

Original Article

Risk factors associated with drug-resistant tuberculosis in prisons in São Paulo State, Brazil (2006-2016)

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Abstract

Introduction: Prisons are high-risk settings for drug-resistant tuberculosis because the prevalence of the tuberculosis (TB) is much higher than in the general population. This study investigated the factors associated with drug-resistant tuberculosis in prisons in the state of São Paulo, Brazil.

Methodology: Retrospective cohort of drug-resistant TB cases for incarcerated people in São Paulo state, reported in the Tuberculosis Patient Control System between 2006 and 2016. To analyze the factors associated with drug-resistant TB, the backward method (likelihood ratio) was used, determining the adjusted odds ratio and respective 95%CI coefficients. Multiple models were proposed to adjust for potential confusion and interaction. The best fit model was selected based on the lowest Akaike information criterion coefficient.

Results: In total, 473 drug-resistant tuberculosis cases were reported in the prison population of São Paulo state, the majority were male. The cases that presented negative results for sputum smear and sputum culture had, respectively, an aOR=0.6 and aOR=0.16 for drug-resistant tuberculosis in relation to the cases with positive results. The cases where the patient had AIDS and reported alcoholism, respectively, an aOR=1.47 and aOR=1.60 for drug-resistant TB. Individuals with a background treatment history for TB presented a stronger association with drug-resistant tuberculosis, aOR=35.08.

Conclusions: Sputum smear, sputum culture, chest X-ray, AIDS, alcoholism and background treatment history for TB were factors associated with resistance to antituberculosis drugs among prisoners. This is useful for the implementation of disease control measures related to the detection and monitoring of cases in the prison system.

Key words: Tuberculosis drug-resistant; tuberculosis multidrug-resistant; prisons; tuberculosis control.

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Introduction

Drug-resistant tuberculosis (DR-TB) remains a public health threat worldwide. According to World Health Organization (WHO) estimates, in 2018 there were about 500,000 new cases of drug-resistant tuberculosis. Among new tuberculosis (TB) cases, which account for most of the global TB burden, an estimated 4.1% have multidrug/rifampicin-resistant tuberculosis (MDR/RR-TB). The proportion is higher among people previously treated for TB, at 19% [1].

Brazil ranks 20th on the list of 30 priority countries for TB, according to the WHO ranking (2016-2020). In 2016, 1,044 cases of drug-resistant TB were reported, 700 of which were new cases and 344 cases were repeat treatments [2]. One of the challenges in controlling

these cases is the high incidence of TB in vulnerable populations, including the people incarcerated in prisons.

Prisons are high-risk settings for TB because the prevalence of the disease is much higher than in the general population, regardless of it being a high- or low-income country [3,4]. A report in Russia showed that the prevalence of drug resistance in new cases in prisons ranged from 7.2% to 38% [5]. In the largest prison in Dhaka, Bangladesh, resistance to isoniazid and rifampicin was 11.4% and 0.8%, respectively [6].

In Brazil, the prevalence of DR-TB among prisoners was not evaluated systematically, but a survey conducted in the state of Rio de Janeiro showed a MDR-TB rate of 1.5% [7], and surveys conducted in different

prisons in the south of the country showed a mono-resistance rate of 8% and 15% [8].

The country had 726,354 people detained in prisons in 2017, the third largest incarcerated population in the world, only behind the United States and China. In relation to the total number of beds available in the prison system, there is a deficit of more than 303,000 beds, with an average occupation rate of 171.62% in the prisons [9]. In Latin American countries with serious socio-political and economic problems, the penitentiary system becomes an indispensable object of intervention, as this system mostly affects economically and socially disadvantaged populations [10].

In this context, there is a high prevalence of transmissible diseases like TB, with improper management of the disease becoming a risk factor for the development of drug-resistant strains and disease transmission in the community [11,12].

A systematic review of the literature showed that cases of TB with previous treatment had a higher prevalence of MDR-TB than new cases of the disease in prisons in countries that were part of the former Soviet Union [13].

Another study conducted in Samara, Russia, found high rates of resistance to first-line drugs among prisoners. The factors associated with drug resistance were background treatment of TB for more than four weeks, smoking (resistance to isoniazid), presence of cavitation in the chest X-ray, and prison [5].

Although understanding the factors associated with drug-resistant TB among prisoners is a relevant object for TB surveillance activities in prisons, in Brazil, there are still few studies focusing on this aspect. Thus, we sought to investigate the factors associated with drug-resistant TB in prisons in the state of São Paulo, Brazil.

Methodology

This is a retrospective cohort study of cases of sensitive and drug-resistant TB in the São Paulo state's prisons. The state of São Paulo is one of 27 federal units in Brazil, located in the Southeast of the country. It has a population of approximately 45 million people distributed across 645 cities, representing 22% of the Brazilian population [14].

The current structure of the prison system in the state of São Paulo is composed of 175 units distributed into five regions: Capital and Greater São Paulo, Vale do Paraíba and Litoral, Central, Northwest and West [15].

The imprisonment rate of the state is 52% higher than the national average, with 536.5 prisoners per 100,000 inhabitants. In the period from 2008 to 2018,

the number of prisoners in the state grew 59% (from 144,425 to 229,556 prisoners) [15].

The cases included in the study were who has been diagnosed as TB-sensitive or bacteriologically confirmed with MDR-TB or RR-TB from January 1, 2006 to December 31, 2016, which was classified as "prisoner" in the "address type" field of the notification form. These cases were obtained through the Tuberculosis Patient Control System (TBWEB) [16], a specific information system in São Paulo state created to the notification of tuberculosis.

The State of São Paulo has its own system for computing information about TB since the 1990s. The State has launched its database even after the national implementation of the Sistema Nacional de Agravos de Notificação Compulsória (National System of Compulsory Notification of Diseases - SINAN) in 1998, access to TBWEB is restricted to professionals responsible for the epidemiological surveillance in the municipality [17].

In the exploratory approach of the database, duplicates were removed, considering the person's name, mother's name, and date of birth. Cases without information regarding the type of resistance and bacteriological confirmation were excluded. In drug-resistant TB cases, the first notification of drug resistance was considered and, in non-resistant TB cases, the most recent notification in the system.

For the study, the following variables were considered: gender (male; female); age group (in years: ≤ 39 ; 40 to 59; 60 and more); education level (< 8 years; ≥ 8 years); race (white; non-white); occupation rate/geographical region of the prison units ($\leq 190\%$; $> 190\%$); clinical form (pulmonary; extrapulmonary); type of screening (active case finding; no active case finding); result of sputum smear culture (positive; negative; not executed); chest X-ray (cavitary; non-cavitary; normal; not executed); HIV serology result (positive; negative; not executed); presence/absence of Acquired Immunodeficiency Syndrome (AIDS), diabetes (type I; type II), illicit drug use, smoking and alcoholism; type of treatment (supervised; self-administered). There was more than one treatment record of the same individual in the study period to determine the presence/absence of previous treatment for TB.

A descriptive analysis of the sociodemographic, clinical and epidemiological characteristics of cases of non-resistant TB and DR-TB among prisoners was carried out in order to characterize the study population by means of absolute and relative frequency

distribution. This analysis was performed in SPSS, version 20.0 (IBM Corp., Armonk, United States).

To analyze the factors associated with drug-resistant TB, the variables were submitted to univariate analysis, calculating the association between the odds ratio (OR) and the respective 95% confidence interval (95% CI), taking as a reference the cases of non-resistant TB of prisoners and, as independent variables, the individual information from the cases reported during the study period.

The variables with $p < 0.20$ in the hypothesis test were selected for inclusion in the multiple regression model and then the backward method (likelihood ratio) was used to select the variables for the best explanatory model, determining their adjusted odds ratio (aOR) and their respective 95%CI values. The absence of multicollinearity among the variables was verified to be a prerequisite. Multiple models were proposed to adjust for potential confusion and interaction. The model with the lowest Akaike information criterion (AIC) was selected [18].

To check the accuracy of the final model and check for significant differences between the classifications of the model and what was observed, we adopted the Hosmer-Lemeshow test ($p > 0.05$) and the area under the receiver operating characteristics curve (ROC) [18,19]. The level of significance of each coefficient in

the model was measured using Wald's test. The pseudo determination coefficient (McFadden's R^2) was calculated to verify the extent to which (%) the set of independent variables belonging to the final model explain the drug-resistant TB outcome. These analyses were performed using the statistical software R version 3.6.0.

This study was approved by the Research Ethics Committee of the Ribeirão Preto College of Nursing, with Ethical Appreciation Certificate (CAAE) 99807018.3.0000.5393.

Results

Between January 2006 and December 2016, 17,187 TB cases were reported in the incarcerated population of São Paulo state. Of this total, 217 (1.3%) were excluded due to lack of information on the type of resistance and bacteriological confirmation, and 16,970 TB cases were confirmed, among which 473 cases of DR-TB were confirmed in the prison system of the state of São Paulo, 2.7% of all TB cases, as presented in Figure 1.

Among the cases of DR-TB, the majority were male ($n = 462$; 97.7%). The most affected age group was ≤ 39 years ($n = 293$; 61.9%). Those non-white race were predominant ($n = 194$; 41.0%) and the majority had less than eight years of education level ($n = 234$; 49.5%), as shown in Table 1.

Regarding the occupation rate, most cases ($n = 298$; 63%) were reported in the prison units of the Capital and Greater São Paulo, Central and Northwest of the state, with an occupation rate of over 190%. The predominant clinical form was pulmonary TB ($n = 472$;

Figure 1. Flowchart of reported tuberculosis cases in prisons in São Paulo State, Brazil, 2006-2016.

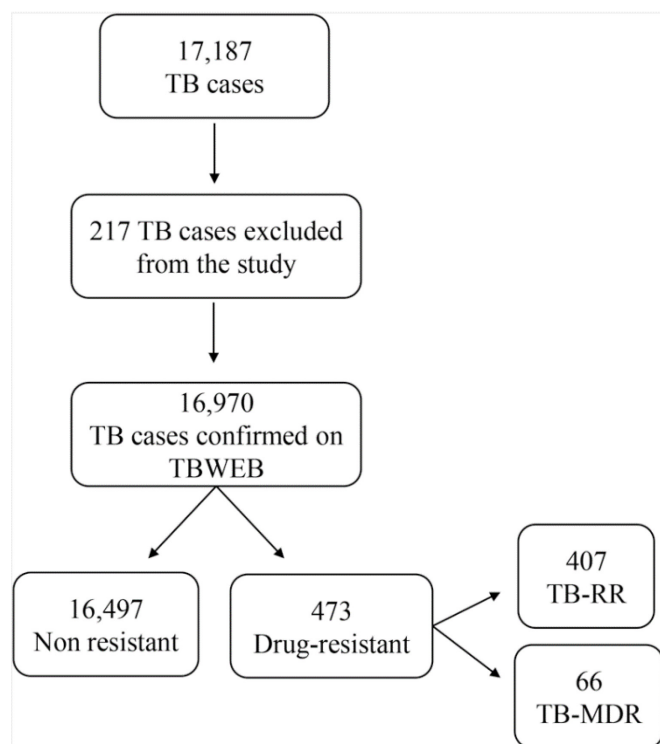


Table 1. Sociodemographic characteristics of drug-resistant tuberculosis cases in the prisons of São Paulo State, Brazil, 2006-2016. ($n = 473$).

Characteristics	Drug-resistant TB cases n (%)
Sex	
Male	462 (97.7)
Female	11 (2.3)
Age group (years)	
≤ 39	293 (61.9)
40-59	168 (35.5)
≥ 60	10 (2.1)
Not given	2 (0.5)
Race	
White	187 (39.5)
Non-White	194 (41.0)
Not given	92 (19.5)
Education level (years)	
< 8	234 (49.5)
≥ 8	118 (24.9)
No information	121 (25.6)

99.8%); the type of screening in most cases was no active case finding (n = 306; 64.7%). At the time of diagnosis, there was a predominance of positive results for sputum smear and sputum culture. A chest X-ray was not executed in most cases (n = 320; 67.6%) and HIV serology was not executed in 52 (11.0%) cases (Table 2).

Table 2. Clinical-epidemiological characteristics of drug-resistant tuberculosis cases in prisons of São Paulo State, Brazil, 2006-2016. (n = 473).

Variables	Drug-resistant TB cases n (%)
Occupation rate/regions of prison units	
≤190%	175 (37.0)
>190%	298 (63.0)
Clinical form	
Pulmonary	472 (99.8)
Extrapulmonary	1 (0.2)
Type of screening	
Active case finding	146 (30.9)
No active case finding	306 (64.7)
No information	21 (4.4)
Sputum smear	
Positive	324 (68.5)
Negative	127 (26.8)
Not executed	22 (4.7)
Sputum culture	
Positive	437 (92.4)
Negative	36 (7.6)
Chest x-ray	
Cavitary	89 (18.8)
Non-cavitary	49 (10.3)
Normal	15 (3.2)
Not executed	320 (67.7)
HIV serology	
Positive	48 (10.2)
Negative	373 (78.8)
Not executed	52 (11.0)
AIDS	
Yes	46 (9.7)
No	427 (90.3)
Diabetes	
Yes	6 (1.3)
No	467 (98.7)
Alcoholism	
Yes	48 (10.1)
No	425 (89.9)
Illegal drugs use	
Yes	88 (18.6)
No	385 (81.4)
Smoking	
Yes	33 (6.9)
No	440 (93.1)
Treatment type	
Supervised	406 (85.8)
Self-administered	67 (14.2)
Treatment background	
Yes	105 (22.2)
No	368 (77.8)

The most frequent comorbidities among DR-TB cases were illicit drug use (n = 88; 18.6%), alcoholism (n = 48; 10.1%), AIDS (n = 46; 9.7%), smoking (n = 33; 6.9%) and diabetes (n = 6; 1.3%). The directly observed treatment (DOT) method was utilized for most of the DR-TB cases (n = 406; 85.8%). A background treatment history for TB was identified in 105 (22.2%) cases (Table 2).

The best fit predictive model with the lowest AIC for DR-TB in the prison system was model 3, as shown in Table 3.

The regression model for DR-TB presented an area under the ROC curve corresponding to 0.79 (95% CI = 0.77-0.81), which represents satisfactory discriminatory power. Moreover, the diagnosis of the final model by performing the tests indicated good fit and no violation of assumptions, according to indices shown in Table 4.

Sputum smear, sputum culture, chest X-ray, AIDS, alcoholism and background treatment history for TB were factors associated with resistance to antituberculosis drugs after adjusted analysis for the variables included in the multiple regression model. On the other hand, occupation rate, clinical form, illicit drug use and type of treatment were no longer significant predictions of drug-resistant TB among prisoners after adjustment of the multiple model, as presented in Table 4.

At the time of diagnosis, the cases that presented negative results for sputum smear and sputum culture had, respectively, an aOR = 0.65 (95% CI = 0.52-0.82) and aOR = 0.16 (95% CI = 0.10-0.26) for drug-resistant TB in relation to the cases with positive results. For chest X-rays, suspected cases without cavity and cases that did not perform the exam showed aOR = 0.19 (95% CI = 0.13-0.28) and aOR = 0.31 (95% CI = 0.23-0.41), compared to suspected cases with cavity.

Cases where the patient had AIDS and reported alcoholism presented, respectively, an aOR of 1.47 (95% CI = 1.03-2.05) and aOR of 1.60 (95% CI = 1.07-2.35) for drug-resistant TB. Individuals with a background treatment history for TB presented a stronger association with the outcome (drug-resistant TB), aOR of 35.08 (95% CI = 25.80-47.74), as shown in Table 4.

Discussion

The study revealed evidence of the association of DR-TB among prisoners with diagnostic tests for suspicion and confirmation of cases (sputum smear, sputum culture and chest X-ray), comorbidities such as

Table 3. Predictive models proposed for drug-resistant tuberculosis in the prisons of São Paulo State, Brazil, 2006-2016.

Models	Explanatory variables	AIC*
Complete	Race, age group, education level, occupation rate/regions of prison units, clinical form, sputum smear, sputum culture, chest x-ray, HIV serology, AIDS, alcoholism, illegal drugs use, treatment type and treatment background	3,549.9
1	Race, age group, education level, occupation rate/regions of prison units, clinical form, sputum smear, sputum culture, chest x-ray, AIDS, alcoholism, illegal drugs use, treatment type and treatment background	3,546.2
2	Age group, occupation rate/regions of prison units, clinical form, sputum smear, sputum culture, chest x-ray, AIDS, alcoholism, illegal drugs use, treatment type and treatment background	3,543.6
3	Occupation rate/regions of prison units, clinical form, sputum smear, sputum culture, chest x-ray, AIDS, alcoholism, illegal drugs use, treatment type and treatment background	3,538.8

*Akaike information criterion.

AIDS and alcoholism, as well as background treatment history for TB.

During the study period, 473 cases of DR-TB were confirmed in the prison system of the state of São Paulo, 2.7% of all TB cases. A study of TB surveillance in prisons in the European region showed a high level of drug-resistant TB among prisoners, with a predominance of cases in Estonia, corresponding to 50% of all cases, which the authors highlight as a warning to review the strategies for disease control in prisons [20].

Sánchez *et al.* [21], when comparing the sociodemographic characteristics of TB cases from different prison units in the state of Rio de Janeiro, showed a young population with a low level of education, similar to the profile found in this study.

Authors point out that the low level of education (less than eight years of study) has been associated with a higher risk of treatment abandonment during the treatment of DR-TB, and this, in turn, is associated with a set of precarious socioeconomic conditions [22].

In Brazil, the National Program for Tuberculosis Control recommends that the health and surveillance teams that operate in the prison system detect new cases of TB through spontaneous demand, based on the questioning of the presence of cough upon entry into the prison system, active systematic search, treatment supervision and raising awareness of the disease among prisoners [23].

The active case-finding in prison units in Brazil must take place at the time of entry and through mass screening, at least once a year, prioritizing prison units with the highest incidences of TB. Two methods can be

Table 4. Determinants associated with drug-resistant tuberculosis in the prisons of São Paulo State, Brazil, 2006-2016.

Explanatory variables	Univariate analysis			Multiple regression			
	OR	95% CI	p-value*	aOR	95% CI	p-value**	
Occupation rate/regions of prison units	≤ 190%	0.79	0.65-0.96	0.018	0.86	0.70-1.06	0.180
	> 190%	1					
Clinical form	Pulmonary	1					
	Extrapulmonary	0.10	0.06-0.45	0.023	0.25	0.01-1.39	0.208
Sputum smear	Positive	1					
	Negative	0.88	0.71-1.08	0.232	0.65	0.52-0.82	<0.001
Sputum culture	Not executed	0.63	0.39-0.95	0.039	0.64	0.39-1.00	0.059
	Positive	1					
Chest x-ray	Negative	0.19	0.12-0.29	< 0.001	0.16	0.10-0.26	< 0.001
	Cavitary	1					
Aids	Non-cavitary	0.17	0.12-0.24	< 0.001	0.19	0.13-0.28	< 0.001
	Normal	0.62	0.34-1.05	0.098	0.52	0.27-0.95	0.042
Alcoholism	Not executed	0.34	0.27-0.44	< 0.001	0.31	0.23-0.41	< 0.001
	Yes	1.54	1.11-2.08	0.005	1.47	1.03-2.05	0.027
Illegal drugs use	No	1					
	Yes	1.96	1.42-2.63	< 0.001	1.60	1.07-2.35	0.019
Treatment type	No	1					
	Yes	1.42	1.12-1.79	0.003	0.99	0.73-1.34	0.991
Treatment background	Supervised	1					
	Self-administered	0.76	0.58-0.99	0.048	0.91	0.67-1.21	0.547
	Yes	39.94	30.08-53.01	< 0.001	35.08	25.80-47.74	< 0.001
	No	1					

* Significance level: < 0.20; ** Significance level: < 0.05; ROC curve = 0.79 (95% CI = 0.77-0.81); Pseudo R² (McFadden R²) = 17%; Wald = 51.1 and *p* < 0.001; Hosmer-Lemeshow = 4.1 and *p* = 0.85.

used to select, in a systematic way, such as: individually interviewing the entire incarcerated population about the presence of cough (of any length) and / or HIV infection or history of previous treatment; subject prisoners to an X-ray examination, regardless of the existence of symptoms [23].

Among resistant cases, 64.7% were identified through strategies such as outpatient demand, urgent/emergency care and hospitalization, defined for the study as "no active case search". It was also observed that, in most cases, chest X-rays were not performed and 11% of the cases did not collect serology for HIV.

Chest X-ray (CXR) is an important tool for TB triaging and screening; it is also a useful aid in TB diagnosis [24]. Studies indicate greater sensitivity in detecting TB cases of radiological screening in prisons [25,26]. However, the availability of equipment and professionals for this purpose is not a reality for most prisons [27].

This finding is related to the data of our study, in which the majority of the prison units do not have equipment to perform screening by image examination, and the only option would be the mobilization of a large number of prisoners to a health service to perform radiological examination, which is an obstacle that is difficult to overcome.

Although, HIV testing is recommended, preferably the gene expert test (RT) for all incarcerated population diagnosed with tuberculosis [23], 11% of the cases in the study did not perform the test, which may be associated with operational difficulties in prisons with overcrowding, as well as trained health professionals. Thus, it is necessary to strengthen and implement measures aimed at early detection and control of the disease, appropriate to the reality of prison units in the country.

Studies indicate that TB control strategies in prison units in Brazil are essentially of a biomedical nature and that the form of discovery occurs upon spontaneous demand when people incarcerated voluntarily seek medical care with acute symptoms of the disease, which reveals weaknesses in case-screening and monitoring, as well as a possible increase in DR-TB in these scenarios [28,29].

Regarding diagnostic tests such as sputum smear, sputum culture and chest X-ray, when the results were positive for sputum smear and sputum culture and there was suspicion of cavities in the chest X-ray, there was an increased chance of drug-resistant TB cases in people incarcerated, which may be related to the higher degree of infectivity and bacillary load with positive

bacteriological tests and the emergence of cavitory processes in the lungs [30].

The most common diagnostic tests for pulmonary TB are bacilloscopy and sputum culture. Bacilloscopy is more used for being simple, fast, and low-cost; however, its sensitivity is low, allows detect 60% to 80% of pulmonary TB cases in adults. Recommendation from Ministry of Health reinforces the need to collect two samples: one in the first visit to the health service and the other in the following morning, regardless of the outcome of the first [23].

On the other hand, sputum culture, both in solid medium (Löwenstein-Jensen and Ogawa-Kudoh) and liquid medium (MGIT – mycobacteria growth indicator tube), is considered the standard diagnostic test, as it detects 70 to 90% of cases, and has virtually 100% specificity. In positive cases, the minimum time for diagnosis is approximately 14 days. In negative cases – when no colonies grow –, the observation period can reach 60 days (incubation period of the microorganism) [23].

Another factor associated with DR-TB among prisoners was alcoholism. A study of the border regions of Brazil, Paraguay and Bolivia identified that individuals with a history of alcoholism represented a 2.1 times greater chance of developing any pattern of resistance, compared to those without alcohol dependence [31]. Although there is not enough evidence to explain this association, research points to alcoholism as a factor associated with the failure of TB treatment, which may explain the greater chance of developing resistance patterns for the disease [32,33].

The association between DR-TB and cases of AIDS identified in the study emerges as a great challenge in confronting and controlling TB/HIV co-infection in incarcerated population. Although different studies [34,35] point out conflicting data on this association in the literature, a systematic review and meta-analysis showed consistent evidence of association and increased risk of MDR-TB among people living with HIV [36].

For this finding, one should consider the rapid progression of the disease in places where drug-resistant TB is prevalent with a higher probability of exposure to drug-resistant *M. tuberculosis* in overcrowded and unhealthy environments, such as prisons [37]. In addition, the malabsorption of drugs, especially rifampicin and etambutol has led to treatment failure in people co-infected with HIV [38].

We have found association between DR-TB and cases with a history of previous treatment for TB. There is a consensus in the world literature that this is a risk

factor for resistance to antituberculosis drugs in prison and even beyond this environment [7,39,40]. In two investigations carried out in prisons in countries of the former Soviet Union, individuals with MDR-TB had five times greater chance of failure during their prior treatment [4,41].

Based on this evidence, the need for effective measures to control the disease in this population is revealed, ensuring adequate medication dosage, use of effective drugs, individual-centered care, improvement in the quality of care and access to drug sensitivity testing. The authors acknowledge that the lack of resources and the presence of operational difficulties have revealed failures in the implementation of case tracking and monitoring strategies in the prison system, which they consider a great challenge for the control of DR-TB [26,42].

In the prisons of Malawi, in east Africa, the best results of progress toward TB control have been evidenced by the effective implementation of active case-finding, Directly Observed Treatment Short-Course (DOTS) strategy, integration of a national TB control strategy with prison health services, qualification of laboratory services, proper inmate screening and isolation, awareness of the disease and the political commitment of the government [43].

The control of TB in prison units follows the general recommendations of the Brazilian Ministry of Health in the prison context. In order to detect cases in this overpopulated environment, it is essential to identify and treat TB cases as quickly as possible, it is then recommended: Passive search based on the spontaneous demand of prisoners, the team investigates the disease; Active search for respiratory symptoms (at the time of entry and mass tracking) [23].

Due to its high accuracy, the Rapid Molecular Test for Tuberculosis (RMT-TB) is the recommended diagnostic test for all incarcerated people with symptoms suggestive of TB, replacing sputum smear microscopy, considering the high frequency of multidrug-resistant forms in this population, culture and the sensitivity test should be performed on the identified respiratory symptoms, in addition to sputum smear microscopy or RMT-TB.

The treatment of TB for prisoners should be Directly Observed and performed exclusively by health professionals, including monthly consultations and regular weight measurement, which may indicate adjustment of medications, in addition to requesting bacilloscopy for control [23]. Unfortunately, this strategies mentioned above are not or only partially applied in developing countries.

Although continued vigilance and prompt investigation of all inmates and staff with suspicious symptoms are called for at all times in a setting with both high TB prevalence and unfavorable environmental factors.

It should be highlighted that this study comes with limitations, such as the use of secondary data from the prison units of São Paulo state, which are not standardized and were not developed for research purposes. This could clarify the reasons that made the individuals involved present their treatment background and the healthcare structure at the investigated units. In addition, there may be cases of underreporting, mainly due to the difficulty diagnosing DR-TB among prisoners.

Conclusions

The study presents evidence regarding the factors associated with DR-TB in persons deprived of their freedom. This is useful for the implementation of disease control measures related to the detection and monitoring of cases in the prison system. Confinement results in the rapid progression of the bacillus and increases treatment costs, directly affecting the Brazilian national health system. Finally, the approach used illustrates the need for further research to understand a singular context in which the access to health should be a priority.

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Authors' contributions

JAC, LHA, ACVR and FLS analyzed the data and drafted the manuscript. TZB, ATIB, LLLS, YMA and MY led the study design. ARS, HLP, FPM, ICP and PFP revised the manuscript critically for important intellectual content. RAA participated in the coordination of data collection and critical review of the manuscript. All authors read and approved the final manuscript.

References

1. World Health Organization (WHO) (2019) Global tuberculosis report. Available: https://www.who.int/tb/publications/global_report/en/. Accessed: 20 February 2020.

2. Brazil. Ministry of Health (2017) Tuberculosis epidemiological bulletin. Brasília (DF): MH. Available: <https://antigo.saude.gov.br/images/pdf/2017/marco/23/2017-V-48-N-8-Indicadores-priorit-rios-para-o-monitoramento-do-Plano-Nacional-pelo-Fim-da-Tuberculose-como-Problema-de-Sa-de-P-blica-no-Brasil.pdf>. Accessed: 15 February 2020. [Article in Portuguese]
3. Balabanova Y, Drobniewski F, Fedorin I, Zakharova S, Nikolayevskyy V, Atun R, Coker R (2006) The Directly Observed Therapy Short-Course (DOTS) strategy in Samara Oblast, Russian Federation. *Respir Res* 7: 44.
4. Biadlegne F, Rodloff AC, Sack U (2015) Review of the prevalence and drug resistance of tuberculosis in prisons: a hidden epidemic. *Epidemiol. Infect* 143: 887-900.
5. Ruddy M, Balabanova Y, Graham C, Fedorin I, Malomanova N, Gusarova G, Zakharova S, Melentyev SA, Krukova E, Golishevskaya V, Erokhin V, Dorozhkova I, Drobniewski F (2005) Rates of drug resistance and risk factor analysis in civilian and prison patients with tuberculosis in Samara Region, Russia. *Thorax* 60: 130-135.
6. Banu S, Hossain A, Uddin MKM, Uddin MR, Ahmed T, Khatun R, Mahmud AM, Hyder KA, Lutfor AB, Karim MS, Zaman K, Khan MAI, Barua PC, Luby SP (2010) Pulmonary tuberculosis and drug resistance in Dhaka Central Jail, the largest prison in Bangladesh. *PLoS ONE* 5: e10759.
7. Sánchez A, Larouzé B (2016) Tuberculosis control in prisons, from research to action: the Rio de Janeiro, Brazil, experience. *Cien Saude Colet* 21: 2071-2080. [Article in Portuguese]
8. Valença MS, Scaini JL, Abileira FS, Gonçalves CV, Von Groll A, Silva PE (2015) Prevalence of tuberculosis in prisons: risk factors and molecular epidemiology. *Int J Tuberc Lung Dis* 19: 1182-1187.
9. Brazil. Ministry of Justice (2017) National survey of penitentiary information. Brasília (DF): MJ; Available: <https://www.gov.br/depem/pt-br/sisdepem/mais-informacoes/relatorios-infopen/relatorios-sinteticos/infopen-jun-2017.pdf> Accessed: 15 February 2020. [Article in Portuguese]
10. Filho MMS, Bueno PMMG (2016) Demography, vulnerabilities and right to health to Brazilian prison population. *Cien Saude Colet* 21: 1999-1201. [Article in Portuguese]
11. Telislinghe L, Fielding KL, Malden JL, Hanifa Y, Churchyard GJ, Grant AD, Charalambous S (2014) High tuberculosis prevalence in a South African prison: the need for routine tuberculosis screening. *PLoS ONE* 9: e87262.
12. Warren JL, Grandjean L, Moore DAJ, Lithgow A, Coronel J, Sheen P, Zelner JL, Andrews JR, Cohen T (2018) Investigating spillover of multidrug-resistant tuberculosis from a prison: a spatial and molecular epidemiological analysis. *BMC Med* 16: 122.
13. Droznin M, Johnson A, Johnson AM (2017) Multidrug resistant tuberculosis in prisons located in former Soviet countries: a systematic review. *PLoS ONE* 12: e0174373.
14. Brazil. Brazilian Institute of Geography and Statistics (IBGE) (2011) 2010 demographic census information base: universe results by census sector. Available: https://www.ipea.gov.br/redeipea/images/pdfs/base_de_informacoess_por_setor_censitario_universo_censo_2010.pdf . Accessed: 20 February 2020. [Article in Portuguese]
15. São Paulo. Secretary of Penitentiary Administration (2019) Prison units. Available: <http://www.sap.sp.gov.br/>. Accessed: 15 January 2019. [Available in Portuguese]
16. Secretariat of Health of the State of São Paulo. Tuberculosis Patient Control System (TBWEB). Available: <http://www.cvetb.saude.sp/tbweb/sistema.jsp>. Accessed: 20 January 2018. [Available in Portuguese].
17. Galesi VMN (2007) Data on tuberculosis in the state of São Paulo, Brazil. *Rev Saude Publica* 41 Supl 1: 121. [Article in Portuguese]
18. Hosmer DW, Lemeshow S, Sturdivant RX (2013) Applied logistic regression, 3rd edition. Hoboken, New Jersey: Wiley 528 p.
19. Šimundić AM (2009). Measures of diagnostic accuracy: basic definitions. *EJICC* 19: 203-211.
20. Aerts A, Hauer B, Wanlin M, Veen J (2006) Tuberculosis and tuberculosis control in European prisons. *Int J Tuberc Lung Dis* 10: 1215-1223.
21. Sánchez AR, Massari V, Gerhardt G, Barreto AW, Cesconi V, Pires J, Espinola AB, Biondi E, Larouzé B, Camacho LAB (2007) Tuberculosis in Rio de Janeiro prisons, Brazil: an urgent public health problem. *Cad Saude Publica* 23: 545-552. [Article in Portuguese]
22. Viana PVS, Redner P, Ramos JP (2018) Factors associated with loss to follow-up and death in cases of drug-resistant tuberculosis (DR-TB) treated at a reference center in Rio de Janeiro, Brazil. *Cad Saude Publica* 34: e00048217. [Article in Portuguese]
23. Brazil Ministry of Health (2019) Guidelines for tuberculosis control in Brazil. Brasília (DF): MH; Available: http://www.saude.sp.gov.br/recursos/cve-centro-de-vigilancia-epidemiologica/areas-de-vigilancia/tuberculose/manuais-tecnicos/tb19_manual-2edrecomendacoes.pdf. Accessed: 14 October 2019. [Article in Portuguese]
24. World Health Organization (WHO) (2020) Global tuberculosis report. Available: <https://apps.who.int/iris/bitstream/handle/10665/336069/9789240013131-eng.pdf>. Accessed: 20 February 2021.
25. Leung CC, Chan CK, Tam CM, Yew WW, Kam KM, Au KF, Tai LB, Leung SM, J Ng (2005) Chest radiography screening for tuberculosis in Hong Kong prison. *Int J Tuberc Lung Dis* 9: 627-632.
26. Sánchez A, Massari V, Gerhardt G, Espinola AB, Siriwardana M, Camachos LAB, Larouzé B (2013) X ray screening at entry and systematic screening for the control of tuberculosis in a highly endemic prison. *BMC Public Health* 13: 983.
27. Vinkeles Melchers NVS, van Elsland SL, Lange JMA, Borgdorff MW, van den Hombergh J (2013) State of affairs of tuberculosis in prison facilities: a systematic review of screening practices and recommendations for best TB control. *PLoS ONE* 8: e53644.
28. Oliveira LG, Natal S, Camacho LA (2015) Analysis of the implementation of the Tuberculosis Control Program in Brazilian prisons. *Cad Saude Publica* 31: 543-554. [Article in Portuguese]
29. Allgayer MF, Ely KZ, Freitas GH, Valim ARM, Gonzales RIC, Krug SBF, Possuelo LG (2019) Tuberculosis: health care and surveillance in prisons. *Rev Bras Enferm* 72: 1304-1310. [Article in Portuguese].
30. Lee HY, Chae KO, Lee CH, Choi SM, Lee J, Park YS, Lee S, Yoo C, Kim YW, Han SK, Yim J (2014) Culture conversion rate at 2 months of treatment according to diagnostic methods among patients with culture-positive pulmonary tuberculosis. *PLoS ONE* 9: e103768.

31. Marques M, Cunha EAT, Evangelista MSN, Basta PC, Marques AMC, Croda J, Andrade SMO (2017). Antituberculosis-drug resistance in the border of Brazil with Paraguay and Bolivia. *Rev Panam Salud Publica* 41: e9. [Article in Portuguese].
32. Przybylski G, Dąbrowska A, Trzcińska H (2014) Alcoholism and other socio-demographic risk factors for adverse TB-drug reactions and unsuccessful tuberculosis treatment – data from ten years' observation at the Regional Centre of Pulmonology, Bydgoszcz, Poland. *Med Sci Monit* 20: 444–453.
33. Theron G, Peter J, Zijenah L, Chanda D, Mangu C, Clowes P, Rachow A, Lesosky M, Hoelscher M, Pym A, Mwaba P, Mason P, Naidoo P, Pooran A, Sohn H, Pai M, Stein DJ, Dheda K (2015) Psychological distress and its relationship with non-adherence to TB treatment: a multicentre study. *BMC Infect Dis* 15: 253.
34. Campos PE, Suarez PG, Sanchez J, Zavala D, Arevalo J, Tucana E, Nolan CM, Hooton TM, Holmes KK (2003) Multidrug-resistant *Mycobacterium tuberculosis* in HIV-infected persons, Peru. *Emerg Infect Dis* 9: 1571–1578.
35. Quy HT, Buu TN, Cobelens FG, Lan NT, Lambregts CS, Borgdorff MW (2006) Drug resistance among smear-positive tuberculosis patients in Ho Chi Minh City, Vietnam. *Int J Tuberc Lung Dis* 10: 160-166.
36. Mesfin YM, Hailemariam D, Biadgilign S, Kibret KT (2014) Association between HIV/AIDS and multi-drug resistance tuberculosis: a systematic review and meta-analysis. *PLoS ONE* 9: e82235.
37. World Health Organization (WHO) (2010). Global report on surveillance and response on multidrug and extensively drug-resistant tuberculosis. Available: https://apps.who.int/iris/bitstream/handle/10665/44286/9789241599191_eng.pdf;jsessionid=4D6E8303A333DAECA7562F6803F31AA9?sequence=1. Accessed: 14 February 2020.
38. Andrews JR, Shah NS, Weissman D, Moll AP, Friedland G, Gandhi NR (2010) Predictors of multidrug- and extensively drug-resistant tuberculosis in a high HIV prevalence community. *PLoS ONE* 5: e15735.
39. Jugheli L, Bzekalava N, Rijk P, Fissette K, Portaels F, Rigouts L (2009) High level of cross-resistance between Kanamycin, Amikacin, and Capreomycin among *Mycobacterium tuberculosis* isolates from Georgia and a close relation with mutations in the *rrs* gene. *Antimicrob Agents Chemother* 53: 5064–5068.
40. Pradipta IS, Forsman LD, Bruchfeld J, Hak E, Alffenaar JW (2018) Risk factors of multidrug-resistant tuberculosis: a global systematic review and meta-analysis. *J Infect* 77: 469-478.
41. Bonnet M, Sizaire V, Kebede Y, Janin A, Doshetov D, Mirzoian B, Arzumanian A, Muminov T, Iona E, Rigouts L, Rüsç-Gerdes S, Varaine F (2005) Does one size fit all? Drug resistance and standard treatments: results of six tuberculosis programmes in former Soviet countries. *Int J Tuberc Lung Dis* 9: 1147-1154.
42. Golub JE, Dowdy DW (2013) Screening for active tuberculosis: methodological challenges in implementation and evaluation. *Int J Tuberc Lung Dis* 17: 856-865.
43. Banda HT, Gausi F, Harries AD, Salaniponi FM (2009) Prevalence of smear-positive pulmonary tuberculosis among prisoners in Malawi: a national survey. *Int J Tuberc Lung Dis* 13: 1557-1559.

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