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TUBERCULOSIS IS OF MAJOR CONCERN AMONG THE POPULATION

Annotation: Tuberculosis (TB) has a long history and being present even before the start of recording history. It has left detrimental effects on all aspect of the life and geared the developments in the science of health. TB is caused by Mycobacterium tuberculosis complex (MTBC) including five species *M. tuberculosis*, *M. bovis*, *M. africanum*, *M. canetti*, and *M. microti*. *M. tuberculosis* and *M. bovis* infect both animals and humans. Therefore, differentiation of these two closely related species is very important for epidemiological and management purpose. In the present study, we aimed to assess the prevalence of bovine tuberculosis (TB) and examine the determinants of disease spread in three high-risk groups in the Ferghana Valley. A prospective cohort study was conducted in the Ferghana Valley between March 2020 and June 2024.

Key words: Mycobacterium tuberculosis, *M. bovis*, polymerase chain reaction, methods.

Based on the necessary inclusion criteria, we recruited a total of 59 participants whose blood samples were subjected to the detection and differentiation of Mycobacterium bovis and Mycobacterium tuberculosis based on polymerase chain reaction. *M. bovis* was found in 11.4%, 8.9% and 12.6% of the selected participants belonging to three different populations (groups A, B and C, respectively). The highest proportion of *M. bovis* infections were observed in group C, which lived in a region with a high level of TB endemicity. Tuberculosis (TB) remains the leading cause of death worldwide, affecting more than 9 million people each year. While Mycobacterium tuberculosis is the most common cause of human tuberculosis, it is believed that unknown proportions of tuberculosis cases are associated with Mycobacterium bovis infection, which is also called bovine tuberculosis [1]. Currently, this infection is of major concern among the population in developing countries, as humans and animals are in the same microenvironment. It has been estimated that zoonotic transmission of *M. bovis* is responsible for 10–15% of new human cases of tuberculosis in developing countries [2]. The disease in humans mainly occurs through close contact with infected cattle or through the consumption of improperly cooked beef and the consumption of unpasteurized milk and dairy products [3,4]. People in certain occupations, such as veterinarians, farmers, and slaughterhouse workers, are thought to be at greater risk [5]. Currently available tests used to identify *M. bovis* are based on bacterial isolation and biochemical tests, which are time-consuming and have low diagnostic accuracy [6]. In addition, TB caused by *M. tuberculosis* In humans, is clinically and radiologically identical to TB caused by *M. bovis* [8]. These problems have been overcome to some extent by molecular methods; however, this method has not been able to identify mycobacterial pathogens at the species level. (MTBC), we targeted areas of difference (RDs) with duplex polymerase chain reaction (PCR) analysis. The analytical sensitivity of duplex PCR assay was determined by 10-fold serial dilutions of 107 fg to 10 fg DNA (equivalent to 10 copies of the genome^{6–10°}) isolated from reference strains of *M. tuberculosis* (ATCC 25177), *M. bovis* (ATCC BAA-935), and *M. bovis* BCG Pasteur (ATCC 35734). To assess specificity, the concentration of DNA templates of each reference strain was adjusted to 10 ng/μL and subjected to PCR. PCR amplicons were analyzed for 2% agarose gel and stained with ethidium bromide. The enhanced foods were then visualized under the influence of ultraviolet radiation. A comparative analysis of the electrophoresis of PCR products produced by two sets of primer pairs showed the ability to distinguish between *M. tuberculosis*, *M. bovis* and *M.*

bovis BCG. Duplex PCR was found to be positive for *M. bovis* when bands of both 176.o. and 110.o. were detected; the result was found to be positive for *M. tuberculosis* when a band of only 110.o. was seen and positive for *M. bovis* BCG when the 176.o. band was visualized on the gel.

A total of 59 patients were included, accounting for 0.4% of TB cases diagnosed in the hospital during the study period. The median age was 45 years (interquartile range [IQR] 27–57 years) and 72% were men. Underlying conditions included diabetes (8/30, 27%), HIV (8/37, 22%; median CD4 T-cell count 42 cells/mm³; IQR 22–108) and malignant disease (1/30, 3%). All of the patients lived in the Buenos Aires metropolitan area. Ninety-three per cent of the patients had at least one risk factor for *M. bovis*. The most frequent was occupational exposure (65%), followed by consumption of unpasteurised milk (4%) and history of living in a rural area (31%). Clinical presentation included cough (84%), expectoration (84%), weight loss (80%), fever (64%), malaise (56%), night sweats (32%), haemoptysis (28%), dyspnoea (28%) and headache (8%). Pulmonary disease was present in 29 cases (74%), extrapulmonary disease in 4 cases (10%) and both in 6 cases (15%). Pulmonary disease was more frequent in those patients with occupational exposure (17/17, 100% vs. non-occupational 6/9, 67%; $P = 0.03$). Chest X-ray showed cavities (10/26), alveolar infiltrates (13/26), miliary pattern (2/26) and pleural effusion (2/26). The Mantoux test was positive in 6/17 patients (35%). Ziehl-Neelsen staining performed in respiratory samples was positive in 77% of cases. All samples grew well in Stonebrink medium and none in LJ. All of the samples were resistant to PZA. Rifampicin resistance and multidrug resistance, defined as resistance to both isoniazid and rifampicin, were each seen in 1/29 cases (3%), both in HIV-infected patients. Empirical treatment was initiated with first-line anti-tuberculosis drugs, including PZA, in 25/27 cases (93%). Twenty-eight per cent of the patients died (7/25). The mortality rate was higher among HIV positive than HIV-negative patients (85%, 6/7 vs. 6%, 1/18; $P = 0.01$).

DISCUSSION The incidence of *M. bovis* infection in our study was low, as previously reported in Latin America.⁶ Although the ingestion of unpasteurised milk is classically described as the most common route of transmission, this was not observed in our study. Based on the fact that the most frequent presentation was pulmonary, our data might suggest that the most likely route of infection was airborne transmission, and that occupational exposure was the most important risk factor. Although we do not deny the possibility of gastrointestinal exposure occurring in these patients—before pasteurisation was established in Argentina *M. bovis* was a food-borne pathogen, and the great majority of patients presented with lesions in the gastrointestinal tract—almost none of our patients with a history of living in a rural area had extrapulmonary lesions, and thus airborne transmission from infected animals rather than consumption of unpasteurised milk could be the more likely route of transmission. Nevertheless, given the small sample size, further research is needed to assess the validity of this observation.

In conclusion, airborne transmission and occupational exposure as risk factors for TB due to *M. bovis* are a very interesting finding. However, due to the limitations related to the small number of cases included, further studies are necessary to confirm these results.

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