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# An overview on Bovine Tuberculosis and its economic significance

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## ABSTRACT

Tuberculosis is Mycobacterial disease caused by *Mycobacterium tuberculosis* complex (MTBC) and is one of the major threats to human health. It has the characteristic feature of acid fast staining which proves the presence of bacterial wall. *Bovine Tuberculosis* is found globally but its presence is not observed in some countries and Antarctica due to its eradication by following strict policies. Economically, the dairy industry was heavily affected, *Tuberculosis* causes high morbidity of cattles and this leads to loss of dairy production. This infection amongst the animals leads to lose of 10-25% of their productive efficiency. This in turn pressurise the international trade to ban animals and animal product. Primarily, the transmission of *Bovine tuberculosis* is by the inhalation of *Mycobacterium bovis* which is the principal route to its infection. It is often facilitated by very close, prolonged contact between infected and healthy animals. No symptoms occur in early stage of disease that is asymptomatic. In advanced cases, the enlargement of lymph nodes may obstruct the air passages, alimentary tract, and blood vessels. Ante mortem examination based on clinical signs can be used for tentative and presumptive diagnosis. *Mycobacterium bovis* is not the major cause of human tuberculosis but it can infect human beings either by consuming infected animal products, by inhaling infective droplets or direct exposure to infected animals. Moreover, advance *tuberculosis* may lead to death of the animals and humans. Therefore, control and prevention of the disease is paramount to save the life of animals and humans and reduce banned trade.

Keywords: Bovine Tuberculosis, Economic Importance, *Mycobacterium bovis*, Zoonosis

## 1. INTRODUCTION

*Tuberculosis* (TB) is recognized as threats to human and animal health causing mortality, morbidity, and heavy economic losses in few decades [1]. It remains a major global health problem and causes ill-health among millions of

people each year and ranked as the second leading death cause from an infectious disease worldwide after the human immunodeficiency virus (HIV) [2].

TB is communicable Mycobacterial disease caused by members of *Mycobacterium*

*tuberculosis complex* (MTBC) [3]. Although, recent studies indicates that *Mycobacterium bovis* are isolated from infected humans and *M. tuberculosis* are isolated from dairy cattle [4-5]. Despite variation in host specificity, the members of MTBC are characterized by 99.9% or greater similarity at nucleotide level and are virtually identical at 16s rRNA sequence [6].

Subsequently *Bovine tuberculosis* (BTB) is a chronic bacterial disease caused by *M. bovis*, which can also infect and cause tuberculosis in badgers, deer goats, pigs, camelids (llamas and alpacas), dogs and cats, including man and other mammals [7].

This disease is still common in developing countries and severe economic losses can occur from livestock deaths, chronic disease and trade restrictions. In some situations, BTB may also be a serious threat to endangered species. Consequently, about 70% of the cattle bred in Latin America are held in areas with high disease prevalence and nearly 17% in areas virtually free from BTB [8].

Therefore, BTB is a contagious disease, which can affect most warm-blooded animals, including human being. Organisms are excreted in the exhaled air, in sputum, faeces (from both intestinal lesions and swallowed sputum from pulmonary lesions), milk, urine, vaginal and uterine discharges, and discharges from open peripheral lymph nodes of infected animals [9].

In cattle, exposure to this organism can result in a chronic disease that jeopardizes animal welfare and productivity and in some countries, leads to significant economic losses by causing ill health and mortality [10]. Moreover, human

TB of animal origin caused by *M. bovis* is becoming increasingly evident in developing countries [11].

In developing countries like Ethiopia, the socio-economic situation and low standard living area for both animals and humans are more contributing in TB transmission between human to human and human to cattle or vice versa [12].

Human infection due to *M. bovis* is thought to be mainly through drinking of contaminated or unpasteurized raw milk and under cooked meat. The high prevalence of TB in cattle, close contact of cattle and humans, the habit of raw milk and meat consumption, and the increasing prevalence of HIV may all increase the potential for transmission of *M. bovis* and other Mycobacteria between cattle and humans [13].

BTB has animal loses 10 to 25% of their productive efficiency; direct losses due to the infection become evident by decrease in 10 to 18% milk and 15% reduction in meat production. Apart from effects on animal production, it has also a significant public health importance [14].

Currently, the disease in human is becoming increasingly important in developing countries, as humans and animals are sharing the same micro environment and dwelling premises, especially in rural areas, and susceptibility of Acquired Immune Deficiency Syndrome (AIDS) patients to tuberculosis [13]. It is estimated that *M. bovis* causes 10 to 15% human cases of tuberculosis in countries where pasteurization of milk is rare and BTB is common [15]. Therefore, the objective of this seminar paper is

to highlight bovine tuberculosis and its economic significance.

## 2. AETIOLOGY

*Mycobacterium bovis* is the main etiological agent of BTB. It is an acid-fast bacterium having characteristic feature of acid fast staining which is due to waxy substance (mycolic acid) present in their bacterial wall [16].

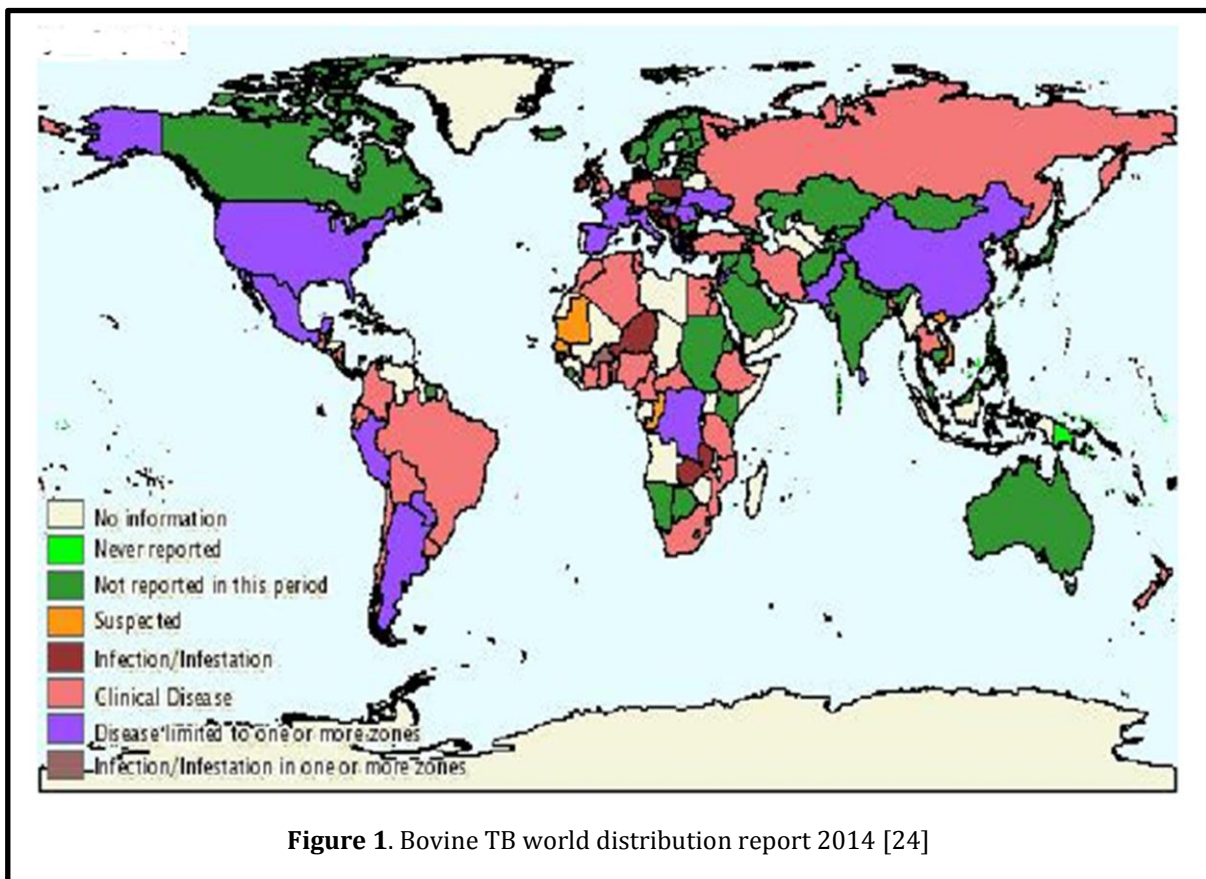
MTBC has seven approved members named as *M. tuberculosis*, *M. bovis*, *M. bovis BCG*, *M. africanum*, *M. microti*, *M. tuberculosis subsp. canetti* and *M. bovis* [17]. Four species (*M. bovis*, *M. tuberculosis*, *M. africanum* and *M. canetti*) of this group cause human tuberculosis [18]. Members of the MTBC have 99.9% genetic similarity on the nucleotide level and even an identical 16rRNA sequence [16].

However, the other two members include *M. caprae* (mostly infect goats) and *M. pinnipedii* (usually infect fur seals and sea lions) of MTBC are also been accepted. These Badgers also act as reservoir for spreading of BTB [19].

## 3. EPIDEMIOLOGY

### 3.1. Geographic Distribution

The disease is found in cattle worldwide, but some countries have been able to reduce or limit the incidence through the process of 'test and cull'. This helped most of European and Caribbean countries (including Cuba) to virtually free from *M. bovis* [11]. *Bovine tuberculosis* is endemic to many developing countries particularly African countries [20]. *M. bovis* combines one of the widest host ranges of all pathogens with a complex epidemiological



pattern, which involves interaction of infection among human beings, domestic animals and wild animals [21]. However, only little is done particularly in developing countries on the epidemiology of this organism and the epidemiological requirements for its control [22].

As BTB was once found worldwide, control programs have eliminated this disease from domesticated animals in many countries [20]. Currently nations like Australia, Iceland, Denmark, Sweden, Norway, Finland, Austria, Switzerland, Luxembourg, Latvia, Slovakia, Lithuania, Estonia, the Czech Republic, Canada, Singapore, Jamaica, Barbados and Israel are classified as TB free [23].

Many eradication programs are in progress in European countries, Japan, New Zealand, the United States, Mexico, and some parts of Central and South America. Bovine TB is still widespread in Africa, Central and South America, parts of Asia and even some Middle East countries [7]. In Africa, although bovine TB is known to be common in both cattle and wildlife, control policies have not been enforced in many countries due to cost implications, lack of capacity, and infrastructure limitations [24]. Therefore, the prevalence of disease is high in the world, tropical and sub-tropical countries [25].

### 3.2. Host range and susceptibility

All species of vertebrates including mammals with various age groups are susceptible to tuberculosis with cattle, goats and pigs being the most vulnerable and sheep and horse showing a high natural resistance [26]. The breed

susceptibility in BTB infections has been reported where *Bos indicus* breeds such as zebu and Brahman may be more resistance to the disease compared to the *Bos taurus* such as Holsteins [27].

Cattle are the main hosts of *M. bovis* but the disease is also found in other species including humans, domesticated animals such as pigs, wild life and African buffalo are also indicating to be susceptible [28]. In African buffalo and cattle, the risk to contract *M. bovis* and consequently, increases with increasing age of the animal and more adult African buffaloes and cattle are affected than calves [29]. Experiments have shown that lions may also become susceptible to bovine TB [30].

TB as a disease may be considered as a single-host, single- pathogen interaction *M. bovis* just like a few other pathogens, may simultaneously interact with multiple species in an ecosystem. This has a huge implication on the dynamics of the disease as factors such as the density of each susceptible host in the ecosystem, the ratio of inter-species transmission rate to intra-species transmission rates as well as the interaction rates between the hosts species, interact at various levels and intensities [29].

## 4. TRANSMISSION

The main reservoirs of *M. bovis* are cattle, which can transmit the infection to many mammalian species including man [31]. Organisms leave the host during respiratory discharges, faeces, milk, urine, semen and genital discharges. These body excretions may contaminate grazing pasture, drinking water, feed, water and feed troughs or

fomites, which may act as source of infection to other animals [32].

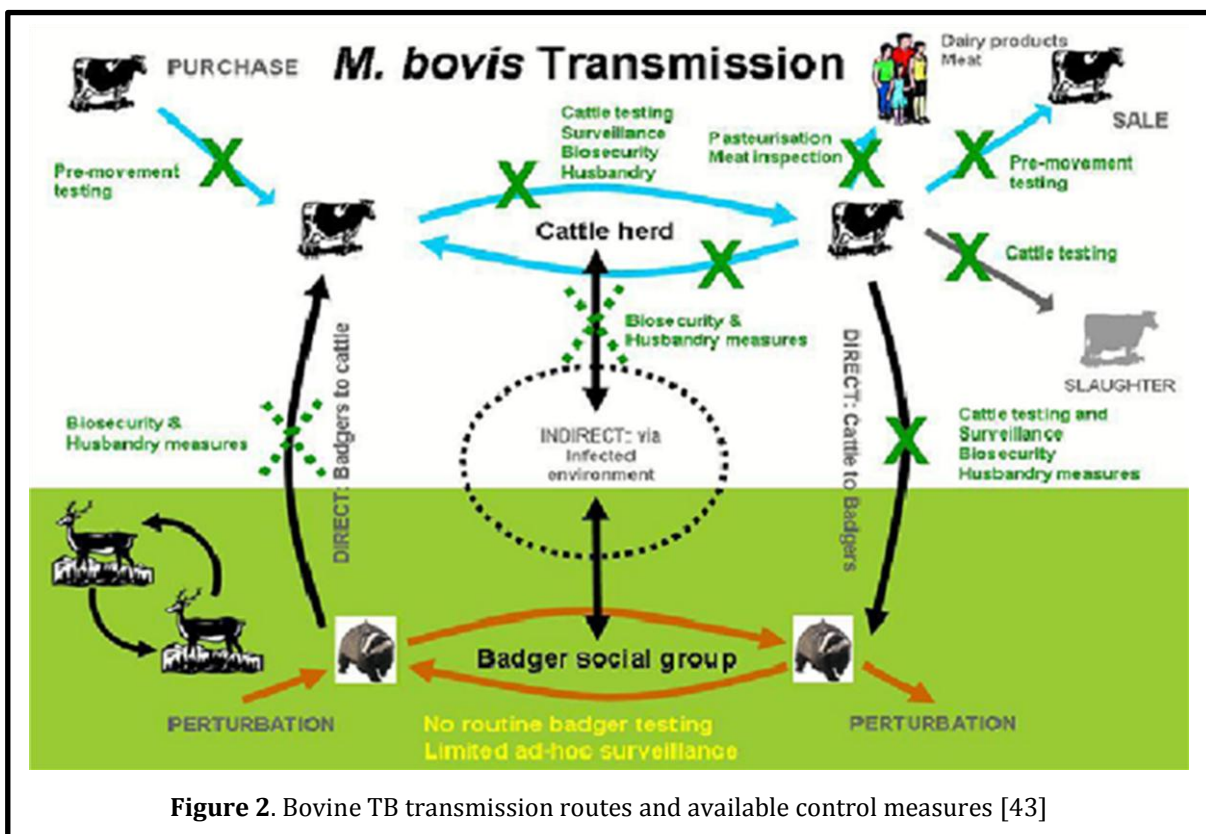
Inhalation of *M. bovis* is the most probable and principal route to bovine infection and is facilitated by close, prolonged contact between infected and healthy animals. Ingestion of *M. bovis* directly from infected and healthy animals or from contaminated pasture, water or utensils may also be very common in some regions. While congenital infections and vertical transmission have been recorded, these routes, like genital transmission, which occurs when reproductive organs are infected, are now rarely seen in regions [33].

## 5. CLINICAL SIGNS AND POST-MORTEM EXAMINATION

TB is a chronic debilitating disease occurs in cattle. No symptoms occur in early stage of

disease that is asymptomatic. However, in late stage, there is progressive emaciation, a mild fluctuating fever, weakness and in-appetence. When infection is present in the lung then dyspnoea, moist cough or tachypnea may occur. In the terminal stage, animal become extremely emaciated and develop acute respiratory distress. Involvement of respiratory tract and its role in pathogenesis of disease is evidenced by the predominant distribution of lesions present in upper respiratory tract, lung and tonsils in affected human as well as in animals [34].

Some cows with extensive miliary tubercular lesions are clinically normal but in most cases progressive emaciation unassociated with other clinical signs occur, inspire of good appetite. A capricious appetite and fluctuating temperature are commonly associated with disease. The hair coat may be rough. Affected animal tend to



become more docile and sluggish but eyes remain bright and alert. These general signs often become more pronounced after calving. Pulmonary involvement is characterized by chronic cough due to bronchopneumonia. Cough occurs only once or twice at a time and is low suppressed and moist which is easily stimulated by squeezing the pharynx or by exercise and is most common in morning and in cold weather [34].

In advanced cases, air passages, alimentary tract, or blood vessels may be obstructed by enlargement of lymph nodes. Lymph nodes of the head and neck may become visibly affected and sometimes rupture and drain. Involvement of the digestive tract is manifested by intermittent diarrhoea and constipation in some instances.

There may be chances of bloat occur due to pressure of enlarged mediastinal glands on the oesophagus. The enlargement of retropharyngeal glands results in dysphagia. Extreme emaciation and acute respiratory distress may occur during the terminal stages of tuberculosis. Lesions on the female genitalia may occur, while male genitalia are seldom involved. Tuberculosis mastitis is of major importance because of danger to public health and of spread of disease to calves and difficulty of differentiating it from other forms of mastitis [9].

In post mortem lesions. It is characterized by the formation of granulomas (tubercles) where bacteria have localized. These granulomas are usually yellowish and extra osseous, or calcified, they are often encapsulated. In some species,

such as deer, the lesion tends to resemble abscesses rather than typical tubercles. Some tubercles are small enough to be missed by the naked eye unless the tissue is sectioned. In cattle, tubercles are found in the lymph nodes, particularly those of the head and thorax. It is common in the lungs, spleen, liver and the surfaces of body cavities [35].

In disseminated case, lesions are sometimes found on the female genitalia, but are rare on the male genitalia. In countries with good control programs, infected cattle typically have few lesions at necropsy. Most of those lesions found in lymph nodes associated with the respiratory system. However, small lesions can often be discovered in the lungs of these animals if the tissues are sectioned [36].

## 6. DIAGNOSIS

Diagnosis of this disease has various challenges and difficulties. Tentative and presumptive diagnosis can be made by Ante mortem examination based on clinical signs. However, disease can be diagnosed more clearly after post mortem examination based on the presence of gross lesions compatible with BTB in the lungs and/or associated lymph nodes and these are not confirmatory [37]. Typical lesion or gross lesions are found at necropsy, microscopic detection and histopathological examination of lesion may confirm the diagnosis but the definitive diagnosis is done only by isolation of *Mycobacterium bovis* from lesion, bacteriologically [38]. The confirmation of disease requires certain laboratory examination.

### 6.1. Laboratory Diagnosis

### 6.1.1. Identification of agent

Organism in clinical samples and tissue samples collected after post-mortem examination may be demonstrated by examination of stained smears or tissue sections and confirmed by cultivation of the organism on primary isolation mechanism [39].

### 6.1.2. Microscopic Examination

*M. bovis* can be demonstrated microscopically on direct smears from clinical samples (blood stained purulent exudates i.e., cough and sputum, pleural fluid) and on prepared tissue materials (lung biopsy). The acid fastness of *M. bovis* is normally demonstrated with the classic Ziehl-Neelsen stain a fluorescent acid-fast staining may also be used. The tentative diagnosis can be made by observing gaseous necrosis, mineralisation, epithelioid cells, multinucleated giant cells and macrophages in the tissue samples on histopathology [39].

### 6.1.3. Culture of *M. Bovis*

The tissue sample is homogenised using a pestle and mortar, followed by decontamination with either detergent, acid or an alkali such as 0.375-0.75% hexadecylpyridiumchloride (HPC), 5% oxalic acid or 2-4% sodium hydroxide. The mixture is shaken for 10 min at room temperature and then neutralised. After that centrifuge the suspension and discard the supernatant. Sediment is used for culture and microscopic examination. For primary isolation, the sediment is usually inoculated on to a set of solid egg-based media such as Lowenstein-Jensen, Coletsos base or Stone brinks; these

media should contain either pyruvate or pyruvate and glycerol. Cultures are incubated for a minimum of 8 weeks (and preferably for 10-12 weeks) at 37 °C with or without CO<sub>2</sub>. The media should be in tightly closed tubes to avoid desiccation. Slants should be examined at regular intervals for presence of any growth. growth is visible, smears are prepared and stained by the Ziehl-Neelsen technique [39].

### 6.1.4. Nucleic acid recognition methods

PCR has been widely used for the detection of *M. tuberculosis* complex in clinical samples (mainly sputum) in human cases and has recently been used for the diagnosis of tuberculosis in animals. The real-time PCR determine the status of infection in cattle for bovine tuberculosis as compare to the IFN gamma mRNA in blood culture [40].

Bacterial culture and post-mortem confirmation of tuberculosis is insufficiently sensitive. So, veterinarians and other health researchers have evaluated other diagnostic approach i.e. immunological including lateral-flow devices and Enzyme-linked Immunosorbent Assay (ELISA) tuberculin skin test and interferon-gamma release assay [39].

### 6.2. Delayed Type Hypersensitivity Reaction

Skin test or Single Intra Dermal test (SID): This is standard test for detection of *bovine tuberculosis* and involves the intradermal injection of bovine tuberculin purified protein derivative (PPD) and the subsequent detection of swelling (delayed hypersensitivity) at the site of injection 72 h later. Generally, this test is conducted on middle of neck and the alternate

site may be the caudal fold of the tail. However, skin of the neck is preferred over tail due to higher sensitivity of skin on neck. During initial stage of infection i.e. 3-6 weeks after infection, this test may give negative reaction. After a SID test, the animals giving a suspicious result should not be tested again before 60 days [41]. This test has poor specificity due to cross-reactions with other non-pathogenic mycobacteria [42].

## 7. TREATMENT

Antimicrobial treatment has been attempted in some species, but the treatment must be long term, and clinical improvement can occur without bacteriological cure. The risk of shedding organisms, hazards to humans and potential for drug resistance make treatment controversial. In some countries, it may be illegal [43]. *M. bovis* is resistant to pyrazinamide, which is widely used in the treatment of infections caused by *M. Tuberculosis Complex* in humans [44]. Cattle should not be treated at all and as such farm animals with tuberculosis must be slaughtered (culled) [43].

## 8. PREVENTION AND CONTROL

In developed countries BTB has nearly been eradicated or drastically reduced in farm animals to low levels by control and eradication programmes [45]. Animal TB is endemic in many African countries because the economic constraints preclude the use of skin test and slaughter control strategies, which have proved effective in the developed world [46].

The basic strategies required for control and elimination of bovine tuberculosis are well

known and well defined. However, because of financial constraints, scarcity of trained professionals, lack of political will, as well as the underestimation of the importance of zoonotic tuberculosis in both the animal and public health sectors by national governments and donor agencies, control measures are not applied or are applied inadequately in most developing countries [47]. The level of testing and control of bovine tuberculosis in Africa is also considerably constrained by the lack of infrastructure, both veterinary and transport related [48].

Bovine tuberculosis can be controlled by test-and-slaughter or test-and-segregation methods. Affected herds are re-tested periodically to eliminate cattle that may shed the organism; the tuberculin test is generally used. Infected herds are usually quarantined, and animals that have been in contact with reactors are traced. Only test-and-slaughter techniques are guaranteed to eradicate tuberculosis from domesticated animals [43]. Animals in traditional African (farming systems are seldom culled and there is a greater chance for chronic tuberculosis in old cows, particularly those subjected to stress [49].

Even when cows are infected, it is difficult to force culling, because the cattle value is deeply interwoven with the social system and they are the savings of the rural poor [49]. Whole herd test and slaughter programmes have been used world-wide for the control of bovine tuberculosis as well as other diseases such as brucellosis and contagious bovine pleuropneumonia. A number of versions of the tuberculin test have been applied, but most



programmes now use a purified protein derivative from culture of *M. bovis* (PPD-B) [27].

## 9. PUBLIC HEALTH IMPORTANCE

Human tuberculosis due to *M. bovis* is usually underestimated or underdiagnosed because of no clinical, radiographical and histopathological differentiation of tuberculosis caused by *M. tuberculosis* and *M. bovis* [50].

*M. bovis* is not the major cause of human tuberculosis but it can infect human beings too either by consuming raw milk, meat and their products from infected animals, or by inhaling infective droplets or direct exposure to infected animals. In an estimate, according to the cases of human tuberculosis are caused by *M. bovis*, while majority are caused by *M. tuberculosis* [50].

In countries, wherein milk is pasteurized and there is effective implementation of bovine tuberculosis programme tuberculosis in human due to *M. bovis* is very rare. But in areas where the disease in bovine is poorly controlled the reporting of the disease is more frequently done. In farmers as well as abattoir workers and others the incidence rate is higher. Exposure to other species apart from cattle can cause infection in human. It has been documented that goats as well as seals, farmed elk and rhinoceros can also act as sources of bovine tuberculosis. A source of infection may be wildlife especially in countries where people use to take bush meat [37].

If the whole carcass is condemned, then it indicates a high degree of tuberculosis infection and its transmission so it requires immediate

attention from both the economic and public health point of view [51]. Being cause of chronic granulomatous disease tubercle bacilli increases susceptibility to bladder and lung cancer. Though BCG induced cytotoxicity of bladder has paved the way towards initiation of BCG immunotherapy for treatment of bladder cancer [52].

## 10. ECONOMIC SIGNIFICANCE OF BOVINE TUBERCULOSIS

Tuberculosis occurs in almost every country of the world and is of major importance in dairy cattle due to high morbidity and loss of production as infected animals lose 10-25% of their productive efficiency. In most developing countries no control programs are implemented, and Bovine TB causes severe economic losses, especially in urban and peri-urban cross breed dairy cattle due to mortality, low productivity, carcass condemnation and trade restrictions [53]. Therefore, the economic impact of bovine TB on livestock production is extremely difficult to determine accurately. The disease reduces livestock productivity in general and may be economically devastating for the cattle industry, especially the dairy sector [54].

Consequently the most important is the impact of the risk of infection to humans, particularly for women and children who appear to be more susceptible to the disease in countries with poor socio-economic conditions and weak veterinary and public health services. Although estimates of the costs associated with bovine TB and its control refer only to specific countries, all data suggest that worldwide economic losses due to the disease are significant. These losses include

those related to animal production, markets and trade as well as the costs of implementing surveillance and control programmes. Losses to TB are also extremely important when endangered wildlife species are involved [55].

In general, BTB affects the national and international economy in different ways. The most obvious losses from BTB in cattle are direct productivity losses (Reduced benefit), which can be categorized into slaughter and “On-farm” losses. Slaughter losses comprise the cost of cattle condemnation and retention, with the loss from condemnation being essentially the purchased value of a slaughter animal and the loss from retention being a fraction of the value of a carcass. On-farm losses comprise the losses from decreased milk and meat production, the increased reproduction efforts and replacement costs for infected cattle [55].

Apart from direct productivity losses, BTB has profound economic consequences for national and international trade. On an international scale, BTB affects access to foreign markets due to import bans on animals and animal products from countries where the disease is enzootic. This situation has also major implications for other economic sectors, which are linked to livestock production. Moreover, BTB can create inefficiencies in the world market as e.g. economically inefficient but disease free exporting countries will receive more revenues than economically efficient countries, which cannot export animal products due to enzootic BTB [56].

The presence of the disease in wildlife has considerable economic consequences. Not only

is disease eradication more difficult and costly but BTB can theoretically affect entire ecosystems with unpredictable impact on many areas of private interest such as e.g. tourism [55].

Crucially, intensive livestock production systems show generally a higher prevalence of BTB than extensive production systems. Second, developing countries lack the financial resources for disease control. This leads to a vicious cycle in which increased poverty affects the means for disease control and vice versa. Third, wildlife reservoirs in Africa are difficult to control; also, contact between transhumant cattle herds and wildlife may be particularly difficult to prevent in Africa. Fourth, African countries have little access to the international trade and sanitary measures in industrialized countries may be used for protectionist purposes. Fifth, the public and political awareness are very low [54].

Alongside the economic impact of BTB in Africa is exacerbated through several factors. First, the fast-growing population, especially in urban areas, causes an increase in demand especially for dairy products and meat and promotes the intensification of livestock production in peri-urban areas as mentioned [55].

## 11. CONCLUSION AND RECOMMENDATIONS

*Bovine tuberculosis* is a contagious disease, which can affect most warm-blooded animals, including human being. Organisms are excreted in the exhaled air, in sputum, faeces (from both intestinal lesions and swallowed sputum from pulmonary lesions), milk, urine, vaginal and uterine discharges, and discharges from open

peripheral lymph nodes of infected animals. The risk of shedding organisms, hazards to humans and potential for drug resistance make treatment controversial. The basic strategies required for control and elimination of bovine tuberculosis are well known and well defined. However, because of financial constraints, scarcity of trained professionals, lack of political will, as well as the underestimation of the importance of zoonotic tuberculosis in both the animal and public health sectors by national governments and donor agencies, control measures are not applied or are applied inadequately in most developing countries. Animal TB is endemic in many African countries because the economic constraints preclude the use of skin test and slaughter control strategies, which have proved effective in the developed world. The level of testing and control of bovine tuberculosis in Africa is also considerably constrained by the lack of infrastructure, both veterinary and transport related. Based on the above conclusion the following recommendations are forwarded:

- Protective cloth should be worn during handling of the diseased animal and infected carcasses.
- Public awareness creation regarding BTB, its routes of transmission, consumption of raw milk and sharing of the same microenvironment with their livestock is very important as it could be potential risk factors for zoonotic transmission of the disease.
- Infected animal should be tested and culled. Because, treatment of infected animals is not economically feasible due to the high cost, and lengthy time. Training of

personnel at all levels of control programmes and the urgent need for further research on the diagnosis and control, immunological, epidemiological and socioeconomic aspects of the disease is paramount.

## 12. ACKNOWLEDGEMENT

NA

## 13. CONFLICT OF INTEREST

The authors have declared that there is no conflict of interest.

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NA

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