



Recent transmission of drug-resistant *Mycobacterium tuberculosis* in a prison population in southern Brazil

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ABSTRACT

We conducted a cross-sectional, retrospective study, characterized by classical and molecular epidemiology, involving *M. tuberculosis* isolates from a regional prison in southern Brazil. Between January of 2011 and August of 2014, 379 prisoners underwent sputum smear microscopy and culture; 53 (13.9%) were diagnosed with active tuberculosis. Of those, 8 (22.9%) presented with isoniazid-resistant tuberculosis. Strain genotyping was carried out by 15-locus mycobacterial interspersed repetitive unit-variable-number tandem-repeat analysis; 68.6% of the patients were distributed into five clusters, and 87.5% of the resistant cases were in the same cluster. The frequency of drug-resistant tuberculosis cases and the rate of recent transmission were high. Our data suggest the need to implement an effective tuberculosis control program within the prison system.

Keywords: Tuberculosis; Prisons; Molecular epidemiology.

Chief among the factors contributing to the increasing incidence of tuberculosis in prison populations are: male gender; a low level of education; coming from a disadvantaged community; illicit drug use; a high prevalence of HIV infection; limited access to health care; overcrowded, poorly lit, and poorly ventilated cells; and a lack of information on tuberculosis.^(1,2) In addition, studies have shown that both a higher frequency of prior arrests and length of incarceration are directly associated with a higher incidence of this disease.^(3,4)

In recent years, the incidence of tuberculosis has decreased worldwide, with a 45% reduction in the number of cases between 1990 and 2012. According to the World Health Organization, Brazil ranks 19th among the 22 countries that collectively account for 80% of all cases of tuberculosis worldwide.⁽⁵⁾ However, the incidence rates of the disease in Brazil and in the Brazilian state of Rio Grande do Sul have remained unchanged. In 2013, a total of 78,628 cases were reported in Brazil, and, of those, 6,378 (8.1%) were reported for the prison population. In the state of Rio Grande do Sul, 6,917 cases were reported in 2014, with 9.4% of those cases being reported for the prison population.⁽⁶⁾

In the prison population, it is possible to determine recent transmission of tuberculosis, characterized by the identification of genetically similar strains, within the prison facilities. Through active surveillance and the aid of molecular biology methods, the clonal relationship among strains can be determined, which is useful for epidemiological investigations, as well as for identification

of genetically related strains and their spread among the prison population.⁽⁷⁾

The increasing incidence of cases of tuberculosis caused by drug-resistant strains of *Mycobacterium tuberculosis* is directly associated with inappropriate treatment or treatment nonadherence. Delayed detection of the disease, in patients with resistance, allows continuing transmission of these strains in a given population.^(8,9)

M. tuberculosis genotyping is a useful tool for epidemiological studies, as well as for identifying clonal spread, any highly prevalent strains, and outbreaks. Among the current genotyping techniques, mycobacterial interspersed repetitive units-variable number of tandem repeats (MIRU-VNTR) has been used because it has similar discriminatory power to that of RFLP and because it employs PCR, which results in reduced completion time and reduced complexity when compared with RFLP.⁽¹⁰⁾

The objective of the present study was to determine the epidemiological profile of cases of tuberculosis in a prison in southern Brazil, by using classical and molecular epidemiology.

We conducted a cross-sectional, retrospective study of *M. tuberculosis* isolates from patients diagnosed with tuberculosis in the Santa Cruz do Sul Regional Prison, in the city of Santa Cruz do Sul, Rio Grande do Sul, Brazil, between January of 2011 and August of 2014. This is a medium-sized prison with health care staff. During the study period, 873 sputum smears were performed, accounting for 379 convicts; of those, 53 were diagnosed with tuberculosis in prison, indicating a prevalence of 80

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cases per 100,000 population. *M. tuberculosis* isolates were obtained from 35 different patients (66%). The clinical isolates from those patients, which were subcultured in Ogawa-Kudoh medium and incubated at 37°C for 4-8 weeks, were derived from a sample bank maintained by the Institute of Biological Research, Rio Grande do Sul State Central Laboratory. The 35 isolates were tested for susceptibility to isoniazid, ethambutol, rifampin, and pyrazinamide by the method of proportions⁽¹¹⁾ and were genotyped by a PCR-based method using 15-locus MIRU-VNTR analysis.⁽¹²⁾

Demographic and prison-related data were obtained from the Integrated System of Penitentiary Information, which is regularly updated by prison officers, who provide data such as length of incarceration, history of incarceration, visits, number of inmates per cell, and changes of cells. The clinical and laboratory data of the patients were collected from the Rio Grande do Sul State Central Laboratory and the Santa Cruz do Sul municipal tuberculosis outpatient clinic. The epidemiological variables analyzed included age, gender, level of education, HIV infection, cell block, length of incarceration, history of incarceration, total length of incarceration, and number of changes of cells. The degree of relatedness among strains (genotype numbers) was compared by constructing a dendrogram.⁽¹³⁾ The epidemiological, clinical, and prison-related data were evaluated with the IBM SPSS Statistics software package, version 20.0 (IBM Corp.,

Armonk, NY, USA). Values are presented as means and standard deviations or as absolute numbers and proportions. Means were compared by the Student's t-test, and categorical variables were compared by Pearson's chi-square test. Values of $p \leq 0.05$ were considered significant. The research project was approved by the Research Ethics Committee of the Rio Grande do Sul State Foundation for Health Science Research (Ruling no. 984.264).

Of the 35 individuals included in the study, all were male (100%), with a mean age of 33.2 years; 31 (88.6%) had had 9 years of schooling (Table 1). A total of 28 (80.0%) had been in prison for more than 3 years, and all (100%) had been arrested more than once, with the mean number of times arrested being 8.9 ± 5.2 . Data regarding changes of cell were obtained for 34 individuals, all of whom had changed cells more than once during their incarceration period. In terms of the spatial distribution of the tuberculosis cases within the prison facility, we found that 10 individuals (27.8%) had remained longer in cell block C than in the other cell blocks.

With regard to clinical characteristics, HIV test results were available for 19 patients (52.8%), 1 (5.3%) of whom tested positive. There were 21 patients (58.3%) with a positive AFB-smear and 35 (100%) with a positive culture, and culture resulted in a 41.7% increase in sensitivity for the diagnosis of tuberculosis.

Table 1. Patient clinical, demographic, and prison-related characteristics by classification as cluster or non-cluster cases.^a

Variable	Cluster	Non-cluster	Total	p
Age, years	34.10 ± 11.85	31.40 ± 7.75	33.20 ± 10.70	0.49
Level of education				
9 years of schooling	20 (64.5)	11 (35.5)	21 (88.6)	0.35
High school	3 (100.0)	0 (0.0)	3 (8.6)	
Illiterate	1 (100.0)	0 (0.0)	1 (2.9)	
Cell block				
A	7 (77.8)	2 (22.2)	9 (25.7)	0.07
B	5 (100.0)	0 (0.0)	5 (14.3)	
C	8 (80.0)	2 (20.0)	10 (28.6)	
D	2 (33.3)	4 (66.7)	6 (17.1)	
Length of incarceration				
Up to 3 years	3 (42.9)	4 (57.1)	7 (20.0)	0.17
More than 3 years	21 (75.0)	7 (25.0)	28 (80.0)	
Number of times arrested				
Up to 10 times	18 (72.0)	7 (28.0)	25 (71.4)	0.68
More than 10 times	6 (60.0)	4 (40.0)	10 (28.6)	
Number of inmates per cell				
Up to 6	5 (100.0)	0 (0.0)	5 (16.7)	0.28
More than 6	17 (68.0)	8 (32.0)	25 (83.3)	
Visits				
Yes	13 (72.2)	5 (27.8)	18 (51.4)	0.72
No	11 (64.7)	6 (35.3)	17 (48.6)	
Conjugal visits				
Yes	10 (83.3)	2 (16.7)	12 (34.3)	0.25
No	14 (60.9)	9 (39.1)	23 (65.7)	

^aValues expressed as n (%) or as mean ± SD.

Of the 35 isolates undergoing genotyping, 24 (68.6%) were found to be grouped into five clusters, named from A to E, each containing 3 to 7 individuals (Figure 1). Patient clinical, demographic, and prison-related data, by classification as cluster or non-cluster cases, are presented in Table 1.

Of the 35 isolates assessed regarding their drug susceptibility profile, 8 (22.9%) were isoniazid mono-resistant. A total of 87.5% of the resistant isolates were in the same cluster (D), with patients being distributed between cell blocks A and B, which are located on the prison same wing. The two largest clusters, B and D, accounted for 52.0% of the strains and contained all cases of drug resistance.

Of the 35 patients whose isolates were tested for antimicrobial susceptibility, 28 (80.0%) had been in prison for more than 3 years and all (100%) had been arrested more than once, with the mean number of times arrested being 8.9 ± 5.2 , a mean that is higher than that reported in a study conducted in southern Brazil.⁽¹⁴⁾

One of the major obstacles to tuberculosis control is the accurate and early detection of cases. The

41.7% increase in sensitivity achieved by culture, when compared with smear microscopy, emphasizes the need to perform culture in order to increase the tuberculosis case detection rate.⁽¹⁴⁾

Although HIV testing is mandatory for patients with tuberculosis, HIV test results were available for only 52.8%, with one case of HIV-tuberculosis coinfection being identified (5.3%), a value that is lower than that reported in studies conducted in southern Brazil.^(15,16)

Of the isolated strains, 24 (68.6%) were found to be grouped into five clusters. In a study conducted in another prison in Rio Grande do Sul, 58.3% of the isolates had an identical genetic profile.⁽¹⁴⁾ Although this high rate of clustering suggests recent transmission, which might have occurred within the prison facility, the lack of studies of isolates obtained from the local extramural population is a limiting factor for the present analysis.^(17,18)

Isoniazid mono-resistance was identified in 8 isolates (22.9%), 7 (87.5%) of which were in the same cluster (p < 0.05), supporting the hypothesis of recent transmission of the bacilli.^(19,20) The high resistance rate

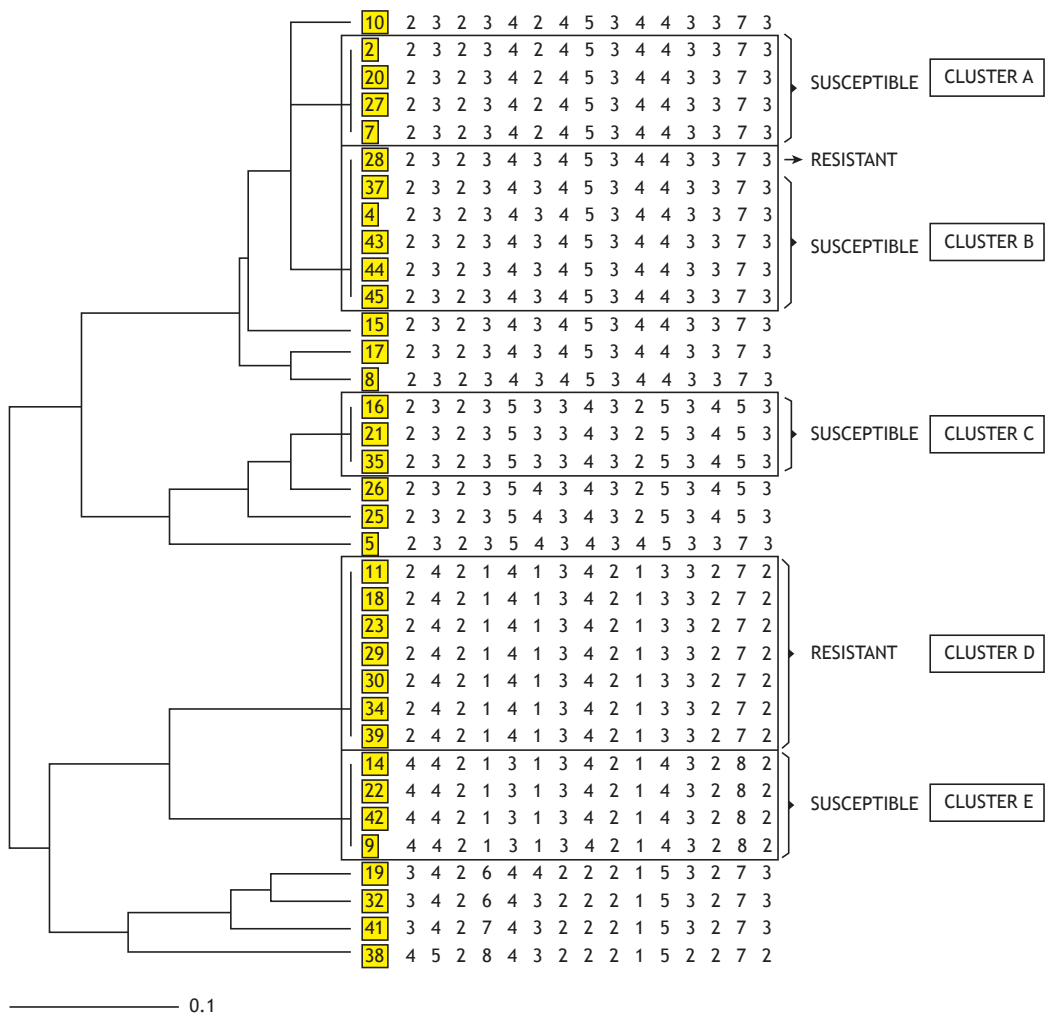


Figure 1. Dendrogram showing the clustering patterns associated with the drug susceptibility profile.

observed in our study is higher than that reported in other studies.^(7,14) Drug resistance is considered to be a major problem in closed institutions, where outbreaks can reach epidemic proportions.⁽¹⁴⁾

Cluster D, consisting of 7 patients who had resistance to isoniazid, was distributed between cell blocks A and B (both of which are located on the same prison wing and have a common exercise yard); although the individuals were not in the same cell, it should be taken into account that contact among inmates can take place in the exercise yard and that changes of cells and cell blocks are common.

The present study showed that the percentage of isoniazid-resistant isolates and the frequency of isolates sharing the same genotype were high. These data support the possibility that transmission of the

bacillus occurred predominantly within the prison facility. Tuberculosis control in prison facilities depends on an effective disease control program, including active search for individuals with respiratory symptoms, prompt diagnosis, and directly observed treatment, within the prison system. In addition, providing continuing education for prison system workers and discussing the topic "prison health care" in other forums, such as community councils, can bring numerous benefits to tuberculosis control in prisons.

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