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Mycobacterium bovis (*M. bovis*) the potential zoonotic challenge for human TB

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Abstract

M. bovis spread Infection among dairy cattle and buffaloes still a zoonotic pathogen threats public heath for all human contactors or those who consume infected products. The present review dealt with the issue focusing on the spread among animals, human transmission routs as well as persons under high risk factors with diect correlation of the *Mycobacterium bovis* infection from cattle to humans and conversely as reverse zoonosis. The work mentioned the obtained previous literatures recommendations as prevent or decline *M.bovis* spread and its globally recommended control programs.

Introduction

Historically in Egypt, tuberculosis more than five Thousand years ago, it was comparatively widespread from the **pre dynastic** (about 3500 –2650 BC) until the late period (around 1450–500 BC),where the disease's defining characteristics, Pott's abnormalities in Egyptian mummies' skeletons **(Amin, 2019)**.On 1882 Koch identified and described the bacillus causing tuberculosis, while on 1892 he mentioned that bovine bacilli were different from the human type. There was no antibiotic treatment for tuberculosis until the 1940s and 1950s.(**Atlanta, Georgia 2019**).

As cases and fatalities decreased, the majority of TB sanatoriums in the United States were closed by the mid-1970s., but by the mid-1980s, it increased again

There are roughly 10 million incident cases of TB, with an estimated 1.2 million TB-related fatalities owing to mycobacterium spp antimicrobial resistance (**WHO 2020).**

Promote **diagnosis of** bovine tuberculosis (**bTB)** among animals is very crucial to detect and eliminate infected cases; if this isn't done, M. bovis can continue to spread throughout herds, increasing the number of public health zoonotic TB cases, which amounted to 142,000 cases out of 10 million cases of tuberculosis, represent 1.4% of the world's TB cases (**WHO, 2016**).

As *M.bovis* is a zoonotic pathogen with various routs of transmission to people (**Toribio *et al.*, 2023**).The present study aimed to put a spot light on *M.bovis* zoonotic view. Additionally, to refer some recommendations as a way forward for controlling TB caused by *M.bovis* in cattle and humans.

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Causes

Mycobacterium bovis is gram positive acid-fast bacilli, aerobic, non-spore-forming, slow-growing, and non-motile, *M. bovis* is a facultative intracellular pathogen that can survive and proliferate inside macrophages and other mammalian cells.

M.bovis is a facultative intracellular pathogen, Gram's positive acid-fast bacilli, aerobic, non-spore-forming, slow growing, and non-motile that can live and grow inside macrophages and other mammalian cells (**Quinn *et al.*, 2011**)

When infect cattle it is accountable for significant financial losses, which have a detrimental effect on both public health as zoonotic pathogen, responsible for considerable economic losses; with consequent negative impact on both public health as zoonotic pathogen, animals and the their product's industry (**Adelakun *et al.,* 2019**).

In Animals

Animals, particularly cattle and buffaloes, are susceptible to the bovine tuberculosis (bTB)as a persistent infectious illness **(Nasr *et al.,* 2016; O'Brien *et al.,* 2023);** mainly dairy sector (**Ameni *et al.,* 2006**) caused by *M. bovis*, with a large and severe financial loss in the production of animals. Granulomas mostly in the kidney, colon, lymph nodes, and lungs are indicative of an active infection. (**Tulu *et al.,* 2021**). But according to bTB control program (test and slaughter), its diagnosis is adopted by tuberculin intradermal cervical test depending on its very high sensitivity character (**O'Brien *et al.*, 2023**). Tuberculin test (TT) is authorized by the World Organization for Animal Health to disclose diseased herds and animals (**O'Brien *et al.,* 2023**). The recirculation of bTB in cattle dairy farms is significantly aided by mixed herds with different species, especially dairy cattle with goats and sheep under intensive management systems (**Tschopp *et al.* 2011** and **Napp *et al.*, 2013**) Infected animal shows mineralization, persistent inflammatory cell aggregation, peripheral fibrosis, and central necrosis (**Salem *et al.,* 2024)**. Among cattle, transmission may be developed as close contact between animals happens during the milking process ,water drinking and eating troughs (**Ghodbane *et al.*, 2014**). The primary routes of infection in cattle are contaminated dust particles or aerosols from animals with open tuberculosis that cough or sneeze. (**Bhembe *et al.,* 2017**). The movement of sick cattle to a non-infected herd is likely another way for the disease to spread among cattle. (**Davies, 2006**). Moreover transmission through crossbreeding between animals that are more vulnerable to bTB than other breeds (**Ameni*al.,* 2007**). Indeed, Unsanitary conditions on a farm could prolong the presence of M. bovis and possibly lead to its proliferation (**Kemal *et al.,* 2019**).

Low farm hygiene as incorrect waste disposal, frequency of waste cleaning or drainage circumstances that could make *M.bovis* infections more persistent by fostering an atmosphere that is conducive to their easy growth and spread (**Mekonnen *et al.,* 2019 and Tulu *et al.*, 2021).**

Human transmission

According to the WHO's 2020 Global Tuberculosis Report, 10 million people (between 8.9 and 11.0 million) contracted TB in 2019, and of those, almost 1.2 million perished (Zoonotoic tuberculosis, 2024). The largest figures were recorded from Africa and South East Asia (**Ramos *et al.*, 2020**) (**WHO, 2020**). Up to 10% of the total human TB cases in developing countries are attributed to *M.bovis* (**Fareed *et al.,* 2024**). *M.bovis* can be transmitted to humans especially in developing countries (**Toribio *et al.,* 2023**) or low and middle-income countries (**Luciano and Roess 2020**). In 2017, *M. bovis* prevalence in cattle or other livestock in parallel with human subjects (**Luciano and Roess, 2020).** Zoonotic potential of bovine TB was established by the direct correlation of *M.bovis* infection between cattle and humans and vice versa as reverse zoonosis in multiple nations **(Messenger *et al.,* 2014, Cosivi *et al.*, 1995, Pal *et al.,* 2022**). Human dietary behaviors, low educational level, population, life style, financial standing, cultivation and the existence of additional other immuno suppressive disease will facilitate transmission and progression to active disease (**Luciano and Roess, 2020**), and living with animals are a couple of these considerations (**Zinsstag *et a*l**

2007).

Despite the the prevalence of bTB has significantly decreased as a result of direct implementing effective programs, mostly by testing and killing of diseased animals (**Pal *et al.*, 2022, Almaw *et al.*, 2022**), it is endemic and is increased (**Davies, 2006**) in many developing, Low-income and middle-income African nations; Nigeria (**Abubakar *et al.*, 2011**), Zambia (**Monde *et al.,* 2023**), Egypt (**Elsabban *et al.*, 1992, Salem *et al.*, 2024**), Ethiopia (**Almaw *et al.*, 2022, Pal *et al.*, 2022**), East Asia – Pakistan (**Fareed *et al.,* 2024) or Latin American nations like Brazil (Avila *et al.*, 2018, Rosa André *et al.,* 2020**) countries mainly due to *M.bovis* antimicrobial resistance as mentioned below with adverse effect on both public health and animal productivity (**Elmonir & Ramadan 2016**). One of the nations with a mid-level incidence rate is Egypt (**Negm *et al.,* 2019**), According to official records from the General Organization of Veterinary Services, Egypt (GOVs), the Nile delta region was the primary site of bTB infection, and the incidence of the disease increased in 2013 when compared to the preceding four years (**Abdellrazeq *et al.*, 2014**). According to a recent report of GOVS, Egypt is seeing an increase in the number of cattle with bTB each year (**Amin, 2019**). The fact that over 20 million Egyptians live in rural areas, where people and farm animals coexist in close proximity, and the lack of adequate extension services in these areas are the main causes of the high prevalence of tuberculosis among the country's human population (**Siam, 1992**). In addition to causing large financial losses in the cattle breeding industry, B BT's etiological agents pose a risk of zoonotic disease. Despite advancements in diagnostics, issues persist, including the possibility of cross-reactivity to test antigens. (**Didkowska, 2021**).

M.bovis mainly affects cattle which be an important reservoir (**Olea-Popelka, 2017 Palmer *et al.*, 2012, Fitzgerald & Kaneene, 2013, Sichewo *et al.,* 2019, Clausi *et al.,* 2021**) threating contact causing human pulmonary and extra-pulmonary infections (**Stephen and Tanya, 2018**). Human TB is mainly caused by Mycobacterium tuberculosis (**Gompo, 2020, Briken *et al.*, 2008, Schöning, 2013).** Since *M. bovis* and *M. tuberculosis* affect human and they are genetically closely related (**World Health Organization, 2017**), there is no prov-ision of differentiating between them (direct conversation with the National TB Center's director in Nepal) (**National Tuberculosis Program Nepal, 2020**).

Occupotional Risks

The most persons contacted TB are those various livestock-related; human-animal proximity or occupational groups particularly in immune-compromised persons (**Okeke *et al.*, 2016, Fareed *et al.*, 2024**) as:-Veterinarians either working in dairy farms or veterinary clinics who are persons at higher risk factor (**Elmonir and Ramadan 2016, Duffy *et al.*, 2020**).

Meat inspectors in abattoirs and **other slaughterhouse staff** (**Mia *et al.*, 2022, Monde *et al.*, 2023**); majority of abattoir's veterinarians may be injured accidentally during meat inspection at least once a week yet they never use gloves (**Elmonir & Ramadan 2016**). Significant relationship link higher work time and zoonotic tuberculosis among slaughterhouse staff (**Khattak *et al.,* 2016**). Since TB is the most common pathology encountered at abattoir meat inspections (**Okeke *et al.,* 2016)**, manual meat inspection is regarded as a useful instrument for detecting ozoonotic illnesses.

Milkers persons of infected animals (**Mia *et al.*, 2022**); awareness of **farm workers or owners** (**Tulu *et al.*, 2021**) and animal husbandry workers (**Luciano and Roess 2020**). Just 30% of workers were taking any preventive measures, and just 15% of workers and herdsmen were aware of bTB. (**Baloch *et al.,* 2020**).

Workers acting with manufacturing dairy products from unpasteurized milk of infected cattle (**Mia *et al.*, 2022**).

Humans other than occupationally affected who can contract bTB; **consumers** of uncooked little processed meat products which are typically consumed fresh after grilling, which presents the risk for humans to develop zoonotic TB (**Clausi *et al.*, 2021**). It is the most typical method of human transmission

(**Toribio *et al.,* 2023**).

Additionally dairy users are susceptible to the spread of infections.
By consuming tainted raw or unpasteurized milk (**Elmonir and Ramadan 2016, Luciano and Roess 2020**). Alimentary route of infection leads to extra-pulmonary TB (**Grange, 2001** (Ingestion of infected food (i.e. milk- or meat-borne) is linked to increase risk of extra-pulmonary tuberculosis (**Kleeberg, 1984**).

Airborne transmission aerogenous through inhalation of infectious droplet nuclei (**Tulu *et al.* 2021**) is often associated with respiratory disease manifestation whereas the aerosol route of *M. bovis* infection during close contact with animals results in pulmonary disease in humans (**Sunder *et al.,* 2009**).

Antimicrobial resistance: The great challenge of TB spreading is manifested in its multidrug resistance as only three new drugs, bedaquiline (BDQ) and the two nitroimidazole derivatives delamanid (DLM) and pretomanid (PMD) were approved in the last decade as the 2019 WHO recommendations (**Müller *et al.,* 2013**). While, *M. bovis* resiststant against pyrazinamide (**Olea-Popelka *et al.,* 2017).** *M. bovis* is naturally resistant to pyrazinamide, one of the four medications used in the standard first-line anti-tuberculosis treatment regimen. It is a big gap behind the patient's effective treatment and timely recovery (**Olea-Popelka, 2017, Ford *et al.,* 2013, Mitsuko Seki 2012 and Djemal *et al.* 2018**). Isoniazid and rifampicin (**WHO, 2013, Sechi *et al.* 2001**), (**WHO, 2020, Cadmus *et al* 2019**), streptomycin (**Djemal *et al.,* 2018**).

Conclusion and Recommendation

The study concluded that bovine *M.bovis* has potential zoonotic impact with great threats for human public health for all contact persons or other consumers of contaminated foodstuffs. It is of high and restricted recommendation to adopt the only successful control program (**TEST & SLAUGHTER**) at all bovine populations (dairy, fattening) either governmental or private communications. It is of serious concern for persons of high risk factor (mainly farm veterinarians or others in abattoir workers) to take the high proportion of precautions when contact with suspected or infected animal. It is of important to avoid consumption of unpasteurized milk or milk products as well as row or uncooked meat.

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