Transboundary and Emerging Diseases, 67*(3), 1306–1314. https://doi.org/10.1111/tbed.13471

Krajewska-Wędzina, M., Radulski, Ł., Waters, W. R., Didkowska, A., Zabost, A., Augustynowicz-Kopeć, E., & Weiner, M. (2022). *Mycobacterium bovis* transmission between cattle and a farmer in Central Poland. *Pathogens, 11*(10), 1170. https://doi.org/10.3390/pathogens11101170

Kuria, J. K. (2019). Diseases caused by bacteria in cattle: Tuberculosis. In *Bacterial Cattle Diseases*. IntechOpen. https://www.intechopen.com/chapters/64814

Little, R. A. (2019). Negotiated management strategies for bovine tuberculosis: Enhancing risk mitigation in Michigan and the UK. *Frontiers in Veterinary Science, 6*, 81. https://doi.org/10.3389/fvets.2019.00081

Maitre, T., Aubry, A., Jarlier, V., Robert, J., Veziris, N., Bernard, C., & Raskine, L. (2017). Multidrug and extensively drug-resistant tuberculosis. *Médecine et Maladies Infectieuses, 47*(1), 3–10. https://doi.org/10.1016/j.medmal.2016.07.006

McKinley, T. J., Lipschutz-Powell, D., Mitchell, A. P., Wood, J. L., & Conlan, A. J. (2018). Risk factors and variations in detection of new bovine tuberculosis breakdowns via slaughterhouse surveillance in Great Britain. *PLoS One, 13*(6), e0198760. https://doi.org/10.1371/journal.pone.0198760

Mitermite, M., Elizari, J. M. U., Ma, R., Farrell, D., & Gordon, S. V. (2023). Exploring virulence in *Mycobacterium bovis*: Clues from comparative genomics and perspectives for the future. *Irish Veterinary Journal, 76*(Suppl 1), 26.

Mohamed, A. (2020). Bovine tuberculosis at the human–livestock–wildlife interface and its control through One Health approach in the Ethiopian Somali pastoralists: A review. *One Health, 9*, 100113.

Nava-Vargas, A., Milián-Suazo, F., Cantó-Alarcón, G. J., & Gutiérrez-Pabello, J. A. (2021). Intracellular survival of *Mycobacterium bovis* strains with high and low frequency in cattle populations in a bovine macrophage model. *Revista Mexicana de Ciencias Pecuarias, 12*(2), 487–502.

Nono, V. N., Nantia, E. A., Mutshembele, A., Teagho, S. N., Simo, Y. W. K., Takong, B. S., & Donfack, V. F. D. (2025). Prevalence of *katG* and *inhA* mutations associated with isoniazid resistance in *Mycobacterium tuberculosis* clinical isolates in Cameroon. *BMC Microbiology, 25*(1), 127.

Olea-Popelka, F., Muwonge, A., Perera, A., Dean, A. S., Mumford, E., Erlacher-Vindel, E., & Fujiwara, P. I. (2017). Zoonotic tuberculosis in human beings caused by *Mycobacterium bovis*—A call for action. *The Lancet Infectious Diseases, 17*(1), e21–e25.

Pal, M., Tolawak, D., & Bikila, U. (2022). Zoonotic importance of bovine tuberculosis in Ethiopia: An overview. *Research in Veterinary Science and Medicine, 2*, 7.

Pascual-Linaza, A. V., Gordon, A. W., Stringer, L. A., & Menzies, F. D. (2017). Efficiency of slaughterhouse surveillance for the detection of bovine tuberculosis in cattle in Northern Ireland. *Epidemiology & Infection, 145*(5), 995–1005.

Pereira, A. C., Ramos, B., Reis, A. C., & Cunha, M. V. (2020). Non-tuberculous mycobacteria: Molecular and physiological bases of virulence and adaptation to ecological niches. *Microorganisms, 8*(9), 1380.

Pérez-Morote, R., Pontones-Rosa, C., Gortázar-Schmidt, C., & Muñoz-Cardona, Á. I. (2020). Quantifying the economic impact of bovine tuberculosis on livestock farms in south-western Spain. *Animals, 10*(12), 2433.

Phipps, E., McPhedran, K., Edwards, D., Russell, K., O'Connor, C. M., Gunn-Moore, D. A., & Morris, J. (2019). Bovine tuberculosis in working foxhounds: Lessons learned from a complex public health investigation. *Epidemiology & Infection, 147*, e24.

Picasso-Risso, C., Alvarez, J., VanderWaal, K., Kinsley, A., Gil, A., Wells, S. J., & Perez, A. (2021). Modelling the effect of test-and-slaughter strategies to control bovine tuberculosis in endemic high-prevalence herds. *Transboundary and Emerging Diseases, 68*(3), 1205–1215.

Pokam, B. D. T., Guemdjom, P. W., Yeboah-Manu, D., Weledji, E. P., Enoh, J. E., Tebid, P. G., & Asuquo, A. E. (2019). Challenges of bovine tuberculosis control and genetic distribution in Africa.

Biomedical and Biotechnology Research Journal (BBRJ), 3(4), 217–227.

Rajesh, J. B., Sunil, B., Prejit, N., Kar, P., & Prasad, H. (2025). A study of antimicrobial usage pattern in dogs at Aizawl, Mizoram, India. *Archives of Current Research International, 25*(6), 155–164.

Ramanujam, H., & Palaniyandi, K. (2023). Bovine tuberculosis in India: The need for One Health approach and the way forward. *One Health, 16*, 100495.

Ramanujam, H., Refaya, A. K., Thiruvengadam, K., Pazhanivel, N., Kandasamy, D., Shanmugavel, A., & Palaniyandi, K. (2025, January). Recovery of *Mycobacterium tuberculosis* complex isolates including pre–extensively drug-resistant strains from cattle at a slaughterhouse in Chennai, India. *Open Forum Infectious Diseases, 12*(1), ofae733. https://doi.org/10.1093/ofid/ofae733

Ramos, B., Pereira, A. C., Reis, A. C., & Cunha, M. V. (2020). Estimates of the global and continental burden of animal tuberculosis in key livestock species worldwide: A meta-analysis study. *One Health, 10*, 100169. https://doi.org/10.1016/j.onehlt.2020.100169

Ramos, D. F., Silva, P. E. A., & Dellagostin, O. A. (2015). Diagnosis of bovine tuberculosis: Review of main techniques. *Brazilian Journal of Biology, 75*(4), 830–837. https://doi.org/10.1590/1519-6984.23613

Robi, D. T., Teklemariam, T., Gebreyes, B. G., Bogale, A., Haile, T., Aleme, M., & Urge, B. (2024). Bovine tuberculosis reactor cattle in Southwest Ethiopia: Risk factors for bovine tuberculosis. *Journal of Clinical Tuberculosis and Other Mycobacterial Diseases, 37*, 100492. https://doi.org/10.1016/j.jctube.2024.100492

Rodrigues, D. L., Amorim, E. A., Ferreira, F., Amaku, M., Baquero, O. S., de Hildebrand e Grisi Filho, J. H., & Ferreira Neto, J. S. (2022). Apparent prevalence and risk factors for bovine tuberculosis in the state of Paraná, Brazil: An assessment after 18 years since the beginning of the Brazilian program. *Tropical Animal Health and Production, 54*(6), 360. https://doi.org/10.1007/s11250-022-03350-0

Shafipour, M., Mohammadzadeh, A., Ghaemi, E. A., Mahmoodi, P., & Mosavari, N. (2025). Investigation of potential relationship between *mazEF3*, *relJK*, and *vapBC3* genes and antimicrobial resistance in *Mycobacterium bovis*. *BMC Infectious Diseases, 25*(1), 1–12.

Shaltout, F. A. (2024). Abattoir and bovine tuberculosis as a reemerging foodborne disease. *Clinical Medical Reviews and Reports, 6*(1), 1–7. https://dx.doi.org/10.26717/BJSTR.2024.54.008545

Sheikh, B. A., Bhat, B. A., Mehraj, U., Mir, W., Hamadani, S., & Mir, M. A. (2021). Development of new therapeutics to meet the current challenge of drug-resistant tuberculosis. *Current Pharmaceutical Biotechnology, 22*(4), 480–500. https://doi.org/10.2174/1389201021666200628021702

Sichewo, P. R., Michel, A. L., Musoke, J., & Etter, E. M. (2019). Risk factors for zoonotic tuberculosis at the wildlife–livestock–human interface in South Africa. *Pathogens, 8*(3), 101. https://doi.org/10.3390/pathogens8030101

Sichewo, P. R., Vander Kelen, C., Thys, S., & Michel, A. L. (2020). Risk practices for bovine tuberculosis transmission to cattle and livestock farming communities living at wildlife–livestock–human interface in northern KwaZulu Natal, South Africa. *PLOS Neglected Tropical Diseases, 14*(3), e0007618. https://doi.org/10.1371/journal.pntd.0007618

Sinclair, J. A., Dawson, K. L., & Buddle, B. M. (2016). The effectiveness of parallel gamma-interferon testing in New Zealand's bovine tuberculosis eradication programme. *Preventive Veterinary Medicine, 127*, 94–99. https://doi.org/10.1016/j.prevetmed.2016.03.020

Singh, V., & Chibale, K. (2021). Strategies to combat multi-drug resistance in tuberculosis. *Accounts of Chemical Research, 54*(10), 2361–2376. https://doi.org/10.1021/acs.accounts.0c00878

Soares Filho, P. M., Ramalho, A. K., de Moura Silva, A., Hodon, M. A., de Azevedo Issa, M., Júnior, A. A. F., & Leite, R. C. (2019). Evaluation of post-mortem diagnostic tests' sensitivity and specificity for bovine tuberculosis using Bayesian latent class analysis. *Research in Veterinary Science, 125*, 14–23. https://doi.org/10.1016/j.rvsc.2019.04.014

Srinivasan, S., Conlan, A. J., Easterling, L. A., Herrera, C., Dandapat, P., Veerasami, M., & Kapur, V. (2021). A meta-analysis of the effect of *Bacillus Calmette-Guérin* vaccination against bovine tuberculosis: Is perfect the enemy of good? *Frontiers in Veterinary Science, 8*, 637580. https://doi.org/10.3389/fvets.2021.637580

Sterling, T. R. (2020). Guidelines for the treatment of latent tuberculosis infection: Recommendations from the National Tuberculosis Controllers Association and CDC, 2020. *MMWR. Recommendations and Reports, 69*(1), 1–11. http://dx.doi.org/10.15585/mmwr.rr6901a1

Thoen, C. O., Kaplan, B., Thoen, T. C., Gilsdorf, M. J., & Shere, J. A. (2016). Zoonotic tuberculosis: A comprehensive One Health approach. *Medicina (Buenos Aires), 76*(3), 159–165. https://pubmed.ncbi.nlm.nih.gov/27295705/

Tora, E., Getachew, M., Seyoum, W., & Abayneh, E. (2022). Public awareness, prevalence and potential determinants of bovine tuberculosis in selected districts of Gamo Zone, Southern Ethiopia. *Veterinary Medicine: Research and Reports*, 163–172. https://www.tandfonline.com/doi/citedby/10.2147/VMRR.S370733?scroll=top

van Der Heijden, E. M., Cooper, D. V., Rutten, V. P., & Michel, A. L. (2020). *Mycobacterium bovis* prevalence affects the performance of a commercial serological assay for bovine tuberculosis in African buffaloes. *Comparative Immunology, Microbiology and Infectious Diseases, 70*, 101369. https://doi.org/10.1016/j.cimid.2019.101369

Vordermeier, H. M., Jones, G. J., Buddle, B. M., Hewinson, R. G., & Villarreal-Ramos, B. (2016). Bovine tuberculosis in cattle: Vaccines, DIVA tests, and host biomarker discovery. *Annual Review of Animal Biosciences, 4*(1), 87–109. https://doi.org/10.1146/annurev-animal-021815-111311

Wright, D. M., Reid, N., Montgomery, W. I., Allen, A. R., Skuce, R. A., & Kao, R. R. (2015). Herd-level bovine tuberculosis risk factors: Assessing the role of low-level badger population disturbance. *Scientific Reports, 5*, 13062. https://doi.org/10.1038/srep13062

Wu, Z., Tan, Q., Zhang, C., Zhao, Y., Liao, Q., Yu, M., & Wei, W. (2022). *mbtD* and *celA1* association with ethambutol resistance in *Mycobacterium tuberculosis*: A multiomics analysis. *Frontiers in Cellular and Infection Microbiology, 12*, 959911. https://doi.org/10.3389/fcimb.2022.959911

Yadav, K., & Prakash, S. (2017). Tuberculosis: An airborne disease. *Global Journal of Microbiology Research, 5*(5), 225–243. https://www.researchgate.net/publication/320042194_Tuberculosis_An_airborn

Zewude, A., Mohammed, T., Terfassa, L., Hunt, W. G., Pan, X., Balada-Llasat, J. M., & Ameni, G. (2019). Evaluation of *Mycobacterium tuberculosis* lipoarabinomannan antigen assay and rapid serology blood test for the diagnosis of bovine tuberculosis in Ethiopia. *BMC Veterinary Research, 15*, 1–8. https://doi.org/10.1186/s12917-019-2114-3

Zhai, W., Wu, F., Zhang, Y., Fu, Y., & Liu, Z. (2019). The immune escape mechanisms of *Mycobacterium tuberculosis*. *International Journal of Molecular Sciences, 20*(2), 340. https://doi.org/10.3390/ijms20020340

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