

## Prevalence of anti-tuberculosis drug resistance in an HIV/AIDS reference hospital in Rio de Janeiro, Brazil

F. Aguiar,\* M. A. Vieira,\* A. Staviack,\* C. Buarque,\* A. Marsico,\* L. Fonseca,\* R. Chaisson,† A. Kristski,\* G. Werneck,<sup>‡§</sup> F. Mello\*

\* Instituto de Doenças do Tórax (IDT)/Clementino Fraga Filho Hospital (CFFH), Federal University of Rio de Janeiro, Rio de Janeiro, Rio de Janeiro, Brazil; † Department of Pulmonary Medicine, Center for Tuberculosis Research, Johns Hopkins University, Baltimore, Maryland, USA; ‡ Instituto de Estudos em Saúde Coletiva, Federal University of Rio de Janeiro, Rio de Janeiro, § Departamento de Epidemiologia, Instituto de Medicina, Social State University of Rio de Janeiro, Rio de Janeiro, Rio de Janeiro, Brazil

### SUMMARY

**SETTING:** A reference hospital for tuberculosis (TB) and human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) with a TB control programme in Rio de Janeiro, Brazil.

**OBJECTIVE:** To estimate the prevalence of resistance to anti-tuberculosis drugs and to identify associated factors.

**DESIGN:** In a cross-sectional study, clinical and laboratory data were collected retrospectively from 2001 to 2005. Patients with isolation of *Mycobacterium tuberculosis* and available drug susceptibility tests were considered eligible. Data on demographic characteristics, risk factors for resistance, HIV serology and past TB history were collected and analysed by  $\chi^2$  Mann-Whitney test and Poisson regression.

**RESULTS:** We analysed 350 treatments, of which 62 were for patients with previous TB. HIV status was positive in

31.2% of cases. Resistance was found in 15.7% and multidrug resistance (MDR) in 4.3% of cases. Previous treatment ( $P < 0.001$ ) and relapse within 2 years were associated with resistance ( $P < 0.03$ ). Pulmonary cavities were associated with MDR ( $P < 0.001$ ). Homelessness was associated with any resistance in newly diagnosed patients ( $P < 0.01$ ). Working in a hospital was not associated with resistance.

**CONCLUSION:** Suspicion of drug-resistant disease is necessary in patients with a history of previous TB in hospitals in Rio de Janeiro. The implementation of an effective hospital TB control programme can prevent transmission even in high TB prevalence settings.

**KEY WORDS:** drug resistance; tuberculosis chemotherapy; hospital infection control programme; multidrug-resistant TB; transmissible disease control

TUBERCULOSIS (TB) is a major public health problem worldwide, particularly in developing countries, where 95% of the world's TB cases and 98% of deaths attributed to TB occur.<sup>1</sup> Brazil ranks sixteenth in the World Health Organization's (WHO's) list of 22 countries that have 80% of the world's TB cases.<sup>2</sup> The city of Rio de Janeiro (RJ) has a high burden of the disease, with over 6000 notified cases in 2003 and an estimated incidence of 105.5 cases per 100 000 population.<sup>3</sup> During the study period, the DOTS strategy was implemented in six TB clinics covering 12% of all TB cases in RJ.<sup>4</sup>

The emergence of multidrug-resistant TB (MDR-TB, defined as resistance to at least isoniazid [INH] and rifampicin [RMP]) is a global threat, making systematic monitoring of the susceptibility of *Mycobacterium tuberculosis* isolates to front-line drugs essential.<sup>5</sup> In developing countries, evaluation of MDR-TB in prisons and hospitals has been neglected by TB con-

trol programmes in the last few decades, and less than 30% of isolates from patients in hospitals and prisons routinely undergo drug susceptibility testing (DST).<sup>6</sup> Data available on drug-resistant TB in these settings show rates of primary and acquired MDR-TB of as high as 7.0% and 33.8%, respectively.<sup>6–17</sup>

In Brazil, few studies have addressed the problem of drug resistance. Countrywide data from patients attending primary health care units were published more than 10 years ago.<sup>18</sup> At that time, resistant TB was found in 10.6% of all cases and MDR-TB in 2.2%. To our knowledge, only two studies have addressed the problem of drug resistance in hospitals in the city of RJ, Brazil. The first study was performed in Ary Parreiras and Clementino Fraga Filho Hospital during 1993 and 1994, and reported a high prevalence of primary resistance to TB drugs, with MDR-TB observed in 4.5% of new patients. Acquired resistance rates were even higher, with the prevalence of

Correspondence to: Fabio Aguiar, Tuberculosis Research Unit (UPT), Clementino Fraga Filho Hospital–Thoracic Diseases Institute, Federal University of Rio de Janeiro. Rua Professor Rodolpho Paulo Rocco 255, Rio de Janeiro, RJ 21941 913, Brazil. Tel: (+55) 21 2562 2426. Fax: (+55) 21 2264 752. e-mail: fsaguiar@hucff.ufrj.br, aguiarMD@gmail.com

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resistance to any drug reaching 35.3%, and MDR-TB in 17.6%.<sup>19</sup> The second study found a prevalence of resistance to any drug of 20%, with 3.5% MDR-TB.<sup>20</sup> The authors concluded that patients attending hospitals have higher resistance rates than those attending primary care units, and that special care should be offered to such patients. However, as in other developing nations, the Brazilian Ministry of Health (MoH) does not provide specific recommendations for dealing with TB control in hospitals. Although the WHO recommends the DOTS-Plus strategy to deal with the problem of anti-tuberculosis drug resistance, to our knowledge no attempt has been made to date to implement DOTS-Plus in Brazil.

In 1998, a TB control programme was implemented in the Clementino Fraga Filho Hospital Thoracic Disease Institute (Instituto de Doenças do Tórax, CFFH/IDT), a teaching hospital, in a novel strategy that consisted of a multidisciplinary approach, with implementation of biosafety measures, prompt diagnosis of the disease and an organised treatment programme, including DOTS in selected cases and screening and treatment for latent TB infection (LTBI). We studied the prevalence of drug resistance in patients who routinely attended CFFH/IDT in RJ, Brazil, from 2001 to 2005, to study rates of resistance to the standard drugs used for anti-tuberculosis treatment.

## METHODS

We performed a retrospective study of all patients registered in the CFFH/IDT TB control programme of the Federal University of RJ (FURJ) from September 2001 to September 2005. Data were collected from the TB clinic files and hospital medical charts. Diagnosis of TB was based on culture of *M. tuberculosis* and/or histopathology results (granulomas with caseous necrosis). In the presence of symptoms of active TB and no clinical possibility of sample collection or culture and histopathologically negative results, presumptive treatment was offered, with close clinical supervision. Patients with *M. tuberculosis* isolates and available DST results were considered eligible. Patients with conflicting DST results were excluded.

CFFH/TDI is a tertiary hospital located in the city of RJ, Brazil. It is a referral centre for the diagnosis and treatment of severe forms of chronic and acute diseases and HIV/AIDS-TB co-infection. With the implementation of the TB control programme in 1998, 13 negative pressure rooms with high efficiency particulate air filters were created for the isolation of suspected infectious cases and a routine was established for the isolation of these cases on hospital admission. The Mycobacteria Laboratory was restructured so that acid-fast bacilli smear results became available within 24 h of receipt of samples, and culture followed by DST was performed for all samples. Quality control is routinely performed by random testing of samples at

FIOCRUZ (Ministry of Health, Brazil) to evaluate the concordance of DST tests. The TB control programme personnel are responsible for the management of all active and latent TB cases.

As CFFH/TDI is not a referral centre for chronic TB cases, no chronic cases were included. TB cases were classified as new cases or relapses according to previous treatment records. Information about previous treatment was obtained from the national government TB database (SINAN).

Data on demographic characteristics, risk factors for drug resistance, HIV status and previous treatment history were collected by trained personnel using a standardised form. MDR-TB was defined as resistance to INH and RMP, disseminated TB as disease in two non-contiguous sites and alcoholism was assessed by the CAGE criteria.<sup>21</sup> HIV status was considered positive if two enzyme-linked immunosorbent assays detected specific antibodies. Data were recorded in a Microsoft Access® database (Microsoft, Redmond, WA, USA), and confidentiality was guaranteed.

Laboratory tests were performed at the CFFH/TDI Mycobacteria Laboratory. Culture for *M. tuberculosis* was performed in Löwenstein-Jensen medium as recommended.<sup>22</sup> Identification of *M. tuberculosis* was performed by biochemical tests and DST was conducted against the first-line anti-tuberculosis drugs INH, RMP, streptomycin, ethambutol and ethionamide using the proportion method as described by Cannetti.<sup>23</sup>

In the bivariate analysis, the prevalence of resistance was analysed by the  $\chi^2$  test for categorical variables and by the Mann-Whitney test for continuous variables. Associations between putative predictive factors and outcome were expressed as prevalence ratios (PRs) and their respective 95% confidence intervals (CIs). Multivariate analysis was performed by Poisson regression with robust variance for all cases and for subgroups according to history of previous treatment.<sup>24</sup>  $P \leq 0.2$  was used to select variables for use in the multivariate regression analysis. A backward stepwise elimination procedure was performed, using a  $P$  value of  $\leq 0.05$  as the criterion for remaining in the model. We included sex, HIV status and previous treatment history in the final models as possible confounders. We used the non-parametric Cuzick's test to analyse trends in the prevalence of resistance. Data were analysed using STATA 9.0 software (StataCorp, College Station, TX, USA).

The study was approved by the Institutional Review Board of the Federal University of Rio de Janeiro.

## RESULTS

During the study period, 432 patients had *M. tuberculosis* isolated on culture. As DST results were not available for 81 patients due to low colony counts, these were not included in the study. One patient with con-

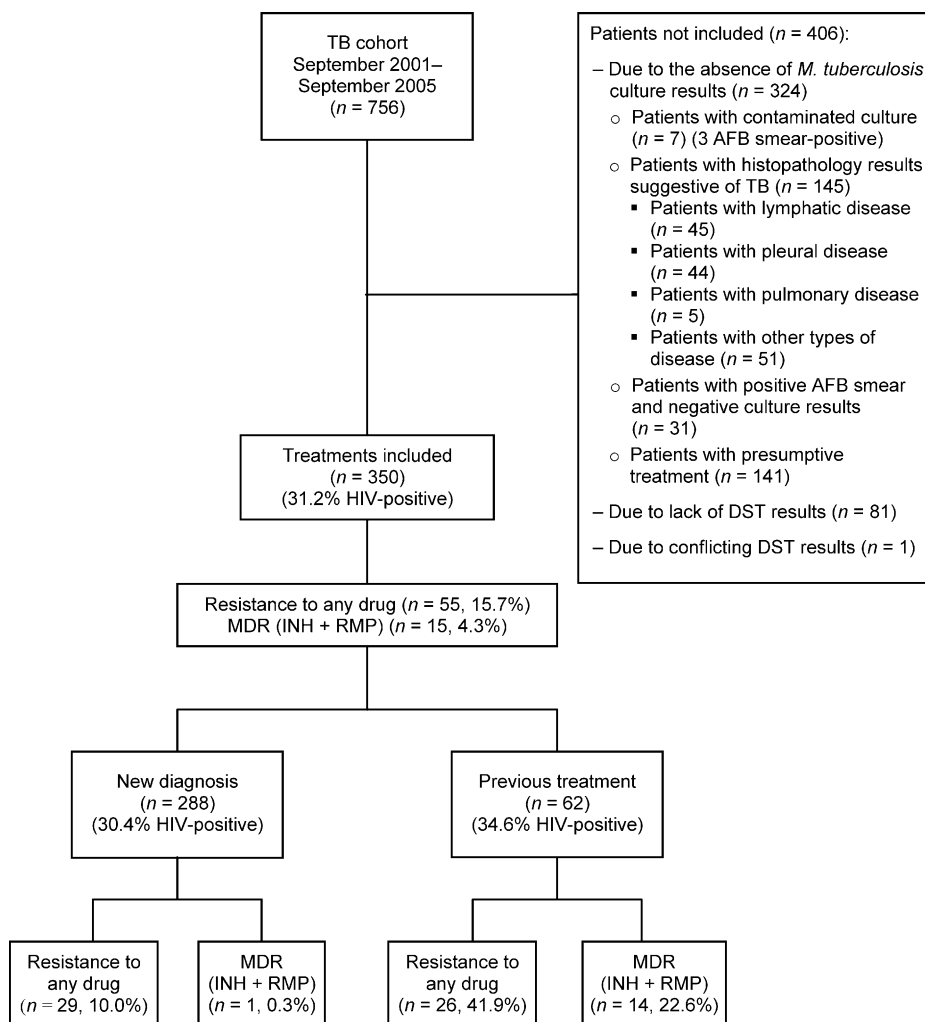
flicting DST results was excluded from the analysis (Figure).

We studied 344 patients who received a total of 350 courses of TB treatment during the study period; 62 (17.7%) of these were patients with a previous history of TB treatment. Six were treated twice at the CFFH/TDI and data from both courses of treatment were analysed. The remaining 56 patients with a history of previous TB had been treated in other health care units in the city.

The median age of the patients was 39 years (interquartile range 28–52) and 223 (63.7%) were male. Around half of the patients were White ( $n = 166$ , 51.5%); among the non-White patients, 87 (27.0%) were Black and 63 (19.6%) were of mixed race. Pulmonary TB was present in 61.8% of cases (73.3% of MDR-TB patients). Disseminated TB was present in 14.5% of cases, and was more common in HIV-positive patients (28.3%). TB-HIV co-infection was found in 31.2% of the cases tested, but HIV status was unknown for 15.7% due to unavailable HIV test results.

Resistance to any drug was found in 47 cases (15.7%); of these, 15 (4.3%) were MDR, corresponding to 4.3% of all cases. The highest prevalence of resistance (10.9%) was to INH, followed by streptomycin (7.7%) and RMP (4.9%). Primary resistance to RMP was found in one case (0.3%), who was also INH-resistant (Figure). Bivariate analysis results are shown in Tables 1 and 2.

Previous TB treatment was associated with a higher prevalence of resistance to one or more drugs and MDR-TB (PR 4.16, 95%CI 2.65–6.55 and PR 65.03, 95%CI 8.71–485.41, respectively). The time between current and previous treatment was associated with resistance to any drug, with a higher risk among those who had relapsed within 2 years of treatment (Table 1). Patients who had not completed their previous course of treatment had a higher risk of resistance, although this was not statistically significant (Table 1). There was no association between resistance and age or clinical presentation of disease, and neither of the two patients with a history of incarceration had resistant strains.



**Figure** Flowchart of patient recruitment and prevalence of resistance. TB = tuberculosis; AFB = acid-fast bacilli; DST = drug susceptibility testing; HIV = human immunodeficiency virus; MDR = multidrug resistance; INH = isoniazid; RMP = rifampicin.

**Table 1** Bivariate analysis results for resistance to any drug in all patients according to history of previous treatment

	All treatments (n = 350)					New diagnosis (n = 288)					Previous treatment (n = 62)							
	n*	% of total	PR	95%CI	P value	n*	% of total	PR	95%CI	P value	n*	% of total	PR	95%CI	P value			
Sex																		
Male	223	63.7	17.0	1		181	62.8	12.1	1		42	67.7	38.1	1				
Female	127	36.3	13.4	0.78	0.46–1.33	0.366	107	37.2	6.5	0.54	0.23–1.21	0.295	20	32.3	50.0	1.31	0.73–2.35	0.30
HIV status																		
No	203	58.0	15.3	1		169	58.7	9.5	1		34	54.8	44.1	1				
Yes	92	26.3	17.4	1.13	0.65–1.97	0.788	74	25.7	13.5	1.42	0.68–2.99	0.268	18	29.0	33.3	0.75	0.35–1.60	0.21
Alcoholism																		
No	276	78.9	15.6	1		225	78.1	9.8	1		51	82.3	41.2	1				
Yes	52	14.9	17.3	1.11	0.57–2.13	0.893	45	15.6	15.5	1.59	0.72–3.49	0.120	7	11.3	28.6	0.69	0.20–2.34	0.694
Illicit drug use																		
No	276	78.9	15.6	1		223	77.4	9.4	1		53	85.5	41.5	1				
Yes	53	15.4	18.9	1.21	0.65–2.25	0.913	47	16.3	17.0	1.80	0.85–3.83	0.137	6	9.7	33.3	0.80	0.24–2.60	0.425
Homeless																		
No	275	78.6	17.4	1		221	76.7	9.9	1		54	87.1	48.1	—				
Yes	5	1.4	40.0	2.29	0.75–6.91	0.143	5	1.7	40.0	4.01	1.27–12.61	0.0179	0	0	0	—	—	
Previous hospitalisation in a general hospital																		
No	151	43.1	17.2	1		122	42.4	9.0	1		29	46.8	51.7	1				
Yes	129	36.9	18.6	1.08	0.65–1.78	0.500	104	36.1	12.5	1.38	0.64–2.96	0.521	25	40.3	44.0	0.85	0.48–1.49	0.968
Cavitary lung disease																		
No	221	63.3	18.1	1		185	64.5	11.9	—		36	58.1	50.0	1				
Yes	74	21.2	5.4	0.29	0.11–0.80	0.006	59	20.6	0	—	15	24.2	26.6	0.53	0.21–1.31	0.079		
Health care worker																		
No	308	88.0	13.9	1		253	87.8	8.7	1		55	88.7	38.2	1				
Yes	18	5.14	11.1	0.79	0.20–3.02	0.590	15	5.2	6.7	0.76	0.11–5.30	0.819	3	4.8	33.3	0.87	0.17–4.47	0.897
Pulmonary disease																		
No	128	36.58	12.5	1		114	39.58	10.5	1		14	22.58	28.6	1				
Yes	216	61.71	18.0	1.44	0.84–2.47	0.106	169	58.68	10.0	0.95	0.47–1.92	0.708	47	75.81	46.8	1.63	0.68–3.95	0.079
Disseminated disease																		
No	294	84.00	15.9	1		240	83.33	9.5	1		54	87.10	44.4	1				
Yes	50	14.29	16.0	1.00	0.50–1.98	0.667	43	14.93	13.9	1.45	0.63–3.36	0.212	7	11.29	28.6	0.64	0.19–2.15	0.560
<2 years between previous and current treatment																		
No	328	95.3	12.2	1		NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Yes	16	4.7	68.7	5.63	3.63–8.75	>0.001	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Previous incomplete treatment																		
No	337	96.29	15.1	1		NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Yes	13	3.71	30.8	2.03	0.86–4.77	0.128	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

\* Full data were not available for all subjects. TB = tuberculosis; PR = prevalence ratio; CI = confidence interval; HIV = human immunodeficiency virus; NA = not applicable.

**Table 2** Bivariate analysis results for multidrug resistance in all patients and according to history of previous treatment\*

	All treatments (n = 350)						Patients with previous history of TB (n = 62)					
	n <sup>†</sup>	% of total	Resistance %	PR	95%CI	P value	n <sup>†</sup>	% of total	Resistance %	PR	95%CI	P value
Sex												
Male	223	63.7	3.1	1			42	67.7	14.3	1		
Female	127	36.3	6.3	2.0	0.74–5.40	0.116	20	32.3	40.0	2.8	1.12–6.98	0.03
HIV status												
No	203	58.0	4.9	1			34	54.8	26.5	1		
Yes	92	26.3	3.3	0.66	0.18–2.34	0.487	18	29.0	16.6	0.62	0.19–2.03	0.24
Alcoholism												
No	276	78.9	4.7	—			51	82.3	23.5	—		
Yes	52	14.9	0	—	—	—	7	11.3	0	—	—	—
Illicit drug use												
No	276	78.9	4.3	1			53	85.5	20.7	1		
Yes	53	15.4	1.9	0.43	0.57–3.26	0.732	6	9.7	16.6	0.80	0.12–5.18	0.912
Homeless												
No	275	78.6	5.4	—			54	87.1	25.9	—		
Yes	5	1.4	0	—	—	—	8	12.9	0	—	—	—
Previous hospitalisation in a general hospital												
No	151	43.1	5.3	1			29	46.8	24.1	1		
Yes	129	36.9	5.4	1.02	0.38–2.74	0.941	25	40.3	28.0	1.16	0.47–2.85	0.507
Cavitary lung disease												
No	221	63.3	4.9	1			36	58.1	27.8	1		
Yes	74	21.2	1.3	0.27	0.35–2.06	0.165	15	24.2	6.7	0.24	0.03–1.71	0.197
Health care worker												
No	308	88.0	3.6	1			55	88.7	20.0	1		
Yes	18	5.14	5.5	1.55	0.21–11.39	0.801	3	4.8	33.3	1.66	0.30–8.99	0.591
Pulmonary disease												
No	128	36.58	3.1	1			14	22.58	28.6	1		
Yes	216	61.71	5.1	1.62	0.53–5.01	0.116	47	75.81	21.3	0.74	0.28–2.01	0.674
Disseminated lung disease												
No	294	84.00	4.4	1			54	87.10	22.2	1		
Yes	50	14.29	4.0	0.90	0.21–3.88	0.978	7	11.29	28.6	1.28	0.36–4.59	0.602
<2 years between previous and current treatment												
No	328	95.3	1.8	1			41	71.9	12.2	1		
Yes	16	4.7	31.2	17.8	5.82–50.0	>0.001	16	28.1	31.2	2.56	0.85–7.67	0.160
Previous incomplete treatment												
No	337	96.29	3.8	1			49	79.03	24.5	1		
Yes	13	3.71	15.4	3.98	1.01–15.88	0.044	13	20.97	15.4	0.62	0.16–2.46	0.699

\* As only one patient had primary MDR-TB, it was not possible to evaluate associations.

<sup>†</sup> Full data were not available for all subjects.

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

The variables selected for inclusion in multivariate regression analysis were the following. All cases: any resistance—race, pulmonary cavities, homelessness, previous incomplete treatment, pulmonary disease and time between current and previous treatment  $\leq 2$  years; MDR-TB—pulmonary cavities, alcoholism, previous incomplete treatment and previous treatment  $\leq 2$  years before. New cases: any resistance—pulmonary cavities, illicit drug abuse and homelessness. Retreatment cases: any resistance—race, pulmonary cavities, previous treatment  $\leq 2$  years before; MDR-TB—pulmonary cavities, alcoholism, previous treatment  $\leq 2$  years before. In the final models, previous treatment history was strongly associated with resistance to any drug and MDR-TB (Tables 3 and 4). Resistance to any drug was independently associated with  $< 2$  years between previous and current treatment (Table 3). For

MDR, we found an independent association with cavities on chest radiograph (Table 4). Among never treated patients, homelessness was found to be independently associated with any resistance (Table 3). No assumptions could be made about acquired resistance, as none of the homeless patients had a history of previous TB treatment. There were no statistically significant trends in resistance rates during the years of the study (data not shown).

## DISCUSSION

Our study found a low prevalence of drug resistance, as previously described in hospitals in developing countries.<sup>7–13</sup> The MDR-TB rate is also similar to those described in the same settings.<sup>8–16</sup> Although our prevalence of primary MDR-TB was lower than those

**Table 3** Multivariate adjusted prevalence ratios and their 95% confidence intervals for the association between any resistance and selected variables

Variables	PR	95%CI	P value
All cases			
Previous TB treatment			
No previous treatment	1.00		
Previous treatment	3.75	2.28–6.17	<0.001
<2 years between previous and current treatment			
No	1.00		
Yes	1.94	1.06–3.56	0.03
Cases with no previous treatment history			
Homeless			
No	1.00		
Yes	4.90	1.69–14.20	0.003
Cases with previous treatment history			
<2 years between previous and current treatment			
No	1.00		
Yes	2.46	1.24–4.89	0.01

PR = prevalence ratio; CI = confidence interval; TB = tuberculosis.

described elsewhere in developing countries, the small number of patients with MDR-TB in this study does not allow further conclusions to be drawn.<sup>7,8,11–13,15,17</sup>

In comparison to previously reported data from Brazil,<sup>18</sup> we found a higher rate of any resistance, mainly due to acquired resistance. It is important to highlight that the prevalence of primary resistance found in our study was similar to that reported in a national survey among clinical isolates from patients who attended primary health care facilities.<sup>18</sup> We also found a lower prevalence of primary resistance, especially MDR, compared to studies performed in other hospitals in the city of RJ.<sup>19,20</sup>

The high prevalence of acquired resistance found in this study suggests that the measures of disease control applied by the TB control programme of the city of RJ are inadequate.<sup>25</sup> The lower rate of primary drug resistance may be due to the implementation of the hospital TB control programme, which helped prevent transmission to the hospital's patients and health care professionals. Three points corroborate this assumption. First, only 10% of the patients with a previous history of TB had been treated in our hospital during the previous episode, suggesting adequate treatment and consequently low rates of relapse. Second, we did not find a higher risk of drug-resistant disease among health care workers, as has been described in another hospital in the city with similar characteristics.<sup>20</sup> Finally, our results show a reduction in the rate of primary resistance, especially MDR, compared to a study conducted in the same establishment before the implementation of the control programme, suggesting low transmission of drug-resistant bacilli to individuals without previous TB.

The implementation of the TB control programme established a risk assessment process through admin-

**Table 4** Multivariate adjusted prevalence ratios and their 95% confidence intervals for the association between MDR and selected variables

Variables	PR	95%CI	P value
All cases			
Previous TB treatment			
No previous treatment	1.00		
Previous treatment	55.4	7.58–405.72	<0.001
Cavities on chest radiography			
No	1.00		
Yes	3.37	1.53–7.46	<0.001
Cases with previous treatment history			
<2 years between current and previous treatment			
No	1.00		
Yes	2.46	1.24–4.89	0.01
Cavities on chest radiography			
No	1.00		
Yes	2.95	1.25–6.92	<0.001

MDR = multidrug resistance; PR = prevalence ratio; CI = confidence interval; TB = tuberculosis.

istrative, environmental and respiratory protection control measures, improving the identification and isolation of patients with infectious TB. Although the implementation of such measures is expensive, we believe the cost is justified, as it is estimated that one third of RJ's new cases of TB are still diagnosed in hospitals.<sup>26</sup>

Resistance was associated with one or more courses of previous TB treatment (PR 3.75, 95%CI 2.28–6.17,  $P < 0.001$ ). Relapse within 2 years of the last TB episode was also associated with resistance (PR 1.94, 95%CI 1.06–3.56,  $P = 0.03$ ), although in the case of MDR-TB the association was not statistically significant. These results were expected: drug resistance has been reported in the literature to be related to previous TB treatment, especially in the case of non-adherence,<sup>27–30</sup> increasing the risk of relapse within a short period of time.

Homelessness was associated with resistance to any drug in patients who had not been treated previously (PR 4.90, 95%CI 1.69–14.20,  $P = 0.003$ ), in agreement with the results of previous studies.<sup>31,32</sup> As we had a small number of homeless patients, all of them newly diagnosed, no further conclusions could be drawn. Patients with cavitory pulmonary disease had a higher association with MDR-TB (PR 3.37, 95%CI 1.53–7.46,  $P < 0.001$ ), a finding also reported by other authors.<sup>30,33,34</sup>

As has been previously described, previous incomplete treatment, alcoholism, drug abuse or admission to a general hospital were not confirmed as independent variables associated with MDR.<sup>27</sup> It is possible that a larger sample would yield different results.

Our study has several limitations. As the study was performed in a tertiary health unit that serves as a reference centre for the treatment of patients with extra-pulmonary TB and HIV/AIDS, the results cannot be generalised to other settings. Information bias may have occurred, as the study was performed retro-

spectively and because incomplete data are common in medical records. Selection bias is another potential problem, as we studied a convenience and not a probabilistic sample, and it is possible that the population studied does not represent the target population, i.e., patients with TB attending general hospitals in the city of RJ. Another limitation of the study is that the DST profile was available only for five drugs, and testing for pyrazinamide was not possible. In addition, the small number of MDR-TB patients limited the analysis of factors associated with this outcome. Nonetheless, the routine TB programme made it possible to study primary resistance, as all patients had DST results available, independent of previous suspected resistance.

This study shows lower drug resistance rates than previously described in other RJ city hospitals.<sup>19,20</sup> However, our data suggest that drug-resistant disease should be suspected when treating TB in RJ city hospitals, especially in patients with a history of previous treatment. The RJ TB control programme has been extending DOTS coverage to improve rates of successful treatment completion; however, in addition to this strategy our data indicate that drug resistance monitoring should also be a priority. Our study also shows that the implementation of an effective hospital TB control programme in developing countries can prevent TB transmission among patients and health care workers, even in referral hospitals located in high TB prevalence settings. Finally, drug resistance surveys should be performed in other RJ health care units to allow data comparisons.

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## RÉSUMÉ

**CONTEXTE :** Un hôpital de référence pour la tuberculose (TB) et le virus de l'immunodéficience humaine/syndrome de l'immunodéficience acquise (VIH/SIDA) dans le cadre d'un programme de lutte antituberculeuse à Rio de Janeiro, Brésil.

**OBJECTIF :** Estimer la prévalence de la résistance aux médicaments antituberculeux et identifier les facteurs qui y sont associés.

**SCHEMA :** Etude transversale. On a colligé les données cliniques et de laboratoire de manière rétrospective entre 2001 et 2005. Ont été considérés comme éligibles les patients chez qui *Mycobacterium tuberculosis* a été isolé et qui disposaient des tests de sensibilité aux médicaments. On a colligé et analysé par le test  $\chi^2$ , les tests de Mann-Whitney et la régression de Poisson les données sur les caractéristiques démographiques, les facteurs de risque de résistance, la sérologie VIH et les antécédents de TB.

**RÉSULTATS :** Nous avons analysé 350 traitements, dont

62 correspondaient à des patients ayant été traités antérieurement pour la TB. Le statut VIH a été positif dans 31,2% des cas. On a trouvé une résistance dans 15,7% des cas et une TB multirésistante dans 4,3% des cas. Un traitement antérieur ( $P < 0,01$ ) et une rechute dans les 2 ans ont été en association avec la résistance ( $P < 0,03$ ). Les cavités pulmonaires sont en association avec la multirésistance ( $P < 0,001$ ). Le fait d'être sans domicile a été trouvé en association avec tout type de résistance chez les patients nouveaux ( $P < 0,01$ ). Le fait de travailler à l'hôpital n'est pas associé à la résistance.

**CONCLUSION :** Dans les hôpitaux de Rio de Janeiro, il est nécessaire de suspecter une maladie à germes résistants aux médicaments chez les patients ayant été traités antérieurement pour une TB. La mise en œuvre d'un programme efficace de lutte contre la TB hospitalière peut prévenir la transmission même dans un contexte à prévalence élevée de TB.

## RESUMEN

**MARCO DE REFERENCIA :** Un hospital de referencia para tuberculosis (TB), infección por el virus de la inmunodeficiencia humana (VIH) y síndrome de inmunodeficiencia adquirida (SIDA) con un programa de control de la TB en Río de Janeiro, Brasil.

**OBJETIVO :** Calcular la prevalencia de resistencia a los medicamentos antituberculosos y definir los factores asociados con la misma.

**MÉTODOS :** Fue este un estudio transvesal en el cual se recogieron datos clínicos y de laboratorio de 2001 a 2005. Se incluyeron pacientes en quienes se había aislado *Mycobacterium tuberculosis* y contaban con pruebas de sensibilidad a los medicamentos. Se copiaron datos sobre las características demográficas, los factores de riesgo de resistencia, el estudio serológico del VIH y los antecedentes de TB y se analizaron mediante las pruebas de  $\chi^2$  y de Mann-Whitney y el modelo regresivo de Poisson.

**RESULTADOS :** Se analizaron 350 tratamientos y 62 de

estos pacientes presentaban antecedente de TB. La prueba serológica del VIH fue positiva en 31,2% de casos. Se encontró farmacoresistencia en 15,7% y multidrogoresistencia en 4,3% de casos. Los antecedentes de tratamiento previo ( $P < 0,001$ ) y de recaída en 2 años ( $P < 0,03$ ) se asociaron con resistencia. La presencia de cavernas pulmonares se asoció con multidrogoresistencia ( $P < 0,001$ ). La falta de domicilio se asoció con cualquier resistencia en pacientes sin antecedente de TB ( $P < 0,01$ ). No se encontró correlación entre trabajo en el hospital y resistencia.

**CONCLUSIÓN :** En los hospitales de Río de Janeiro, se debe considerar la presunción de enfermedad farmacoresistente en pacientes con antecedente de TB. La aplicación de un programa hospitalario eficaz de control de la TB puede prevenir la transmisión, incluso en entornos con una alta prevalencia.