Human Tuberculosis Caused by Mycobacterium Bovis in India: Present Situation, Problems, and Opportunities

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Abstract

One of the infectious diseases that claim most lives worldwide is tuberculosis, which is brought on by the bacteria, Mycobacterium tuberculosis. Mycobacterium Bovis, an animal pathogen, has also been linked to tuberculosis infections. The condition can be contracted by close contact with livestock or by consuming infected meat or raw milk. The principal source of M. bovis infection has traditionally been thought to be infected animals. The disease "bovine tuberculosis (bTB)" is documented in every country that raises livestock, regardless of socioeconomic status of the nation, although little is known about its global distribution. Current efforts have been made to control bTB in the hopes of reducing the prevalence of human infection globally. In India, instances of tuberculosis (TB) are reported quite infrequently. In India, there have only been a relatively small number of epidemiological studies conducted in the context of the M. bovis-induced human TB, and even fewer have focused on the management of this specific disease. The purpose of this review was to shed light on the most significant challenges and opportunities for action that exist in India in relation to mitigating the threat of M. bovis infections to individuals and maximizing public safety. In this paper, a review of the evidence that is currently available, the current condition of M. bovis-induced zoonotic TB is as well discussed.

Keywords: Tuberculosis, Zoonosis, Mycobacterium Tuberculosis, Mycobacterium Bovis, Bovine Tuberculosis, Prevalence.

INTRODUCTION

From ancient times, tuberculosis (TB) has remained a significant illness affecting both humans and animals. Three thousand year old Egyptian mummies and bison fossils that are 17,000 years old contain TB traces.[1] Both domestic and wild animals specifically cattle are susceptible to TB. Mycobacterium tuberculosis causes TB in humans. Around a third of the population is infected with tuberculosis, which also causes nearly 2 million fatalities per year globally and can live under extremely unfavourable conditions in the host. Mycobacterium bovis share 99.5% of their genetic sequences with M. tuberculosis and it is still unclear what percentage of human TB cases worldwide are brought on by this bacillus.[2-4] M. Bovis, can infect nearly all animal species.[5] In the majority of species, M. Bovis may go years without showing any symptoms in infected animals, yet it slowly deteriorates their health. Bovine TB (bTB) when infected to the animals is challenging to diagnose and screen the animals.[6]

The clinical symptoms of the illness, "*Tuberculin Skin Test* (TST)", and the isolation of pathogen are the three key components of an accurate diagnosis of bTB.[7] Common method for diagnosis is TST, however the accuracy of the test is debated and the result interpretations needs expertise. Novel assays were introduced to overcome the problems of TST's accuracy, but these tests are expensive and their application in developing countries is contentious. The "gold standard test" for bTB diagnosis is regarded to be bovis on pyruvate-containing culture medium. It does, however, have several drawbacks, such as a lengthy turnaround time and decreased sensitivity.[8] Utilizing molecular methods to find M. Bovis offers a quick replacement for culture. A multiplex PCR can identify these two variants of TBs.[9] Several molecular assays, including PCR-RFLP, 16S-23S rRNA, and genes encoding M-specific proteins. For the detection of bTB in animals, tuberculosis complexes such hsp65, MPB64, MPB70, and have been created and utilised.[10] "*Pulsed-field gel electrophoresis"* and

"Spoligotyping" are two methods of molecular typing for rapid identification of the M. bovis animal cases. The advantages of using molecular typing assays for animal herds include the competency to simultaneously detect infection and the dynamics of transmission of the infection. Nevertheless, there are restrictions on the sensitivity of the test when using molecular typing methods on paucibacillary samples.[11]

M. bovis induced TB among people is a significant public health issue on a global scale. Proximity to the cattle that is infected or consuming animal-sourced foods (such as raw milk and undercooked meat) are the two main ways that people become infected.[12] Even though the mechanism of infection in humans is not fully understood, it is hypothesised that the alimentary route of infection results in extra-pulmonary TB whereas the aerosol route of M. bovis infection during close contact with animals produces pulmonary disease in people. The fate of the disease largely hinges on how these macrophages react to the approaching threat. There is evidence that M. Bovis can spread disease by multiplying inside host cells, altering the macrophage's antimicrobial defenses.[13]

Mendum et al.,[14] reported the genetic make-up of the M. Bovis that allows for the longer infectivity of these pathogens in the host. M. bovis induced TB mimics M. Tuberculosis for all the clinical and diagnostic presentations. The occurrence of zoonotic TB is rare in industrialized nations due to the adoption of bTB control programs. As a result, most of bTB cases are seen in the developing nations where the control programs are unavailable.[15] In India, bTB has always been regarded as a rare disease. However in recent years, domestic livestock species from various regions of the nation have frequently been found to have bTB. In India, domestic livestock had a modest (7.3%) prevalence of bTB, according to a recent meta-analysis.[16] Animals' resistance to bTB varies depending on breed, according to several researchers. In West Bengal, Das et al.,[17] found that exotic crossbred animals had a considerably greater frequency of bTB ($P < 0.001$) than native cattle. In India, samples of the environment (soil and water) and milk obtained from animals have both been shown to contain M.bovis. In India, incidents of zoonotic transmission have been documented often due to sporadic and ineffective control measures. [18,19] M. bovis exposure continues to be a concern for the human population through food products and direct contact. The current review discusses the situation of M. bovis infection and is based on information that has been published in the human population and identifies major obstacles to reducing M. bovis infections among humans in India.

DISEASE IN THE INDIAN CONTEXT

M. bovis infection in people causes the same illness as TB brought on by M. tuberculosis. Conferring to estimates, the prevalence of the M. Bovis-induced human TB is ten times more in the countries like India, than the USA which is developed. The "*World Health Organization (WHO)*"[4] reported ten percent mortality due to this zoonotic tuberculosis, primarily in African and South-East Asian nations. Due to the clinical, radiographic, and histological similarities between M. bovis-caused human TB cases and the TB (common), bovis-derived human TB cases are typically underreported.[20] The majority of TB cases worldwide are in India. Cases involving M. Bovis-induced human TB were documented early in the last century, India.[21] Unfortunately, the condition has not gotten much attention, and there are no statistics to assess the M. Bovis-induced human TB in India. This could be as a consequence of the challenges due to the lack of adequate laboratory facilities to separate and isolate the two different strains of M.tuberculosis and M.bovis. Because the various M. tuberculosis complex members respond to anti-TB medication in very different ways, species identification is crucial for directing treatment.[22-24] When treating TB patients, failing to distinguish between M.tuberculosis and M.bovis complex might be lethal.[25]

Several investigations have indicated intermittent occurrence in recent years, cases of probable tuberculosis with M.bovis infection from various parts of India. Bapat et al.,[26] concluded from their study that M. Bovis is seen among those who have a close association with the animals like cattle farmers and zoo-keepers. They have supported their research using a duplex PCR. A substantial risk factor for zoonotic TB in the surrounding human population, according to the study, was intake of raw milk and past contact with TB patients who were still actively infected. Jain[27] using the PCR found the hupB gene in majority of the M.TB cases, followed by the M. Bovis-induced human TB among the subjects who were infected with extrapulmonary TB. Using PCR targeting the hupB gene, Kohli et al.,[28] found that half of their subjects who were infertile women, had M.bovis or co-infection with both the Mycobacterium species causing the tuberculous endometritis.

Much of the information regarding the existence of M. Bovis-induced human TB in India is from the observational studies done on limited sample size. As a result, these investigations might not accurately reflect the general public and might understate the prevalence of M. Bovis-induced human TB in the nation.[29] These studies indicate that between 10% and 15% of extrapulmonary TB cases in India may be caused by M. bovis; as a result, public health officials in the nation should pay them more attention. Priority should be given to investigating the epidemiology and clinical signs of M. bovis-induced TB, as well as any occurrences of non-tuberculous mycobacteria or co-infection with M. tuberculosis, in order to better manage and plan for the control of TB in the nation's human population.

ISSUES WITH THE DISEASE MANAGEMENT IN THE INDIAN CONTEXT

There are difficulties that are seen in the Indian context for the management of the M. Bovis-induced human tuberculosis like the Routine diagnostic test limitations and inadequate laboratory infrastructure for zoonotic tuberculosis diagnosis, lack of knowledge regarding patient recovery and effective treatment, high density of people and frequent contact between people and animals, infection common among those with compromised immune systems, and infection of those with reduced immune resistance and the religious and Sociocultural values.

The majority of laboratory tests used to diagnose TB do not distinguish between M. tuberculosis and M. bovis, and they may thus miss cases of zoonotic TB. It is challenging to make an accurate diagnosis of zoonotic TB caused by M. bovis, and clinical samples must be used to isolate and characterise the bacilli. Now, the nation has implemented "*National Tuberculosis Elimination Programme (NTEP)"* approved culture and DST laboratories for the diagnosis of TB.[30] For this well-equipped laboratory infrastructure are required. Almost 3 million TB patients live in India, which accounts for 27% of all newly diagnosed TB cases worldwide.[4] To stop the spread of TB in the community, the NTEP primarily focuses on early detection and treatment initiation. Owing to the overwhelming burden of pulmonary TB, the majority of NTEP-culture labs utilise non-pyruvate culture medium instead of pyruvate-containing media, which are thought to be the preferred media for initial isolation of M. bovis from clinical samples.[31] As a result, for better zoonotic TB identification and control in India, laboratory infrastructure upgrading and enhanced laboratory diagnostic tests are paramount.

Therapy for M. bovis-induced TB differs from that for M. tuberculosis-induced pulmonary TB, and it presents significant difficulties for the patient's recovery and efficient care. One of the most significant first-line anti-TB medications utilised in the treatment regimen, pyrazinamide, has been discovered to be inherently resistant to M. bovis.[32,33] Without understanding the precise Mycobacterium species involved, the majority of healthcare professionals in India begin treating TB patients based only on the detection of acid-fast bacilli in clinical samples. Since both M. TB and M. bovis are members of the M. tuberculosis complex, the findings of the "*Cartridge-Based Nucleic Acid Amplification Test* (CBNAAT or GeneXpert)", which is used with universal DST, cannot distinguish between the two. In these circumstances, patients with TB caused by M. bovis receive insufficient care, which may have negative effects on the management of TB patients and even cause the development of drug resistance to anti-TB medications.[20] Thus, it is important to establish the differential identification of M. tuberculosis from M. bovis and routine testing of pyrazinamide resistance for patients suspected of having zoonotic TB. M. TB and M. bovis co-infections were also documented in earlier studies.[34,35] To effectively manage patients in our nation and in the nations where bTB is common, it is necessary to examine the clinical differences and treatment outcomes of co-infection.

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One of the most significant risk factors for M. bovis infection in people is a suppressed immune system. Prior research has demonstrated that HIV-positive people are more vulnerable to M. bovis infection, which affects the disease's mortality rate and clinical manifestations.[33,36]

According to reports among immune-reduced and even immune-competent people in the UK, suppressed immunity also encourages interpersonal transmission of M. bovis.[37] In a retrospective analysis of 86 cases of TB and HIV co-infection, Park et al. (1989)[38] found that 34.9% of patients in San Diego, had M. bovis infection. The number of HIV/AIDS cases in India as well as other immune-compromised conditions patients is staggering.[39] Although unpasteurized milk and dairy products are the primary source of M. bovis infection in humans, immune deficient patients in India are at a high risk of exposure due to M. bovis contamination of these products.[40,41,42] The status of M. bovis infection in HIV patients or other immune challenged individuals is unknown at this time in India, hence this issue has to be looked into. Precautions must be taken in the current situation to prevent the transmission of live M. bovis to humans. Healthcare establishments in India should make it mandatory to counsel immune-compromised patients about zoonotic TB and risk factors for contracting M. bovis infection.

The stratification of society in India as a result of cultural variation in daily life is based on religious traditions, dietary preferences, and healthcare needs. Raw cow's milk has just recently gained popularity as a healthful beverage, and certain families and civilizations now consume it regularly. An intriguing case of tuberculosis among the animals and people on a dairy farm as a result of drinking raw milk was documented in 2009.[43] Hence, through raising awareness among the rural and tribal populations, the custom of boiling milk before drinking, should be revived and spread. According to a recent study by Srinivasan et al.,[16] 6.3% of the nation's cattle are infected with bTB. The bioburden of M. bovis in India is predicted to rise as diseased cows can spread the virus to humans and other animals. The State and Central Governments in India must work together to create quarantine facilities for affected cattle and launch a bTB control programme.

In order to tackle zoonotic infections in both humans and animals, the major international health agencies have pushed for the "One Health" strategy.[44] The efforts of TB eradication programmes in high-endemic nations like India may be jeopardised by the spread of TB from animals to humans or vice versa. Under the aegis of "One Health," the nation's current TB elimination programme can establish comprehensive measures to combat both human and zoonotic TB. The rapid eradication of human TB and the ambitious target of TB eradication in India by 2025 would both benefit from the application of this strategy.

CONCLUSION

The WHO designated zoonotic TB as a priority disease back in the 1950s, but it has not gained the attention it deserves in India. This could be for a number of reasons, including the dearth of thorough studies on zoonotic TB in people and bTB in animals. The research that was provided demonstrated that bTB is a "insidious disease" among domestic cattle species in India and that M. bovis exposure is a possibility among people. In order to quantify the prevalence and monetary damages brought on by M. bovis-induced TB, a surveillance program is urgently required. This knowledge, together with other particular actions, may be essential for enhancing bTB control tactics and reducing the spread of M. bovis infection to the human population in India.

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