

Major Article

A diagnosis of pulmonary tuberculosis and drug resistance among inmates in Mato Grosso do Sul, Brazil

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Abstract

Introduction: High endemic levels of pulmonary tuberculosis in prisons result from overcrowding, limited access to healthcare, delayed diagnosis, sustained transmission owing to poor control measures, and multidrug resistance. This study evaluated locally implemented measures for early pulmonary tuberculosis diagnosis and evaluated resistance to anti-tuberculosis drugs. **Methods:** This transversal study employed data from the Mato Grosso do Sul State Tuberculosis Control Program obtained from 35 correctional facilities in 16 counties for 2 periods (2007-2010 and 2011-2014). **Results:** Statewide prevalence (per 100,000) was 480.0 in 2007 and 972.9 in 2014. The following indicators showed improvement: alcohol–acid-fast bacillus testing (from 82.7% to 92.9%); cultures performed (55.0% to 81.8%); drug susceptibility testing of positive cultures (71.6% to 62.4%); and overall drug susceptibility testing coverage (36.6% to 47.4%). Primary and acquired resistance rates for 2007-2014 were 21.1% and 30.0%, respectively. Primary and acquired multidrug resistance rates were 0.3% and 1.3%, respectively. **Conclusions:** Prevalence rates increased, and laboratory indicators improved as a result of capacity building and coordination of technical teams and other individuals providing healthcare to inmates. Resistance rates were high, thereby negatively affecting disease control.

Keywords: *Mycobacterium tuberculosis*. Laboratory diagnosis. Prisons. Transnational borders. South America.

INTRODUCTION

Despite recent advances in control measures, tuberculosis is the principal infectious disease among inmates in Brazil¹, surpassing by up to 81 times the national average prevalence rate in the general population^{2,3}, indicating that controlling the disease remains a neglected priority⁴.

In the midwestern State of Mato Grosso do Sul, the risk of pulmonary tuberculosis (PTB) is 25.3 times higher in prison population than in the general population⁵. In the prison population, a number of vulnerabilities—overcrowding, late detection of the disease, poorly ventilated facilities, malnutrition, inadequate control of cases and contacts, high HIV prevalence, alcohol, and illicit drugs—are likely to interact, facilitating

infection with *Mycobacterium tuberculosis* and progression of disease^{2,6-9}. In addition, a high turnover rate within and across prisons¹⁰, poor access to healthcare, and low adherence to treatment contribute to delayed diagnosis^{2,7}, maintenance of the transmission chain, and emergence of multiresistant strains¹⁰.

Efforts to provide healthcare to inmates is often hampered by logistical challenges, underfunding, lack of political commitment, and governmental negligence¹¹. However, improving the physical structure of prisons (with gains in natural ventilation) and reducing cell crowding should mitigate the burden of disease in this population^{9,12} and indirectly, mitigate the burden of a disease in the society as a whole^{3,4,13}.

Along with the urgency of improving the early diagnosis capacity in Mato Grosso do Sul prisons, strategies to detect cases and reduce transmission among present inmates and recently released inmates have been reported¹³.

In a mass screening of 12 prisons in the state, 691 inmates who presented with cough were evaluated using sputum smear microscopy and sputum cultures. Sputum smear

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Received 3 August 2017

Accepted 6 June 2018

microscopy failed to confirm 74% of tuberculosis cases, which were subsequently confirmed by culturing two samples¹⁴, demonstrating the effectiveness of this approach in early diagnosis.

In 2010, smear testing along with cultures was implemented for suspected tuberculosis cases among inmates serving sentences in the state. Comparing laboratory results obtained before and after the implementation of these measures and expanding the investigation of resistance to antituberculosis drugs in this population can reveal the impact of these changes.

METHODS

Study type

This transversal study employed secondary data of the prison population of Mato Grosso do Sul.

Overview

Of the 2,382,083 residents estimated in the 78 counties in Mato Grosso do Sul in 2007, 9,322 (0.4%) were serving sentences in 35 correctional facilities subordinated to the Mato Grosso do Sul State Penal System Administration Agency (AGEPEN-MS) in 16 counties. By 2014, those numbers had risen to 2,619,657 residents and 14,904 inmates (0.5%). From January 2007 to December 2014, 8,032 PTB cases were reported to the state's branch of the Brazilian Information System of Notifiable Hazards (SINAN-SES-MS), with 1,012 cases being inmates held in AGEPEN-MS-managed prisons. Duplicate notifications for the same episode or for inmates transferred from other states or held at police precincts were excluded.

Ethical considerations

The study was approved by the Research Ethics Committee of the Universidade Federal de Mato Grosso do Sul (opinion 252,447).

Variables investigated

Alcohol-acid-fast bacillus (AAFB) testing, *M. tuberculosis* culture, and drug susceptibility testing (DST) results were retrieved from the Central Public Health Laboratory of Mato Grosso do Sul (LACEN-MS) or the Mato Grosso do Sul Laboratory Environment Management Database (LAG-MS) and double-checked. Cases were grouped by year for the entire state and for the following three groups: cases originating from the Jair Ferreira de Carvalho Correctional Facility (JFCCF), in Campo Grande, the state capital (Group 1); cases from other correctional facilities in Campo Grande (Group 2); and cases from prisons in other counties in Mato Grosso do Sul (Group 3). We distributed cases into these three groups because 2006 samples for AAFB testing that were collected outside of Campo Grande were locally processed at municipal laboratories and subsequently sent to the LACEN-MS in Campo Grande for culturing and DST. Samples from the JFCCF were processed for AAFB testing in the Campo Grande municipal laboratory and subsequently cultured at the LACEN-MS. However, since 2010, the LACEN-MS has been responsible for processing AAFB testing for all samples originating from the JFCCF. Furthermore,

the JFCCF accounted for 65.2% of cases in Campo Grande and 39.9% of cases in the entire state, which might have biased the results if cases were pooled together into fewer groups.

Laboratory testing routine

Sputum samples from suspected cases of PTB were tested for AAFB at local municipal laboratories and subsequently cultured in Bactec *Mycobacterial Growth Indicator Tube 960* (MGIT 960; Becton-Dickinson, Sparks, MD, USA) or Löwenstein-Jensen solid medium¹⁵ at the LACEN-MS. However, samples from four counties (Amambai, Corumbá, Dourados, and Ponta Porã) were tested locally for AAFB, seeded in Ogawa-Kudoh medium, and sent to the LACEN-MS.

Since 2010, smear testing has been shared by the LACEN-MS and the Campo Grande Municipal Laboratory with a consequent increase in the number of cultures and DST.

Positive cultures were subsequently tested at the LACEN-MS for susceptibility to rifampicin, isoniazid, streptomycin, and ethambutol using the proportion method¹⁶.

Resistance patterns detected on DST were validated at the Tuberculosis and Mycobacterial Testing Center of the Instituto Adolfo Lutz (São Paulo) or the Hélio Fraga Reference Center of the *Fundação Oswaldo Cruz* (Rio de Janeiro).

Five operational indicators (AAFB testing, *M. tuberculosis* culturing, positive *M. tuberculosis* cultures, DST on positive cultures, and DST on notified cases) and two epidemiological indicators which included the resistance rate ratio between new (primary resistance) and treated (acquired resistance) cases and multidrug resistance (MDR; resistance to both rifampicin and isoniazid) rate ratio between new and treated cases¹⁷, were examined for two periods: 2007-2010 and 2011-2014 which represent the period before and the period after suspected cases in Group 1 began to be tested at the LACEN-MS, respectively.

Statistical analysis

We used the chi-square test to evaluate associations between correctional facilities and other variables with Bonferroni correction for pairwise comparison of proportions when *p* values were significant in the overall analysis. Student's *t*-test compared quantitative variables between periods. The chi-square test detected associations between facilities and rates of drug sensitivity/resistance, AAFB testing, cultures performed, DST performed, and susceptibility profiles, with Bonferroni correction for pairwise comparison of proportions when associations proved significant. Cross-period comparisons for mean rates of sensitive and resistant cases per group were performed using Student's *t*-test. Data of other variables were subjected to descriptive statistical analysis. The SigmaPlot Exact Graphs and Data Analysis software, version 12.5, was used for statistical analysis with a significance level of 5%¹⁸.

RESULTS

In the 35 prisons investigated, PTB cases increased from 358 in 2007-2010 to 654 in 2011-2014 (an 82.7% increase), representing prevalence rates (per 100,000 inmates) of 480 and 972.9, respectively. Most of these 1012 cases (885) were

concentrated in five counties: Campo Grande (620), Dourados (122), Corumbá (63), Amambai (42), and Ponta Porã (38).

Across periods, operational indicators evolved as follows in Group 1: AAFB testing, 71.4 to 98.4% ($p < 0.001$); cultures performed, 60.2 to 98.4% ($p < 0.001$); positive cultures, 96.6 to 98.3% ($p = 0.716$); DST for positive cultures, 82.5 to 60.8% ($p = 0.003$); and DST coverage, 48.0 to 58.8% ($p = 0.035$). In Group 2, none of these five indicators showed any increase. In Group 3, increases were observed in cultures performed (54.4 to 74.5%, $p < 0.001$) and DST coverage (32.2 to 43.2%, $p = 0.039$). No changes in positive culture rates were detected, whether within groups or statewide (Table 1 and Table 2).

Across groups, no significant differences were found in DST performance on positive cultures (~60%; $p = 0.523$) or in the resistance profiles of tested cultures (~70% sensitive, ~20% resistant; $p = 0.700$) (Table 3).

Across periods, the rates of sensitive cases fell in all three groups, while those of resistant cases increased. The same patterns were seen in statewide rates (Table 4).

Overall, resistance rates of 21.1% (76/361) and 30% (24/80) were observed among new and treated cases, respectively, with a 22.7% mean rate for all cases (100/441). Among uncombined drugs, primary resistance was highest for streptomycin

(11.9%; 43/361) and was also observed in nine cases of MDR (2.5%; 9/361). Among treated cases, resistance was highest for streptomycin (15%; 12/80) and ethambutol (11.3%; 9/80). Primary and acquired MDR rates were 0.3% (1/361) and 1.3% (1/80), respectively (Table 5).

DISCUSSION

Increasing from 480.0 in 2007 to 972.9 in 2014, the PTB prevalence rates per 100,000 inmates in Mato Grosso do Sul were similar to the national rates reported for prisons¹⁹. A study comprising 59% of inmates in 12 prisons in the state throughout 2013 revealed prevalence and incidence rates per 100,000 prisoners of 951 and 1839, respectively¹⁴, with the latter being similar to the 830.6 rate found in a sample of 2237 prisoners in São Paulo in 2008²⁰. Our findings, however, reflect cases reported from a range of correctional facilities (closed, semi-open, and open conditions, but not police precincts).

In 2014, Mato Grosso do Sul had the highest incarceration rate (568.9 per 100,000 population) and the fourth highest prison occupancy rate (216%), ranking 11th among the 28 Brazilian state-level administrative divisions in number of prisoners¹⁹. Overcrowding, compounded by poorly ventilated cells deprived of sunlight, potentiates the likelihood of bacillus transmission^{6,7,9}.

TABLE 1: Laboratory indicators for pulmonary tuberculosis and drug resistance diagnosis with respect to correctional facility and study period.

Variable	Group 1					Group 2					Group 3				
	2007-2010 (n = 98)		2011-2014 (n = 306)		p value	2007-2010 (n = 111)		2011-2014 (n = 105)		p value	2007-2010 (n = 149)		2011-2014 (n = 243)		p value
	n	%	n	%		n	%	n	%		n	%	n	%	
AAFB testing															
yes	70	71.4	301	98.4	<0.001	88	79.3	90	85.7	0.288	138	92.6	211	86.8	0.107
no	28	28.6	5	1.6		23	20.7	15	14.3		11	7.4	32	13.2	
culturing															
yes	59	60.2	301	98.4	<0.001	57	51.4	53	50.5	0.994	81	54.4	181	74.5	<0.001
no	39	39.8	5	1.6		54	48.6	52	49.5		68	45.6	62	25.5	
positive cultures															
yes	57	96.6	296	98.3	0.716	54	94.7	46	86.8	0.264	72	88.9	155	85.6	0.604
no	2	3.4	5	1.7		3	5.3	7	13.2		9	11.1	26	14.4	
DST on positive cultures															
yes	47	82.5	180	60.8	0.003	36	66.7	25	54.3	0.292	48	66.7	105	67.7	0.993
no	10	17.5	116	39.2		18	33.3	21	45.7		24	33.3	50	32.3	
DST on notified cases															
yes	47	48.0	180	58.8	0.035	36	32.4	25	23.8	0.209	48	32.2	105	43.2	0.039
no	51	52.0	126	41.2		75	67.6	80	76.2		101	67.8	138	56.8	

Group 1: Jair Ferreira de Carvalho Correctional Facility, Campo Grande. Group 2: other prison facilities in Campo Grande. Group 3: prisons located elsewhere in the state. n: notified cases of pulmonary tuberculosis; AAFB: alcohol-acid-fast bacilli; DST: drug sensitivity testing. P values as per the chi-square test.

TABLE 2: Laboratory indicators for pulmonary tuberculosis and drug resistance diagnosis in Mato Grosso do Sul, 2007-2014.

Variable	Period				p value
	2007-2010 (n = 358)		2011-2014 (n = 654)		
	n	%	n	%	
AAFB testing					
yes	296	82.7	602	92.0	<0.001
no	62	17.3	52	8.0	
Culturing					
yes	197	55.0	535	81.8	<0.001
no	161	45.0	119	18.2	
Positive cultures					
yes	183	92.9	497	92.9	0.873
no	14	7.1	38	7.1	
DST of positive cultures					
yes	131	71.6	310	62.4	0.032
no	52	28.4	187	37.6	
DST of notified cases					
yes	131	36.6	310	47.4	0.001
no	227	63.4	344	52.6	

n: notified cases of pulmonary tuberculosis; **AAFB**: alcohol–acid-fast bacilli; **DST**: drug sensitivity testing. p-values as per the chi-square test.

TABLE 3: Performance of DST of *Mycobacterium tuberculosis* cultures with respect to correctional facility in Mato Grosso do Sul, 2007-2014.

Testing	Group 1	Group 2	Group 3	p value (chi-square test)
DST of positive cultures				
yes	64.7 (227)*	61.0 (61)*	67.4 (153)*	0.523
no	35.3 (124)*	39.0 (39)*	32.6 (74)*	
Drug sensitivity profile				
sensitive	78.9 (179)*	77.0 (47)*	75.2 (115)*	0.700
resistant	21.1 (48)*	23.0 (14)*	24.8 (38)*	

*Data expressed as relative frequencies (followed by absolute frequencies). Values in the same row followed by various letters differ significantly (chi-square test, $p < 0.05$, Bonferroni correction).

In 2014, Mato Grosso do Sul had the highest incarceration rate in the country (568.9 per 100,000 residents) and the fourth-highest occupancy rate (216%), ranking 11th among the 28 Brazilian state-level administrative units in terms of number of inmates¹⁹. In Mato Grosso do Sul, correctional facilities have operated at up to 500% capacity with cells holding between 35 and 40 detainees who have an average of 2.1m² of space per

prisoner (less than half the minimum recommended standard), representing a pressing problem both in terms of human rights and public health⁹.

With a mean 82.7% increase between the first and the last year of study, the increase in the number of cases varied considerably across groups, from 212.2% cases in Group 1 (closed conditions) to 63.1% cases in Group 3 (three incarceration conditions) to

TABLE 4: Mean percentages of sensitive and resistant cases with respect to study period and correctional facility in Mato Grosso do Sul, 2007-2014.

Testing	Group 1	Group 2	Group 3	Mato Grosso do Sul
Cases tested for drug sensitivity	227 (51.5%)	61 (13.8%)	153 (34.7%)	441 (100.0)
Sensitive samples (%)				
2007-2010	84.08 ± 5.87	90.0 ± 10.0	77.64 ± 7.76	82.10 ± 5.54
2010-2014	77.14 ± 4.72	70.54 ± 11.14	73.21 ± 3.64	75.75 ± 4.26
<i>p</i> value	0.393	0.241	0.623	0.398
Resistant samples (%)				
2007-2010	15.93 ± 5.87	10.00 ± 10.0	22.36 ± 7.76	17.90 ± 5.54
2010-2014	22.86 ± 4.72	29.46 ± 11.14	26.80 ± 3.64	24.25 ± 4.26
<i>p</i> value	0.393	0.241	0.623	0.398

Data expressed as means ± standard error of means. *p* values as per Student's *t*-test.

TABLE 5: Resistance profiles in Mato Grosso do Sul, 2007-2014.

Resistance profile	New cases (361)		Treated cases (80)		Total cases (441)		Means*
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	
Resistant samples	76	21.1	24	30.0	100	22.7	21.76 ± 2.95
Monoresistance							
S	43	11.9	12	15.0	55	12.5	11.40 ± 2.45
I	17	4.7	7	8.8	24	5.4	5.05 ± 0.57
R	3	0.8	2	2.5	5	1.1	1.55 ± 0.78
E	2	0.6	9	11.3	11	2.5	0.34 ± 0.23
Multidrug resistance							
R + I	1	0.3	1	1.3	2	0.5	0.74 ± 0.55
Polyresistance							
S + I	7	1.9	1	1.3	8	1.8	1.80 ± 0.51
S + R	1	0.3	0	0.0	1	0.2	0.20 ± 0.20
I + E	1	0.3	0	0.0	1	0.2	0.20 ± 0.20
S + R + E	1	0.3	0	0.0	1	0.2	0.35 ± 0.35
S + I + E	0	0.0	1	1.3	1	0.2	0.15 ± 0.15

S: streptomycin; I: isoniazid; R: rifampicin; E: ethambutol. *Means ± standard error of means.

no variation in cases in Group 2 (also three conditions). The overall increase may have resulted from the 59.9% growth in the prison population (9,322 in 2007 to 14,904 in 2014) reported for the state^{19,21}. Furthermore, specificities in this population may have also contributed. Although PTB incidence and mortality rates in Mato Grosso do Sul are similar to the national averages, the risks of morbidity and death from the disease are higher among indigenous individuals and residents

of international border regions²². Moreover, the state's location on a cross-national land route of drug and arms trafficking may be a potential contributing factor to increased local detention rates with a greater likelihood of detainees originating from neighboring countries (*e.g.*, Peru and Bolivia) where endemic multidrug-resistant tuberculosis rates are high²³. In 2010, 243 out of 9688 inmates in Mato Grosso do Sul were foreigners (mostly Bolivians, Paraguayans and Peruvians)²⁴.

Difficulties searching for respiratory symptomatic inmates in the entire state during the study period limited this task to two prisons in Campo Grande that jointly held 2300 inmates. In 2010–2014, the LACEN-MS performed 3621 AAFB testing and cultures (an average 724 exams per year) on samples originating from the prisons investigated which represented a coverage rate of 31.4%. However, this rate was lower than the 38.7% rate found for inmates in Carapicuíba, São Paulo State¹¹.

In the present study, culturing confirmed 523 PTB cases or 39% of early diagnosis, which was within the 30–40% range advocated by the World Health Organization (WHO) (where culturing is available¹⁵) and was similar to the 32.3% of early diagnosis found in southern Brazil²⁵. Early treatment of paucibacillary forms interrupts the transmission chain, which is a desirable outcome in prison settings as paucibacillary forms facilitate propagation both of sensitive and resistant strains²⁶. The rate of culture-confirmed cases in the present sample (>90%) proved similar to that found for inmates in Espírito Santo State in 2003–2006²⁷.

In Mato Grosso do Sul, the availability of culturing and DST for populations at a higher risk of drug resistance¹⁵ and the recommendation of both procedures for all tuberculosis cases detected among inmates²⁸ predated national guidelines. In mid-2010, the LACEN-MS was imposed the extra burden of performing AAFB testing, cultures, and DST for the Jair Ferreira de Carvalho Correctional Facility (Group 1), which was previously done by the Campo Grande municipal laboratory, but the change does not appear to have biased our analysis since this prison accounted for 40% of cases reported for the state. No significant differences in DST-related aspects were observed among groups.

The measures implemented also addressed informing the medical and nursing teams of the JFCCF on the importance of promoting a continuous, systematic search for inmates presenting with cough for the purpose of sputum collection. Measures implemented also addressed improvements to the operational routine of sample transit and processing, prompt communication of positive results via telephone call, and providing JFCCF technicians access to the LACEN-MS Information System for obtaining examination results.

Among new cases, resistance rates—streptomycin, 14.4%; isoniazid, 6.9%; rifampicin, 1.4%; ethambutol, 1.1% (whether uncombined or in association, for each drug)—were roughly twice those observed for the state's general population, probably reflecting recent intra-institutional transmission²⁹, a trait not devoid of consequences for the general population¹³. Molecular biology studies have revealed clustering in over 68%²⁹ and 87%³⁰ of strains. Among the state's general population, primary monoresistance (including the four drugs considered here) has been associated with border regions and comorbidity (diabetes and alcoholism)³¹, features that may apply to the prison population of Mato Grosso do Sul. However, MDR rates of 0.3% among new cases and 1.3% among treated cases were both lower than among the state's general population (0.6% and 6.3%, respectively)³¹.

In the present study, the overall resistance rate exceeded those found for inmates in other Brazilian states^{25,29–33}, except

for MDR, which proved four times lower in our sample. The stability of resistance rates from the first to the second period may be indicative of effectiveness in control measures^{15,28}. The high positivity rate of resistant-strain smears (66.0%) was lower than that reported for prisoners in São Paulo³².

In Dourados county of Mato Grosso do Sul, 54% of *M. tuberculosis* strains detected in the general population had the same profile as that found in inmates¹² drawing attention to the risk of spread across populations.

The high prevalence of PTB among prisoners in Mato Grosso do Sul may reflect not only poor ventilation and overcrowding conditions, but also reflect the overall growth of the population and the effects of ongoing measures toward the active search of suspected cases. Ongoing investments in the provisions of culturing, DST, and technical training, efforts combining state and municipal human resources, facilitated access to service indicators, and raised awareness among prison managing boards on the urgency of controlling communicable diseases may have helped shape the results found in this investigation. Nevertheless, the findings highlight the need for health policies that prioritize laboratory diagnosis of suspected cases and monitoring of sensitive and resistant treatments (measures unfeasible without sufficiently trained technical staff to follow every diagnosed case) in order to interrupt the chain of transmission and attenuate the endemic character of the disease.

Recent studies have stressed the need for early diagnosis based on new technologies, as well as the importance of architectural interventions in improving natural ventilation and reducing overcrowding in correctional facilities. Additional studies might identify aggravating factors such as unmet healthcare demand for suspected cases, delayed treatment, outcomes of treated cases, and operational and logistical issues affecting care provision.

While acknowledging the limitations of studies based solely on secondary data, which tend to preclude the investigation of features such as behaviors, attitudes, and clinical histories, we believe the data used in the present study are sufficient for evaluating the effectiveness of an intervention implemented in the diagnosis of tuberculosis among inmates in Mato Grosso do Sul.

Conflict of interest

The authors declare that there is no conflict of interest.

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