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This study aimed to evaluate possible factors associated respectively to *M. bovis* co-infections (study 1) and evidences of *M. avium-intracellulare* presented alone or in co-infections (study 2) by means of two case-control nested in a cross-sectional study. In the latter study we defined the mycobacteria involved in 191 patients. The cross-sectional study was implemented in two health centers in Minas Gerais, Brazil, from March 2008 to February 2010. In both studies we selected 15 controls (TB due to *M. tuberculosis*) for each *M. bovis* co-infection or *M. avium-intracellulare* evidence, respectively. In both studies, controls were matched by age group (cutoff point 38 years) and sex (Study 1) and by age group (cutoff point 38 years), sex and type of entry into service (study 2). In one study, *M. bovis* co-infections were associated ($p \leq 0.05$) both with zoonotic exposure (OR=16,85, CI 95% = 0,64-275,18) and with the clinical form of tuberculosis (OR = 16.00, 95% CI = 1.21 to 209.94). In Study 2, *M. avium-intracellulare* evidences presented an association ($p \leq 0.05$) with HIV / AIDS (OR = 13.36, 95% CI = 1.26 to 140.93). We verified a high rate of current consumption (44%) of unpasteurized cheese among the subjects in this study. Additionally, *M. bovis* was identified in the subpopulation of extrapulmonary TB, and the possible source of infection for these patients was unpasteurized cheese. Therefore, the potential health hazards of several microorganisms, including *M. bovis*, which can be carried through unpasteurized milk and milk derivates, should be emphasized.

Key-words: zoonotic tuberculosis, risk factors, Brazil

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Risk factors for *Mycobacterium bovis* and *M. avium-intracellulare* human infections in Brazil

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INTRODUCTION

Although most cases of human tuberculosis (TB) are caused by *My-cobacterium tuberculosis*, concerns over *Mycobacterium bovis* have been expressed and are based on several observations. First, there have been outbreaks of multidrug-resistant (MDR) *M. bovis* strains among hospitalized patients with human im-munodeficiency virus (HIV) (*1*). These outbreaks highlight the high risk that MDR *M. bovis* could spread, especially in parts of Africa where animals with *M. bovis* and humans with HIV co-exist. Second, the reemergence of zoonotic tuberculosis among immigrants from regions where bovine tuberculosis is still prevalent have been documented (*2*).

In Latin America, the estimated proportion of zoonotic TB due to *M. bovis* accounts for 2% and 8% of pulmonary (PTB) and extrapulmonary (EPTB) forms, respectively (*3*), while in Brazil, the proportion of zoonotic cases due to *M. bovis* was estimated to be 3.5% of all TB cases in 1974 (*4*). As a standard procedure, sputum acid-fast bacilli (AFB) microscopy and histopathology are the major criteria for TB diagnosis in Brazil which may overlook potential cases of zoonotic TB cases in endemic areas of the country. This potential is reinforced as 0.85% of the cattle in Minas Gerais State (MG), Brazil, was demonstrated to be tuberculin reactors by the Brazilian Ministry of Agriculture .

This study aimed to evaluate possible factors associated respectively to *M. bovis* co-infections (study 1) and evidences of *M.*ycobacterium *avium-intracellulare* (MAI) infections (study 2) by means of two case-control nested in a cross-sectional study. In the cross-sectional study we defined the mycobacteria involved in 191 patients.

MATERIAL AND METHODS

The cross-sectional study was implemented in two health centers in Minas Gerais, Brazil, from March 2006 to February 2010.

In both studies of case-control we selected 15 controls (TB due to *M. tuberculosis*) for each *M. bovis* co-infection or *M. avium-intracellulare* evidence, respectively. In both studies, controls were matched by age group (cutoff point 38 years) and sex (Study 1) and by age group (cutoff point 38 years), sex and type of entry into service (study 2).

RESULTS AND DISCUSSION

In study 1, *M. bovis* co-infections were associated ($p \leq 0.05$) both with zoonotic exposure (OR=16,85; CI 95% = 0,64-275,18) and with the clinical form of tuberculosis (OR = 16.00, 95% CI = 1.21 to 209.94).

In Study 2, *M. avium-intracellulare* evidences presented an association ($p \leq 0.05$) with HIV / AIDS (OR = 13.36, 95% CI = 1.26 to 140.93).

We verified a high rate of current consumption (44%) of unpasteurized cheese among the subjects in this study. Two (11.7%) of the 17 extrapulmonary TB and one (0.6%) of the 170 pulmonary TB patients presented an *M. bovis* profile.

Figure 1 shows molecular profiles of *M. bovis* isolated from extrapulmonary TB patients. Possible sources of *M. bovis* infection were unpasteurized cheeses, goats or slaughterhouse

Therefore, the potential health hazards of several microorganisms, including *M. bovis*, which can be carried through unpasteurized milk and milk derivates, should be emphasized.

Furthermore, isolates of MAI were found respectively from sputum of four patients. Nevertheless, as three of these four cases were HIV/AIDS, it could be accepted that these were really co-infection cases.

CONCLUSION

M. bovis co-infections were associated both with zoonotic exposure and with the clinical form of tuberculosis.

Furthermore, *M. avium-intracellulare* evidences presented an association with HIV / AIDS.

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Mtb: (…)CAGACGCTCGATGCTGCCCAACACCCGGGCGGTGTGGCTGGCCACCG
MB: (…)CAGACGCTCGATGCTGCCCAACACCCGGGCGGTGTAGCTGGCCACCG
P1 (…)CAGACGCTCGATGCTGCCCAACACCCGGGCGGTGTAGCTGGCCACCG
P2 (…)CAGACGCTCGATGCTGCCCAACACCCGGGCGGTGTAGCTGGCCACCG

Figure 1 Comparison of homology for *oxyR* pseudogene partial sequences extracted from biopsies, Juiz de Fora County, Mth. *oxyR* pseudogene partial sequence of reference *Mycobacterium tuberculosis* H37Rv strain (GenBank); MB, *oxyR* pseudogene partial sequence of reference *Mycobacterium bovis* BCG Pasteur 1173P2 strain (GenBank); P1, *oxyR* pseudogene partial sequence of *M. bovis* strain from biopsies, patient 1, P2, *oxyR* pseudogene partial sequence of *M. bovis* strain from biopsies, patient 2, (…), DNA sequence omitted; ▮ and ▮, position 285 of *oxyR* pseudogene.

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