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Prevalence of latent *Mycobacterium tuberculosis* infection in prisoners

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ABSTRACT

Objective: To determine the prevalence of and the factors associated with latent *Mycobacterium tuberculosis* infection (LTBI) in prisoners in the state of Minas Gerais, Brazil. **Methods:** This was a cross-sectional cohort study conducted in two prisons in Minas Gerais. Tuberculin skin tests were performed in the individuals who agreed to participate in the study. **Results:** A total of 1,120 individuals were selected for inclusion in this study. The prevalence of LTBI was 25.2%. In the multivariate analysis, LTBI was associated with self-reported contact with active tuberculosis patients within prisons (adjusted OR = 1.51; 95% **CI:** 1.05-2.18) and use of inhaled drugs (adjusted OR = 1.48; 95% **CI:** 1.03-2.13). Respiratory symptoms were identified in 131 (11.7%) of the participants. Serological testing for HIV was performed in 940 (83.9%) of the participants, and the result was positive in 5 (0.5%). Two cases of active tuberculosis were identified during the study period. **Conclusions:** Within the prisons under study, the prevalence of LTBI was high. In addition, LTBI was associated with self-reported contact with active tuberculosis patients and with the use of inhaled drugs. Our findings demonstrate that it is necessary to improve the conditions in prisons, as well as to introduce strategies, such as chest X-ray screening, in order to detect tuberculosis cases and, consequently, reduce *M. tuberculosis* infection within the prison system.

Keywords: Prisons; Tuberculin test; Latent tuberculosis, HIV.

INTRODUCTION

It is estimated that there were 9.4 million new cases of tuberculosis worldwide in 2014, 12% of which were HIV-infected, as well as 1.5 million tuberculosis-related deaths.[1] Brazil is one of the 22 countries that collectively account for 80.0% of the global burden of this disease.[1] Minas Gerais ranks fourth among the states with the highest number of tuberculosis cases in Brazil.[2] The main global strategy for tuberculosis control, proposed by the World Health Organization (WHO) and known as Stop TB,[1] highlights, in one of its components, the need to promote tuberculosis control activities targeting prisoners because such individuals are at high risk for latent *Mycobacterium tuberculosis* infection (LTBI) and for developing tuberculosis disease, given that this a serious public health problem in penal institutions.[3-6]

The presence of tuberculosis within the prison system has been described as a threat. Some authors have suggested that it will not be possible to control tuberculosis in the community unless effective measures are taken to combat the disease in prisons. In those places, tuberculosis is not limited to prisoners only, because it also affects the community with which they interact, family members, and prison staff, during and after incarceration.[3,5-9] In Brazil, the incidence of tuberculosis within the prison system is 28-fold higher than that in the general population.[10] The prevalence of LTBI is also high in those places,[5,7-9,11-13] a reality that remains unknown in most Brazilian regions since there are no studies on the subject.

Identifying LTBI in prisoners should be given priority so that preventive measures can be adopted, especially in groups with conditions associated with high risks of developing tuberculosis, such as HIV seropositivity, diabetes mellitus, chronic renal failure, use of immunosuppressants, etc.[6,9,14] The method for identifying suspected tuberculosis cases should be decided upon on a scenario-by-scenario basis, depending on the local context and the existing resources.[3,8,9,15-17] The main screening strategies are based on symptoms, chest X-ray, and the tuberculin skin test (TST).[3,8,9,14,15] Each has advantages and limitations.[3,8,9,15-18] Active surveillance for cases of tuberculosis disease, through screening, should be undertaken not only upon entry into the prison system, but also afterwards. The purpose of this surveillance is to examine individuals who are more likely to develop the disease, such as those with respiratory symptoms (RS), identify active cases, and treat them accordingly. Such measures break the chain of transmission and decrease the incidence of the disease.[6,11,18] The objective of the present study was to estimate the prevalence of and the

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factors associated with LTBI in prisoners in the main prison area in Minas Gerais.

METHODS

Study design

This was a cross-sectional cohort study conducted in the two largest prisons (condemned prisoners) in the main prison area in the state of Minas Gerais, both of which are located in the city of Ribeirão das Neves and house 8.4% of the prisoners in the state. A total of 1,492 inmates were included in the present study (67.0% of the prisoners in the prisons under study and 5.8% of the prisoners in the state)[19-21] between April and June of 2013. The eligibility criteria were as follows: having had no previous treatment for tuberculosis; having no tuberculosis disease at the study outset; and having never undergone a TST.

Administering and reading TSTs

TSTs were performed by the Mantoux method, which consists of administration of 0.1 mL (2 tuberculin units) of *M. tuberculosis* PPD RT23 (State Serum Institute, Copenhagen, Denmark) on the left forearm. TSTs were read 72 h after being administered, by measuring the maximum transverse diameter of induration with a millimeter ruler. An induration of ≥ 10 mm was considered a positive result for HIV-uninfected individuals, whereas an induration of ≥ 5 mm was considered a positive result for HIV-infected individuals.[14] Isoniazid preventive therapy was recommended to all prisoners at risk for developing active tuberculosis.[6] All TSTs were administered and read by trained and certified professionals for research project participation.

Sampling and bacteriological tests

Sputum samples were collected from individuals with a history of cough, regardless of length of history, for smear microscopy and mycobacterial culture. Drug susceptibility testing was performed if culture was positive, in accordance with the WHO laboratory guidelines.

Serological testing for HIV

Serological testing for HIV was offered to all participants, along with pre- and post-test counseling.[22] Positive results by ELIZA were confirmed by the Western Blot method.

Data collection

Educational and awareness-raising activities regarding *M. tuberculosis* infection were developed for the prison health team and the prisoners. The study participants completed a questionnaire addressing sociodemographic characteristics (age, gender, marital status, schooling, occupation before incarceration, and length of incarceration); behavioral characteristics (use of licit and illicit drugs, alcoholism—assessed by the **C**ut down, **A**nnoyed, **G**uilty, and **E**ye-opener screening questionnaire—[23]smoking, and contact with active pulmonary tuberculosis patients inside or outside prison); health history (previous treatment for active tuberculosis, BCG vaccination, HIV infection, presence of diabetes mellitus or other diseases, and use of medications); and symptoms suggestive of pulmonary tuberculosis (cough, cough duration, expectoration, hemoptysis, fever, adynamia, cyanosis, anorexia, weight loss, and night sweats). The health records available in the prisons were consulted to fill in missing information.

Statistical analysis

The selected characteristics were analyzed descriptively by gender, with results being presented as frequencies, and by univariate and multivariate analysis, with results being presented as measures of central tendency and dispersion. The mean differences for continuous variables were compared using the Student's t-test, whereas the proportions of categorical variables were compared using Pearson's chi-square test. The IBM SPSS Statistics software package, version 21.0 (IBM Corporation, Armonk, NY, USA) was used for statistical analysis, and the data were recorded in tables. The magnitude of the association between the selected explanatory variables and the event of interest, that is, LTBI, was estimated by calculating ORs with 95% CIs. Variables with a p value of ≤ 0.25 in univariate analysis, as determined by the Wald test, were manually selected to build a multivariate model via a stepwise regression selection procedure. The significance level required for inclusion in the final model containing the selected variables was set at 0.05 to adjust for potential confounders properly. Only the variables showing a significant independent association with the event of interest remained in the final model. The likelihood ratio test was used to compare the models. The goodness of fit of the final models was assessed using the Hosmer-Lemeshow test.

Ethical guidelines

The study was approved by the Research Ethics Committee of the Federal University of Minas Gerais (Protocol no. 0617.0.203.000-09) on April 5, 2010.

RESULTS

Characteristics of the population

Most of the prisoners agreed to participate in the study (N = 1,431; 96.0%), and, of those, 1,120 (78.0%) were included in the final sample. Of the total number of individuals excluded from the study (n = 311), 68 (21.8%) had undergone a TST previously, whereas 243 (78.1%) had not because of previous tuberculosis (35/243; 14.4%), tuberculosis treatment (4/243; 1.6%), transfer to another prison (13/243; 5.3%), or refusal (191/243; 78.6%; Figure 1).

In the study population (Table 1), the mean age was 29 ± 7 years and most individuals had had less than 7 years of schooling (90.0%). The length of incarceration was longer than 12 months for 57.0%

of the participants (mean, 28 ± 25 months). Contact with active pulmonary tuberculosis patients occurred outside and inside prison, respectively, in 10.0% and 15.0% of the cases. The proportions of smoking and pre-incarceration alcoholism were, respectively, 61.1% and 24.8%. The use of illicit drugs was reported by 75.0% of the inmates. Of those, 97.0% reported using inhaled drugs, 2.0% reported using injected drugs, and 1.0% reported using inhaled and injected drugs.

Diabetes mellitus, chronic renal failure, silicosis, and use of immunosuppressive medications were reported, respectively, by 1.2%, 0.7%, 0.1%, and 2.9% of the prisoners. Serological testing for HIV was performed in 83.9%, and the result was positive in 0.5%.

In the univariate analysis, LTBI was found to be associated with the following variables: gender; marital status; contact with active tuberculosis patients outside prison; pre-incarceration alcoholism; use of inhaled illicit drugs; diabetes mellitus; chronic renal failure; and chronic use of corticosteroids and/or immunosuppressants (Tables 1 and 2).

Prevalence of and factors associated with LTBI

The prevalence of LTBI was 25.2%. In the multivariate analysis, the occurrence of LTBI was associated with self-reported contact with active tuberculosis patients inside prison (adjusted OR = 1.51; 95% CI: 1.05-2.18) and with the use of inhaled drugs (adjusted OR = 1.48; 95% CI: 1.03-2.13; Table 2). The results of the TSTs were negative for all individuals who tested positive for HIV.

Measures of frequency of symptoms suggestive of tuberculosis infection and of tuberculosis disease

At least one of the symptoms suggestive of tuberculosis (cough, weight loss, loss of appetite, and chest pain) were reported by 68.0% of the study population. Cough and weight loss were the most common symptoms, occurring in 27.0% and 25.0% of the participants, respectively. Of those who reported cough, 43.0% had had the symptom for two weeks or more, corresponding to 131 individuals of the total number of prisoners (11.7%). Two cases were diagnosed with tuberculosis, and the strains were susceptible to rifampin, streptomycin, isoniazid, and ethambutol.

DISCUSSION

The magnitude of LTBI within the Brazilian prison system, as previously mentioned, remains mostly unknown. The prevalence observed in this study (25.2%) was higher than those reported for prisons in countries such as the USA (17.0%),[24] Australia

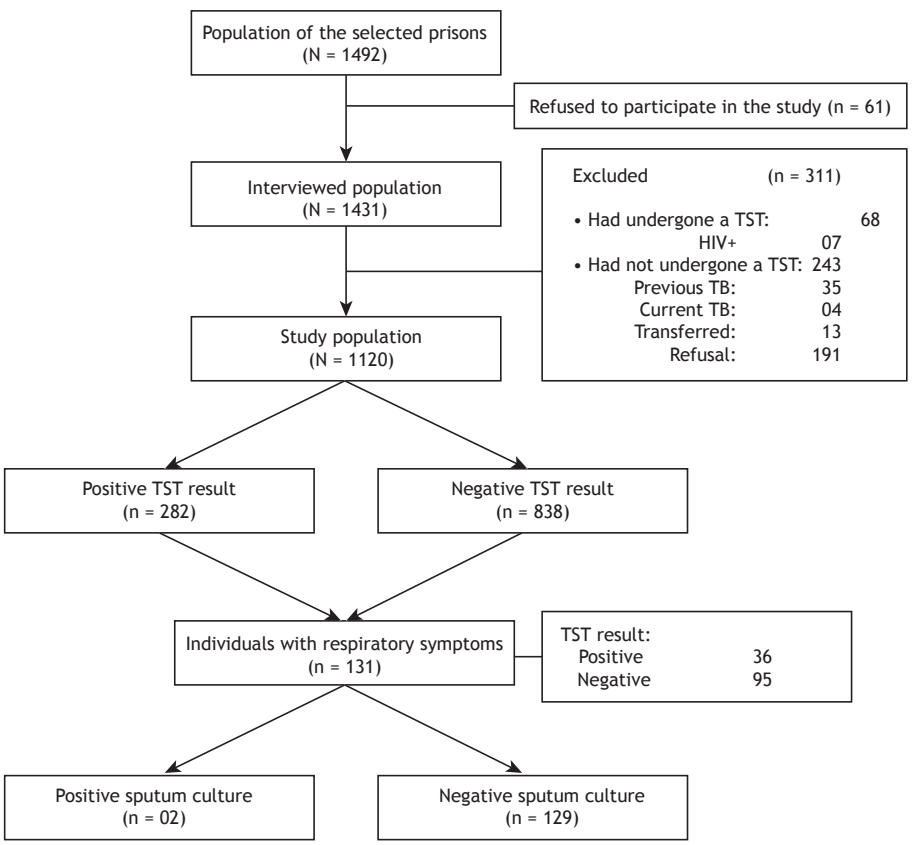

Figure 1. Individuals selected for inclusion in the study, Minas Gerais, 2013 (N = 1,120). TST: tuberculin skin test; and TB: tuberculosis.

Table 1. Descriptive characteristics of the sample of prisoners under study, by gender, Minas Gerais, Brazil, 2013 (N = 1,120).[a]

Characteristics	Gender		p
	Female	Male	
Sociodemographic characteristics			
Age, years			0.165
< 30	53 (53.0)	608 (60.1)	
≥ 30	47 (47.0)	403 (39.9)	
Marital status			< 0.001
Single	80 (80.0)	584 (57.3)	
Married/steady partner	20 (20.0)	436 (40.7)	
Schooling, years			0.089
< 7	85 (85.0)	920 (90.4)	
≥ 7	15 (15.0)	98 (9.6)	
Occupation before incarceration			0.714
Yes	93 (93.0)	938 (92.0)	
No	7 (7.0)	82 (8.0)	
Length of incarceration, months			0.389
≤ 15	55 (55.0)	515 (50.9)	
> 15	45 (45.0)	505 (49.5)	
Behavioral characteristics			
Contact with active TB patients outside prison			< 0.001
Yes	24 (24.0)	83 (8.1)	
No	62 (62.0)	850 (84.1)	
Does not know	14 (14.0)	87 (16.8)	
Contact with active TB patients inside prison			0.054
Yes	7 (7.0)	162 (15.9)	
No	70 (70.0)	754 (73.9)	
Does not know	23 (23.0)	104 (10.2)	
Pre-incarceration alcoholism			0.047
Yes	33 (33.0)	245 (24.0)	
No	67 (67.0)	775 (76.0)	
Smoking			0.203
Yes	67 (67.0)	617 (60.5)	
No	33 (33.0)	403 (39.5)	
Use of inhaled drugs			< 0.001
Yes	49 (49.0)	789 (77.4)	
No	51 (51.0)	231 (22.6)	
Use of injected drugs			0.511
Yes	3 (3.0)	27 (2.6)	
No	97 (97.0)	993 (97.4)	
Health history			
Diabetes mellitus			0.031
Yes	4 (4.4)	9 (1.1)	
No	86 (95.6)	815 (98.9)	
Chronic renal failure			0.027
Yes	3 (3.1)	5 (0.5)	
No	95 (96.9)	1002 (99.5)	
Chronic use of corticosteroids and/or immunosuppressants			0.004
Yes	8 (8.2)	25 (2.4)	
No	89 (91.8)	993 (97.6)	
Presence of at least one symptom suggestive of TB[b]			0.113
Yes	75 (75.0)	686 (67.3)	
No	25 (25.0)	334 (32.7)	
Individuals with respiratory symptoms[c]			0.126
Yes	7 (7.0)	124 (12.2)	
No	93 (93.0)	896 (87.8)	

TB: tuberculosis. [a]Values expressed as n (%). The total number of patients varied according to the amount of ignored information. [b]Cough, expectoration, hemoptysis, dyspnea, chest pain, cyanosis, fever, asthenia, night sweats, recent weight loss, and loss of appetite. [c]Individuals with cough for two weeks or more.

Table 2. Univariate and multivariate analyses of factors associated with latent *Mycobacterium tuberculosis* infection in the study population, Minas Gerais, Brazil, 2014 (N = 1,120).[a]

Factors	LTBI		Univariate analysis		Multivariate analysis*	
	Yes n (%)	No n (%)	p	OR (95% CI)	p	aOR (95% CI)
Sociodemographic factors						
Gender						
Female	26 (26.0)	74 (74.0)	0.843	1	-----	-----
Male	256 (25.1)	764 (77.9)		0.954 (0.597-1.524)		
Age, years						
< 30	166 (25.1)	495 (74.9)	0.934	1	-----	-----
≥ 30	114 (25.3)	336 (74.7)		1.012 (0.768-1.333)		
Marital status						
Married/steady partner	108 (23.7)	348 (76.3)	0.340	1	-----	-----
Single	174 (26.2)	490 (73.8)		1.144 (0.868-1.509)		
Schooling, years						
≥ 7	24 (21.2)	89 (78.8)	0.305	1	-----	-----
< 7	258 (25.7)	747 (74.3)		1.281 (0.798-2.054)		
Occupation before incarceration	260 (25.2)	771 (74.8)	0.917	1	-----	-----
Yes	22 (24.7)	67 (75.3)		0.974 (0.590-1.608)		
No						
Length of incarceration, months	135 (23.7)	435 (76.3)	0.241	1	0.543	1.096 (0.816-1.471)
< 15	147 (26.7)	403 (73.3)		1.175 (0.897-1.540)		
≥ 15						
Behavioral factors						
Contact with active TB patients outside prison	230 (25.2)	682 (74.8)	0.672	1	-----	-----
No	29 (27.1)	78 (72.9)		1.102 (0.702-1.732)		
Yes						
Contact with active TB patients inside prison	193 (23.4)	631 (76.6)	0.030	1	0.026	1.516 (1.052-2.185)
No	53 (31.4)	116 (68.4)		1.494 (1.039-2.147)		
Yes						
Alcoholism						
No	209 (24.8)	633 (75.2)	0.632	1	-----	-----
Yes	73 (26.3)	205 (73.7)		1.079 (0.791-1.470)		
Smoking						
No	98 (22.5)	338 (77.5)	0.097	1	0.207	1.221 (0.896-1.666)
Yes	184 (26.9)	500 (73.1)		1.269 (0.958-1.682)		
Use of inhaled drugs						
No	61 (21.6)	221 (78.4)	0.111	1	0.034	1.483 (1.031-2.133)
Yes	221 (26.4)	617 (73.6)		1.307 (0.940-1.817)		
Use of injected drugs						
No	273 (25.0)	817 (75.0)	0.286	1	0.072	2.249 (0.931-5.430)
Yes	9 (30.0)	21 (70.0)		1.574 (0.684-3.621)		
Health history						
Diabetes mellitus						
No	215 (23.9)	686 (76.1)	0.947	1	-----	-----
Yes	3 (23.1)	10 (76.9)		0.957 (0.261-3.510)		
Chronic renal failure						
No	273 (24.9)	824 (75.1)	0.418	1	-----	-----
Yes	3 (37.5)	5 (62.5)		1.811 (0.430-7.627)		
Use of immunosuppressants						
No	275 (25.4)	807 (74.6)	0.395	1	-----	-----
Yes	6 (18.8)	26 (81.2)		0.677 (0.276-1.663)		
HIV infection						
No	233 (24.9)	702 (75.1)	-----	-----	-----	-----
Yes	0 (0.0)	5 (100.0)				

LTBI: latent *Mycobacterium tuberculosis* infection; TB: tuberculosis; and aOR: adjusted OR. [a]The total number of patients varied according to the amount of ignored information.*Hosmer-Lemeshow test; $\chi^2 = 0.679$; degrees of freedom = 2; p = 0.712.

(14.0%),[25] and Italy (17.9%),[26] and in the state of Mato Grosso do Sul, Brazil (20.8%).[13] However, it was lower than those found in Spain (40.3%)[27] and Switzerland (46.9%),[28] and in other states in Brazil (Bahia, Mato Grosso do Sul, and São Paulo; range, 30.9-61.5%).[29-31] These differences highlight the need for studying LTBI in different regions. There have been no studies showing the prevalence of LTBI in the region where the prisons selected for this study are located. In addition, the results of the present study are important not only to Minas Gerais, but also to other regions in Brazil where the prisons have the same scenarios.

Although there has been considerable debate about the use of the TST in places where there is mass vaccination with BCG, the WHO suggests the use of this test to detect LTBI in places where the TST is recommended, especially in adults. In the present study, 89.2% of the participants had been vaccinated more than 10 years prior (mean, 30 years). Therefore, BCG vaccination probably contributed little to TST positivity, because the response to the TST is nearly nonexistent 8-10 years after vaccination.[32,33] The TST may yield false-negative results in people who live with HIV and are not receiving antiretroviral therapy, because the response to the TST is based on the immune response of the individual[14]; this is probably the reason why LTBI was not identified in the prisoners recently diagnosed with HIV infection.

Several factors create a favorable context for increasing the prevalence of LTBI in prisoners.[11,30,34] As discussed, this population consists predominantly of young adults from socioeconomically disadvantaged communities with high rates of active tuberculosis. Among other elements posing an increased risk for the development of tuberculosis, the rate of alcoholism (24.8%) was lower than that reported in other studies (39.2-44.1%),[30] whereas the rate of smoking (61.1%) was similar.[30] The use of inhaled illicit drugs (97.0%) was higher than that reported by other authors (25.2-45.2%), whereas the use of injected illicit drugs (2.0%) was lower (7.5-13.1%).[27]

The rate of HIV infection found in our study sample (0.5%) was similar to the mean estimated rate for the Brazilian population (0.4%)[35]; however, it was lower than those reported by other authors (1.0-11.3%).[18,27,34,36] Therefore, it is important to detect LTBI in the HIV-infected population so that preventive measures can be taken, because HIV-infected individuals with LTBI have an 8.0-10.0% annual risk of developing active tuberculosis, as do users of inhaled illicit drugs with LTBI. In contrast, HIV-uninfected individuals with LTBI have a 10.0% lifetime risk of developing tuberculosis.[18,37]

In the prisons selected for this study, treatment of LTBI was not given to prisoners with diabetes mellitus, those with chronic renal failure, or those receiving immunosuppressants, although preventive therapy is recommended for these groups, which are considered at high risk for developing tuberculosis.[6,9,14]

Chief among the conditions of the prison environment that can favor the spread of the disease are limited exposure to sunlight,[5,6] overpopulation,[5,6,8,18,30,34] and inadequate ventilation.[5,6,30] To this context, we can add lack of training in tuberculosis control activities among prison health teams[5] and limited access to health care in prisons.[30,34] Therefore, changes should be made to the physical structures of prisons, and training in tuberculosis control should be provided to prison health teams.

In the present study, the likelihood of LTBI was found to be increased when the prisoners reported contact with someone with tuberculosis disease, a finding that has also been observed by several authors.[3,13,34] This might indicate an increased perception by the prisoners of the health risk related to the disease, since there is a high frequency of tuberculosis in the environment.[38] There was an association between the use of inhaled illicit drugs and LTBI, but no association was found between smoking and LTBI; the use of inhaled illicit drugs probably leads to greater tissue damage and greater impairment of mucociliary activity, which is the body's first line of protection when the bacilli enter the airways.[39]

The expected rate of individuals with RS in Brazil is 1.0% in the general population.[6] Among the prisoners included in this study, the proportion of individuals with RS was found to be 11.7-fold higher than that in the general population; however, it was lower than those reported in other studies conducted in Brazil (20.6-36.1%).[13,30,34] This can be explained by the poor infrastructural conditions in the prisons and by the high rates of smoking and use of inhaled illicit drugs.

There is no consensus in the scientific literature regarding an ideal mechanism for identification of people who are more likely to develop tuberculosis among prisoners.[5,6,9,15,16] However, the identification of chronic cough is used as a screening tool.[15,16,36] Some authors have reported that this symptom alone is not relevant to raising a suspicion of tuberculosis in this population.[38] Surveillance for cases of pulmonary tuberculosis should preferably include a combination of symptoms (fever, weight loss, and asthenia, for instance) rather than consider chronic cough alone.[30,40] The symptom approach is the only screening tool available in most resource-poor settings.[5,6,8,15-18] In addition, symptoms suggestive of tuberculosis may be nonspecific where there are high rates of other conditions associated with respiratory diseases, such as smoking.[8]

Minas Gerais, despite having the second largest overall population in the country, has the fourth lowest incidence rate of tuberculosis. It is possible that the prevalence rates of LTBI and active tuberculosis for the prisons selected for this study are not as high as those reported for other prisons because of the local epidemiological context.

One of the limitations of the present study is the fact that data on exposure and outcome were collected at the same time, which makes it difficult to understand

the temporal relationship between them and provides a static view of the dimension of the problem. Another limitation was that the incidence rates of LTBI and tuberculosis disease were not evaluated.

In conclusion, the prevalence of LTBI was high among the prisoners of the two largest prisons in Minas Gerais, as well as being associated with self-reported contact with active tuberculosis patients inside prison and with the use of inhaled drugs. Our findings demonstrate that it is necessary to improve the conditions in prisons, as well as to introduce strategies, such as chest X-ray screening, in order to detect tuberculosis cases and, consequently, reduce *M. tuberculosis* infection within the prison system.

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