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Prevalence of tuberculosis in prisons: risk factors and molecular epidemiology

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SUMMARY

SETTING: Tuberculosis (TB) in prisons is a challenge for the public health system. Active and passive case screening are important tools for TB case detection.

OBJECTIVE: To characterise TB in a southern Brazil prison in terms of epidemiological variables, diagnostic approaches and clinical isolate genotypes.

DESIGN: Inmates of a southern Brazilian prison were assessed using active and passive TB case screening. Sputum microscopy, culture, drug susceptibility testing and genotyping were performed. Data were analysed using descriptive statistics and multivariable logistic regression.

RESULTS: TB prevalence was 4712 per 100 000 inmates, and was associated with low educational level, time incarcerated, productive cough, previous TB history, smoking and human immunodeficiency virus (HIV) infection. Overall, 27.8% of TB cases were detected by culture only; the prevalence of drug-resistant strains was 7.8%; 58.3% of clinical isolates had an identical genotypic profile.

CONCLUSION: The study showed extensive circulation of *Mycobacterium tuberculosis* strains in a highly endemic prison. It is recommended that priority be given to the evaluation of prison inmates with longer jail times, those who are HIV-positive, those with symptoms and those with a previous history of tuberculosis. We observed that active case finding induced passive case detection.

KEY WORDS: *Mycobacterium tuberculosis*; diagnosis; genotyping; multidrug resistance; prisons

THE GLOBAL PREVALENCE of tuberculosis (TB) in 2013 was estimated at 159 cases per 100 000 population.[1] In prisons, the average prevalence was 1913/100 000 inmates.[2] Most prisons are overcrowded, with poor ventilation and lighting, favouring the transmission of *Mycobacterium tuberculosis*. In 2012, Brazil had 309 074 places for 508 357 inmates,[3] and this, among other factors, contributed to the high TB incidence rate reported in its prisons in 2013 (1080/100 000).[4] Factors associated with TB in prisons include cough of >4 weeks, sharing cells with other TB-infected cases or inmates with chronic cough,[5] repeated incarceration, human immunodeficiency virus (HIV) infection and alcohol use.[6]

The use of diagnostic tools with high sensitivity and specificity improves case detection. Microbiological methods such as culture and molecular approaches should be used for TB screening in prisons.[6] Molecular epidemiology provides a better understanding of the dynamic of *M. tuberculosis* transmission. Knowledge of the ways in which the microorganism is dispersed in the population is of particular interest for prevention strategies. The high proportion of isolated clusters suggests that intra-institutional transmission of the bacillus contributes substantially to high TB prevalence.[7]

The objective of the present study was to characterise TB cases in a southern Brazilian prison in terms of epidemiological variables, diagnostic approaches and clinical isolate genotypes.

MATERIALS AND METHODS

Study design

A cross-sectional study was carried out in a prison with 764 inmates, where the following interventions were performed: active and passive TB case screening, microscopy, culture, drug susceptibility testing (DST) and clinical isolate genotyping.

Background

Of the 26 Brazilian states, Rio Grande do Sul has the seventh highest TB rate;[4] a significant proportion of these cases are found in prisons.[6,8,9] The prison in

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which our study was conducted is located in a priority city for TB control; the prison is organised into six galleries comprising 10–22 cells. Although the cells are designed to hold six inmates, there are usually on average nine inmates per cell (range 4–20).

The study was conducted from November 2012 to December 2013. The Research Ethics Committee Federal University of Rio Grande, Rio Grande, RS, Brazil approved the study (report no 66/2012).

Study participants

Sample calculations took into account a 10% TB prevalence rate[6,10] and 95% confidence intervals (CIs). The study sample, which included 285 prisoners (increased by 10% for possible losses), was selected by drawing lots, and only included inmates on the closed regime (full confinement). The sample was proportional to the number of inmates per cell and gallery. A pre-coded questionnaire was used to collect sociodemographic information, prison history and clinical data. The randomly selected inmates ($n = 285$) constituted the active case finding (ACF) group. During ACF, a group of 133 inmates with respiratory symptoms presented at the medical service for evaluation and sputum collection. These subjects constituted the passive case finding (PCF) group.

Among the 418 inmates evaluated for TB symptoms using ACF ($n = 285$) and PCF ($n = 133$), only 304 answered the pre-coded questionnaires, as we were unable to mobilise a greater number of inmates during the study period. All ACF participants ($n = 285$), but only TB cases diagnosed by PCF ($n = 19$), were interviewed, totalling 304.

Study variables

The main observed variables were clinical diagnosis, microbiological confirmation, new cases, retreatment cases with previous documented cure, treatment completion and loss to follow-up.[1] Productive cough of $\geqslant 2$ weeks was used to define cases with respiratory symptoms.[11] Subjects were evaluated for HIV infection as well as alcohol, tobacco and other drug use. Sociodemographic characteristics evaluated included age, sex, education, ethnicity and monthly income. Subjects' penal profiles, current and overall prison terms, history of incarceration, number of previous arrests, prisons at which they were previously incarcerated and cell exchanges during the current period of detention were also taken into account.

Diagnosis, drug susceptibility testing and genotyping

Two sputum samples were collected for microscopic Ziehl-Neelsen examination and Ogawa-Kudoh culture for all of the cases with respiratory symptoms. If microbiological tests were negative, they were repeated; if persistent TB was suspected, a clinical diagnosis and radiological approach was used.[11]

Characteristic growth of *Mycobacterium* spp. was identified using a molecular approach that evaluated the *M. tuberculosis* complex.[12] The resazurin microtitre assay was used for DST.[13] Clinical isolates were genotyped using 12-locus mycobacterial interspersed repetitive units–variable number of tandem repeats (MIRU-VNTR).[14] All of the confirmed TB cases received treatment, and follow-up routines were established by the health service council.

Data analysis

Sociodemographic, prison and clinical characteristics were analysed using Epi Info™ version 6.04 (Centers for Disease Control and Prevention, Atlanta, GA, USA), which was used for crude analysis, prevalence ratios, 95%CIs and P value calculations; differences with $P < 0.05$ were considered statistically significant. We also used Pearson, χ^2, Fisher's exact and linear trend testing.

In multivariate analysis, Poisson's regression technique was applied, and the adjusted prevalence ratio (PR) and its 95%CIs were calculated according to a hierarchical analysis model comprising two levels of determination, the most distal of which was formed by the variables education, duration of incarceration and previous TB episodes; at the second-most proximal level, respiratory symptoms at the time of onset, HIV status and smoking were also considered. Each variable with $P < 0.05$ was retained in the model to fit at the next level.

Diagnostic variables were analysed according to laboratory results, the contribution of culture[15] and WHO ranking.[1] For the genetic relationship analysis, built-up dendrograms[16] and MIRU-VNTR discriminatory power were determined using the Hunter Gaston Discriminatory Index (HGDI).[17]

RESULTS

Inmates' penal, sociodemographic and clinical characteristics

The average age of the inmates was 31.2 years (±8.4); 8.9% (27/304) were females and 91.1% (277/304) males, of whom respectively 2 (7.4%) and 34 (13.3%) were diagnosed with TB. The majority (59.2%) were White, and 73.7% had $\leqslant 7$ years of education. Of the 288 who were able to report an income, 78% received 250–500 USD/month.

The average current detention time was 26 months, with three cell or gallery changes; 70.1% had been arrested previously at least once and 44.3% $\geqslant 3$ times. The total length of incarceration (current + previous detention time) was on average 55 months.

In terms of clinical characteristics, 8.9% were HIV-positive, of whom 41.2% (7/17) were diagnosed with TB; 11.5% of the inmates reported previous TB, of whom 16.1% were lost to follow-up.[1] Drug use was reported in 70%, of whom 44.6% were crack users.

Table 1 Prevalence and distribution of TB cases by gallery

Gallery	Prevalence of TB cases by gallery Cases/number of respondents* (%)	Distribution of confirmed cases by gallery *n/N* (%)
A	11/47 (23.4)	11/36 (30.6)
B	5/66 (7.6)	5/36 (13.9)
C	8/88 (9.1)	8/36 (22.2)
D	7/52 (13.5)	7/36 (19.4)
Gallery for workers	3/24 (12.5)	3/36 (8.3)
Female gallery	2/27 (7.4)	2/36 (5.6)

* 304 inmates interviewed (answered the pre-coded questionnaire).
TB = tuberculosis.

The use of alcohol and tobacco was reported by respectively 9.5% and 68.4%.

TB prevalence and characteristics of cases

TB prevalence was 4712/100 000; 36/279 (12.9%) subjects with symptoms were diagnosed with TB. TB prevalence in the ACF and PCF groups was respectively 17/146 (11.6%) and 19/133 (14.3%). Sixteen (44.4%) cases were microscopy- and culture-positive; respectively 10 (27.8%) and five (14%) were diagnosed using culture or microscopy alone. Five TB cases were diagnosed clinically. The contribution of culture to TB diagnosis was 32.3%.

The prevalence of drug-resistant TB was 7.8% (2/26): one case had multidrug-resistant TB (MDR-TB) and the other was resistant to isoniazid and ethambutol. Both cases had a history of retreatment and were detected by PCF. The TB-HIV co-infection rate was 18% (7/36), and most of the TB cases were concentrated in Gallery A (Table 1).

There were no statistically significant differences between groups detected by ACF and those detected by PCF in terms of age, ethnicity, education level, total prison time, previous history of incarceration, duration of respiratory symptoms, previous TB, HIV status or alcohol use, which justified the inclusion of 19 TB cases detected by PCF in the analysis comparing the two groups.

Bivariate analysis of the groups with and without a TB diagnosis indicated significant associations for schooling, prison time, duration of respiratory symptoms, previous TB, HIV status and smoking. The group with $\leqslant 7$ years of schooling had a four-fold higher risk of TB (95%CI 1.24–12.46, $P = 0.009$). Patients with >3 years of incarceration had a two-fold higher risk of TB than those with prison stays of $\leqslant 1$ year (95%CI 0.98–5.40, $P = 0.038$).

Linear trend analysis showed a relation between longer duration of symptoms and higher probability of having TB, with a 10-fold greater risk in the group with respiratory symptoms for $\geqslant 5$ weeks (95%CI 3.20–31.76, $P < 0.001$). TB risk was also higher among the group with at least one previous TB episode (95%CI 2.43–7.77, $P < 0.001$) and being HIV-positive (95%CI 1.27–4.74, $P = 0.023$). A significant association between being a smoker and development of TB was also observed: smokers had almost a two-fold increased risk (95%CI 0.76–3.41, $P < 0.001$) (Table 2).

On multivariate analysis model analysis, however, only the following final variables remained associated with higher risk of TB: previous TB (95%CI 1.92–16.29, $P = 0.002$), respiratory symptoms for 3–4 weeks (95%CI 1.75–12.14, $P = 0.002$) and respiratory symptoms for $\geqslant 5$ weeks (95%CI 5.07–79.55, $P < 0.001$) (Table 3).

Transmission dynamics of M. tuberculosis

Genotyping was performed on 24/26 (92.3%) clinical isolates; most (14/24, 58.3%) shared an identical genotypic pattern, comprising two clusters: one with 12 and one with 2 isolates (Figure). MIRU-VNTR showed HGDI 0.996.

Cluster 2 comprised strains from two inmates who were in the same gallery at the time of diagnosis, while Cluster 1 represented 85.7% of clustered cases (12/14): at the time of diagnosis, 5 were in Gallery A (42%), 3 in Gallery C (25%) and 3 in Gallery D (25%), while 1 case occurred in the female gallery (8%); 67% (8/12) of inmates reported having changed cells or galleries.

Four of the patients with Cluster 1 strains had HIV and three had previously had TB in the same prison. Five had never been arrested, while the remaining seven had previously been in the same prison. The median duration of incarceration of these 12 cases was 54 months. All were culture-positive, but only half were microscopy-positive.

DISCUSSION

The high TB prevalence in the study prison, 69-fold higher than in the general population, is alarming, but similar to findings reported elsewhere.[5,6,8,10,18] This finding indicates the urgent need for strategies to reduce the TB burden in prisons.

The floating population in the prisons makes inter-study comparisons difficult, and is a challenge for the measurement of the magnitude of TB in prisons.[19] Nevertheless, the prevalence rate in our study was similar to that recently determined in another prison in the state of Rio Grande do Sul.[7]

Other studies have suggested that in penal institutions the sensitivity of TB screening is higher when radiology is used, followed by microscopy and culture;[20–24] however, symptom evaluation followed by microbiological confirmation was found to be appropriate in our study. Culture contributed to early detection in 32.3% of TB cases. This result is within the expected rate of 30–40% in locations where samples are cultured;[15] it is also similar to that reported among the general population of the city of the study prison, Pelotas.[25]

Table 2 Analysis between groups with and those without a TB diagnosis in the prison by socio-demographic, prison and clinical variables

Sociodemographic profile, penal and clinical variables	Comparison between groups with and those without a TB diagnosis: Inmates with TB ($n = 36$) n (%)	Comparison between groups with and those without a TB diagnosis: Inmates without TB ($n = 268$) n (%)	Bivariate analysis: PR (95%CI)	Bivariate analysis: P value
Age, years ($n = 304$)				
⩾31	13 (9.8)	119 (90.2)	1.0	0.346*
⩽30	23 (13.4)	149 (86.6)	1.36 (0.72–2.58)	
Ethnicity ($n = 304$)				
Caucasian	21 (11.7)	159 (88.3)	1.0	0.909*
Non-Caucasian	15 (12.1)	109 (87.9)	1.04 (0.56–1.93)	
Educational level, years of schooling ($n = 304$)				
⩾8	3 (3.8)	77 (86.2)	1.0	0.009*
⩽7	33 (14.7)	191 (85.3)	3.93 (1.24–12.46)	
Total incarceration time,† months ($n = 295$)				
⩽12	6 (7.7)	72 (92.3)	1.0	0.038*
13–36	7 (8)	80 (92)	1.05 (0.37–2.98)	
⩾37	23 (17.7)	107 (82.3)	2.30 (0.98–5.40)	
Previously incarcerated ($n = 304$)				
No	9 (9.9)	82 (90.1)	1.0	0.491*
Yes	27 (12.7)	186 (87.3)	1.28 (0.63–2.62)	
Duration of respiratory symptoms, weeks ($n = 164$)				
⩽2	3 (4.8)	59 (95.2)	1.0	<0.001‡
3–4	11 (18)	50 (82)	3.73 (1.09–12.71)	
⩾5	20 (48.8)	21 (51.2)	10.08 (3.20–31.76)	
Previous TB ($n = 304$)				
No	23 (8.6)	246 (91.4)	1.0	<0.001§
Yes	13 (37.1)	22 (62.9)	4.34 (2.43–7.77)	
HIV¶ ($n = 190$)				
Negative	29 (16.8)	144 (83.2)	1.0	0.023§
Positive	7 (41.2)	10 (58.8)	2.46 (1.27–4.74)	
Cigarette smoking ($n = 301$)				
No	8 (8.4)	87 (91.6)	1.0	<0.001*
Yes	28 (13.6)	178 (86.4)	1.61 (0.76–3.41)	
Alcohol use: CAGE ($n = 304$)				
Negative	33 (12)	242 (88)	1.0	0.541§
Positive	3 (10.3)	26 (89.7)	0.86 (0.28–2.64)	

* χ^2 test.
† Current + previous incarceration.
‡ Linear trend.
§ Fisher's exact test.
¶ Cases with known HIV serology. New TB cases underwent HIV testing as recommended by the National TB Control Programme.
TB = tuberculosis; PR = prevalence ratio; CI = confidence interval; HIV = human immunodeficiency virus; CAGE = Have you ever felt you needed to cut down on your drinking? Have people annoyed you by criticising your drinking? Have you ever felt guilty about drinking? Have you ever felt you needed a drink first thing in the morning (eye-opener) to steady your nerves or to get rid of a hangover? (alcohol use disorders screening test).

The five cases diagnosed by microscopy alone may indicate that the use of 2% sodium hydroxide for sample decontamination, although effective, is drastic for micro-organisms and may affect the viability of bacteria in culture.[15] In these cases, response to treatment confirmed the TB diagnosis.[11]

Although none of the variables studied were significantly different between the ACF and PCF groups, the PCF group had a higher TB case prevalence, which allows us to infer that those who seek treatment have a higher probability of being sick. The fact that 11.6% would have presented asymptomatically and would not have been diagnosed without ACF strengthens the importance of implementing ACF, not only as a tool for detection but also as a stimulus for PCF.

On multivariate analysis, only previous TB and duration of respiratory symptoms were associated. Greater length of incarceration, lower educational levels and previous TB episodes increased the risk four-fold, while smoking and HIV positivity doubled the risk. These data can be used to address strategies aimed at high-risk groups, especially in larger prisons.[22,26]

We have found that longer duration of respiratory symptoms leads to a 10-fold increase in TB risk. Given that subjects may underestimate cough symptoms, the duration of productive cough can be difficult to determine.[27]

Studies in Brazilian prisons have shown an average rate of drug-resistant TB of 9.7%,[7,8,10,28] similar to that observed in this study. The two cases with drug-

Table 3 Multivariate analysis of risk factors for TB in prison

Sociodemographic profile, penal and clinical variables	Multivariate analysis	
	PR (95%CI)	*P* value
Educational level, years of schooling		
⩾8	1.0	0.107
⩽7	3.12 (0.78–12.48)	
Total period of incarceration, months		
⩽12	1.0	
13–36	0.79 (0.25–2.44)	0.691
⩾37	1.01 (0.31–3.22)	0.985
Duration of respiratory symptoms, weeks		
⩽2	1.0	0.002
3–4	4.61 (1.75–12.14)	<0.001
⩾5	20.08 (5.07–79.55)	
Previous TB		
No	1.0	
Yes	5.59 (1.92–16.29)	0.002
HIV		
Negative	1.0	
Positive	1.57 (0.47–6.48)	0.397
Cigarette smoking		
No	1.0	
Yes	1.26 (0.42–3.76)	0.678

TB = tuberculosis; PR = prevalence ratio; CI = confidence interval; HIV = human immunodeficiency virus.

resistant TB were identified among patients with previous treatment histories. The spread of drug-resistant strains is a serious problem in enclosed areas, where the possibility of intra- and extramural outbreaks can reach dramatic proportions.

The fact that most clinical isolates share the same genomic profile indicates that transmission of the bacillus within the institution contributed to the high TB prevalence rate observed in the study. When supplemented with information about the galleries and passages in the prison, it may be inferred that contact relationships were established between Cluster 1 cases, although it is not possible to say when the infection occurred in the index case or when the index case became acid-fast bacilli-positive. Although none of the cluster isolate cases were observed among cellmates, contact among inmates in the same gallery could also occur in the courtyard. Cluster 1 dispersion in four of the six prison galleries can be traced, as 67% of inmates had exchanged cells; it is therefore possible to establish a relationship among all of the cases and a hypothetical route of dispersion. It should also be noted that the genotype of these 12 strains had previously been identified in the same prison.[25]

While it is possible that some cases may have developed from latent infections, recent infection has been considered an important problem in other molecular epidemiology studies in prisons.[7,8,26] 12-locus MIRU-VNTR has been used in other studies in this region and shown high discriminatory power;[25,29,30] it is therefore a suitable tool for molecular epidemiology studies in this scenario. Further studies regarding community isolates may show how extramural transmission occurs and provide eventual links with the prison.

CONCLUSIONS

The study showed extensive circulation of *M. tuberculosis* in a highly endemic prison. ACF and PCF of TB cases based on respiratory symptoms, followed by microbiological diagnosis and genotyping, suggests that priority should be given to the evaluation of inmates with longer jail times, those

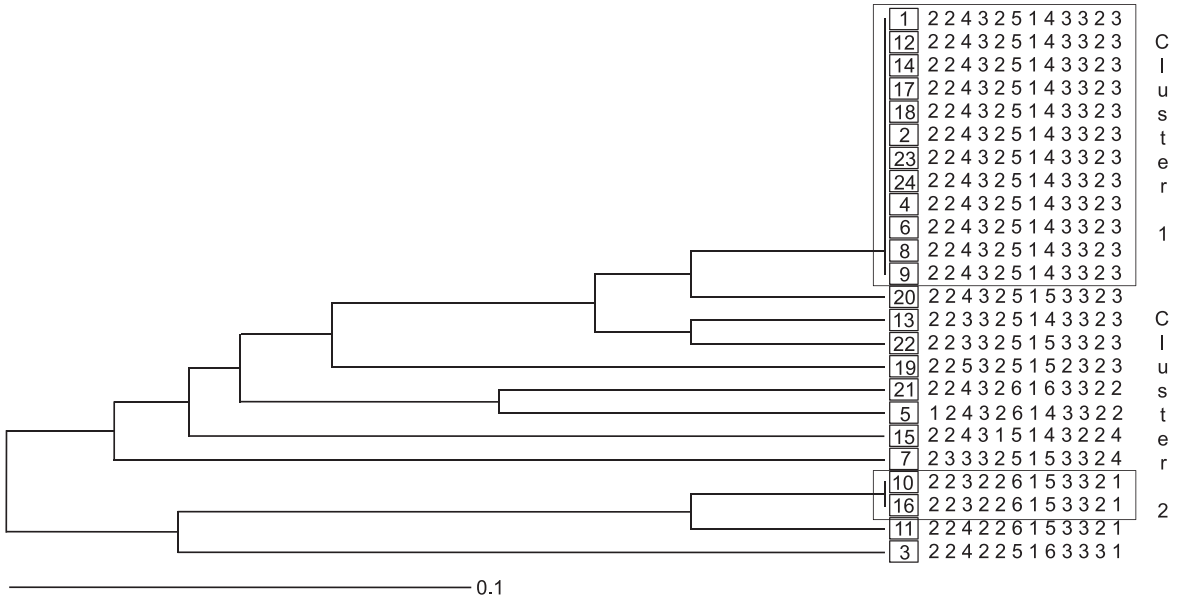

Figure Dendrogram of clinical isolates from the prison using 12-locus MIRU-VNTR. Dendrogram performed using clustering[15] using UPGMA. Clusters were defined as at least two *M. tuberculosis* strains with identical patterns isolated from different patients. UPGMA = unweighted pair group method with arithmetic mean; MIRU = mycobacterial interspersed repetitive units; VNTR = variable number of tandem repeats.

who are HIV-positive, those with symptoms and those with previous TB. The use of ACF to induce PCF is essential to increase TB detection.

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RESUME

CONTEXTE : La tuberculose (TB) en prison constitue un défi majeur pour le système de santé publique. Le dépistage actif et passif des cas est un outil important pour la détection des cas de TB.

OBJECTIF : Caractériser la TB dans une prison du sud du Brésil en termes de variables épidémiologiques, d'approches diagnostiques et de génotypes des isolats cliniques.

SCHÉMA : Cette étude a été réalisée dans une prison du sud du Brésil. Les détenus ont été évalués grâce aux approches de dépistage actif et passif des cas. On a réalisé une microscopie de crachats, une culture, un test de pharmacosensibilité et un génotypage. Les données ont été analysées grâce à des statistiques descriptives et à une régression logistique multivariée.

RÉSULTATS : La prévalence de la TB a été de 4712 pour 100 000 détenus et a été associée à un faible niveau d'instruction, à la durée de la détention, à une toux productive, à des antécédents de TB, à l'usage du tabac et au virus de l'immunodéficience humaine (VIH). Dans l'ensemble, 27,8% des cas de TB ont été détectés par culture seule et la prévalence de souches de TB résistantes a été de 7,8%. De plus, 58,3% des isolats cliniques avaient un profil génotypique identique.

CONCLUSIONS : Cette étude a mis en évidence une circulation extensive de *Mycobacterium tuberculosis* dans une prison hautement endémique. On suggère de donner la priorité à l'évaluation des détenus anciens, ceux qui sont VIH positifs, ceux qui ont des symptômes et ceux qui ont déjà eu la TB dans le passé. De plus, nous avons constaté que le dépistage actif des cas induisait une détection passive des cas.

RESUMEN

MARCO DE REFERENCIA: La tuberculosis (TB) en las prisiones representa un gran problema del sistema de salud pública. La detección activa y pasiva de casos es un instrumento importante en la detección de los casos de TB.

OBJETIVO: Caracterizar la TB en una prisión del sur del Brasil mediante el análisis de las variables epidemiológicas, los enfoques diagnósticos y los genotipos de los aislados clínicos.

MÉTODOS: El estudio se llevó a cabo en una prisión del sur del Brasil. La investigación de los reclusos siguió estrategias de búsqueda activa y pasiva de casos. Se practicaron la baciloscopia del esputo, el cultivo, las pruebas de sensibilidad a los medicamentos y la genotipificación. Los datos se analizaron mediante estadísticas descriptivas y análisis de regresión logística multifactorial.

RESULTADOS: Se observó una prevalencia de TB de 4712 por 100 000 reclusos y la enfermedad se asoció con un bajo nivel educativo, el tiempo de permanencia en prisión, la tos productiva, el antecedente de TB, el tabaquismo y la situación frente al virus de la inmunodeficiencia humana (VIH). En general, el 27,8% de los casos de TB se detectó solo mediante el cultivo y la prevalencia de cepas farmacorresistentes fue 7,8%. Además, el 58,3% de los aislados clínicos presentó un perfil genotípico idéntico.

CONCLUSIÓN: El estudio puso de manifiesto una extensa circulación de *Mycobacterium tuberculosis* en una prisión con alta endemia. Se recomienda dar prioridad a la evaluación de los prisioneros con un tiempo más prolongado de encarcelamiento, los que presentan una serología positiva frente al VIH, los que refieren síntomas y los que presentan un antecedente de infección tuberculosa. Además, el estudio indicó que la búsqueda activa de casos favorece la detección pasiva.