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## Abstract

**Objective:** to analyze the association between tuberculosis mortality and socio-demographics and health indicators in the capitals of Brazilian states and the Federal District. **Methods:** this is an ecological study whose outcome was the standardized coefficient of tuberculosis mortality in the 2008-2010 period; the independent variables comprised 16 indicators, grouped into three blocks; Pearson correlation test and multiple linear regression were applied for analysis. **Results:** 4,744 deaths from tuberculosis were registered in the 27 municipalities (2.7 deaths per 100,000 inhabitants); the following indicators were associated with tuberculosis mortality ( $p < 0.10$ ): income inequality (Gini index of monthly income of individuals over 10 years old:  $\beta = 0.454$ ; 95%CI 6.21;28.51), proportion of migrants in the municipality ( $\beta = 0.537$  95%CI 0.12;0.31), poor black-skinned individuals ( $\beta = 0.302$  95%CI 0.004;0.109) and coefficient of Tb/HIV coinfection ( $\beta = 0.449$  95%CI 0.05;0.28). **Conclusion:** tuberculosis mortality was higher in capitals with greater income inequality, migration, poverty among black-skinned individuals and occurrence of Tb/HIV coinfection.

**Keywords:** Tuberculosis; Mortality; HIV Infections; Health Inequalities; Ecological Studies.

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## Introduction

Tuberculosis is an important Public Health problem worldwide, being one of the main causes of death in adults among the communicable diseases. The high prevalence, associated with the potential of dissemination, turned tuberculosis into an emerging condition, with high and increasing levels of morbidity and mortality, especially in poor countries, where 95% of new cases and 98% of deaths are registered.<sup>1</sup>

In 2014, 9.6 million cases of tuberculosis were estimated, with 6 million new cases and 1.5 million deaths worldwide. Despite the 45% decrease in prevalence since the 1990s, 11 out of the 22 countries that host 80% of the cases have not achieved the target settled by the World Health Organization (WHO), which was to reduce by half the incidence, prevalence and mortality due to the disease until 2015.<sup>2</sup> Among the reasons for such failure, we can highlight the relation between tuberculosis and poverty and social exclusion, core issues from vulnerability to sickness.<sup>3</sup>

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In Brazil, from 2005 to 2014, there was a decrease in the coefficient of tuberculosis incidence, from 41.5 cases to 33.5 new cases *per* 100 thousand inhabitants. A reduction in mortality coefficients was also registered: from 2.8 to 2.3 deaths/100 thousand inhabitants, between 2004 and 2013, representing an average decrease of 2.3% per year in this period. Brazilian state capitals with the highest incidence coefficients in 2013 were, respectively, Porto Alegre, Cuiabá, Recife, Manaus and Belém.<sup>2</sup>

Since they are urban centers with higher job offers, state capitals constitute great agglomerates of populations and migrants concentration, characteristics which are prone to increasing social inequalities, freedom deprivation and homeless.<sup>4,5</sup> These groups, together with individuals co-infected by the human immunodeficiency virus (HIV) and those who abandon treatment, are the most affected individuals by the disease who and present the highest levels of mortality.<sup>6-13</sup>

Considering mortality as a marker for the effectiveness of the disease's prevention and control strategies, the aim

of this study was to analyze the ecological association between tuberculosis mortality and socio-demographic indicators, as well as indicators of health and access to health services in Brazilian state capitals and the Federal District.

## Methods

This is an ecological study with database from the Ministry of Health's Mortality Information System (SIM) and of the Primary Health Care Information System (SIAB), as well as of the National Household Sample Survey (PNAD), from the Brazilian Institute of Geography and Statistics (IBGE), which had as units of analysis the 26 Brazilian state capitals and the Federal District (27 municipalities), and the 2008 to 2010 period.

The dependent variable was the average standardized coefficient of tuberculosis mortality *per* 100 thousand inhabitants in the Brazilian state capitals, from 2008 to 2010. To calculate the coefficient, we used the number of deaths from tuberculosis and the population size in the period analyzed. Tuberculosis mortality rates were adjusted through the direct method of standardization, using the standard-population provided by WHO for the 2000-2025 period. Standardization enables the comparison between different regions with different demographic and age groups patterns, which is the case of Brazilian state capitals. The number of deaths due to tuberculosis was obtained from SIM, based on the code-records A15 to A19 from the International Statistical Classification of Diseases and Related Health Problems – 10th Revision (ICD-10).<sup>14</sup>

The independent variables comprised 16 indicators, grouped into three blocks (Figure 1). The coefficients of tuberculosis mortality and the explanatory variables were described using average, standard deviation, maximum and minimum value. The association between the variables was analyzed through Pearson correlation coefficient. The independent variables which presented statistic association ( $p < 0.10$ ) with the outcome in the bivariate analysis were included into the multiple linear regression model, through the "backwards" method.

The regularity in the variables distribution was analyzed by applying Shapiro-Wilk test. The analyses were performed with the Statistical Package for the Social Sciences (SPSS) version 18.0. The research was approved by the Ethics and Research Committee from the Federal University of Rio Grande do Sul (UFRGS): Report No. 572.013.

Block	Indicators	Indicator's Description	Source, Year
Socio-demographic Indicators	Gini Index	Assesses the monthly income inequality of people over 10 years old	PNAD, <sup>a</sup> 2008
	Human Development Index	Compound Index, which incorporates three dimensions of human development: income, education and health	IBGE, <sup>b</sup> 2008
	Proportion of poor individuals	Proportion of poor individuals <sup>c</sup>	PNAD, 2008
	Proportion of poor light-skinned or white people	Percentage of people of light color or white race that are poor	IBGE, 2008
	Proportion of poor black-skinned individuals	Percentage of black-skinned individuals who are poor	IBGE, 2008
	Illiteracy rate	Percentage of people who cannot read or write	IBGE, 2008
	Unemployment rate	Percentage of EAP <sup>d</sup> who are unemployed (open but secret)	IBGE, 2008
	Migration rates	Percentage of people who are not from that municipality	PNAD, 2008
	Proportion black-skinned individuals	Percentage of black individuals (black plus brown-skinned)	PNAD, 2008
Health Indicators	Coefficient of AIDS mortality	Number of deaths by AIDS <i>per</i> 100 thousand inhabitants	SIM, <sup>e</sup> 2008-2010
	Ill-defined causes of death	Number of deaths by ill-defined causes <i>per</i> 100 thousand inhabitants	SIM, 2008-2010
	Coefficient of hospitalization due to tuberculosis	Number of hospitalizations due to tuberculosis <i>per</i> 100 thousand inhabitants	SIH, <sup>f</sup> 2008-2010
	Coefficient of HIV/Tuberculosis co-infection	Number of individuals infected with HIV and tuberculosis <i>per</i> 100 thousand inhabitants	Sinan, <sup>g</sup> 2008-2010
Access to Health Services Indicators	Population coverage by the Family Health Strategy	Percentage of individuals covered by the Family Health Strategy team	Siab, <sup>h</sup> 2008-2010
	Population coverage by health community agents	Percentage of individuals covered by the health community agents	Siab, 2008-2010
	Number of physicians	Number of physicians <i>per</i> 1 thousand inhabitants	SIRH, <sup>i</sup> 2008-2010

a) PNAD: National Household Sample Survey

b) IBGE: Brazilian Institute of Geography and Statistics

c) Household income *per capita* of up to BRL150.00 per month, according to parameters of the Institute for Applied Economic Research (Ipea)

d) EAP: economically active population

e) SIM: Mortality Information System

f) SIH-SUS: National Hospital Information System

g) Sinan: Information System for Notifiable Diseases

h) Siab: Primary Health Care Information System

i) SIRH: SUS Human Resources Information System

**Figure 1 – Socio-demographic, health and services access variables**

## Results

In the 2008-2010 period, 4,744 deaths due to tuberculosis were registered in the 26 Brazilian state capitals and the Federal District; 23% of the Brazilian population lived in those municipalities and they concentrated 33% of the deaths due to tuberculosis that had occurred in the country. The standardized coefficient of tuberculosis mortality was of 2.5 deaths per 100 thousand inhabitants in the analyzed period, ranging from 6.4/100 thousand inhabitants in Manaus to 0.1/100 thousand inhabitants in Palmas (Figure 2).

In 13 Brazilian state capitals, the coefficients of tuberculosis mortality were above average: Manaus and Belém (North region); Recife, Maceió, São Luís, Salvador and Teresina (Northeast region); Cuiabá (Midwest region); Rio de Janeiro (Southeast region); and Porto Alegre (South region) (Figure 2).

In the description of independent variables (Table 1), the high proportion of poor individuals (33%), migrants (38%) and of mortality due to AIDS (18 deaths/100 thousand inhabitants) was evident. The proportion of black-skinned poor individuals was higher than the proportion of white-skinned poor individuals, and approximately 50% of the population living in state capitals was covered by actions of the community health agents and the Family Health Strategy (FHS) (Table 1).

When the correlation test between the standardized coefficient of tuberculosis mortality and the independent variables presented in Table 2 was applied, the association between tuberculosis mortality and income inequality measured by the Gini index of income of people over 10 years old. The following variables also demonstrated association with tuberculosis mortality, according to Table 2 ( $p < 0.10$ ): proportion of poor individuals, proportion of poor black-skinned individuals, proportion of poor white-skinned individuals, migration rate, HIV/tuberculosis coefficient of co-infection, population coverage of the Family Health Strategy and of community health agents.

After applying the multiple linear regression model, and adjusting it (Table 3), we observed that four variables remained significantly associated with tuberculosis mortality: Gini index ( $\beta = 0.454$ ;  $p = 0.001$ ), migration rate ( $\beta = 0.537$ ;  $p = 0.002$ ), HIV/tuberculosis coefficient of co-infection ( $\beta = 0.449$ ;  $p < 0.006$ ) and proportion of poor black-skinned individuals ( $\beta = 0.302$ ;  $p = 0.065$ ). The model presented a predictive capacity of the outcome of 62% ( $r^2 = 0.620$ ).

## Discussion

Tuberculosis mortality was higher in capitals with higher income inequality, higher migration rates, higher proportion of poor black-skinned individuals and greater HIV/tuberculosis co-infection coefficients.

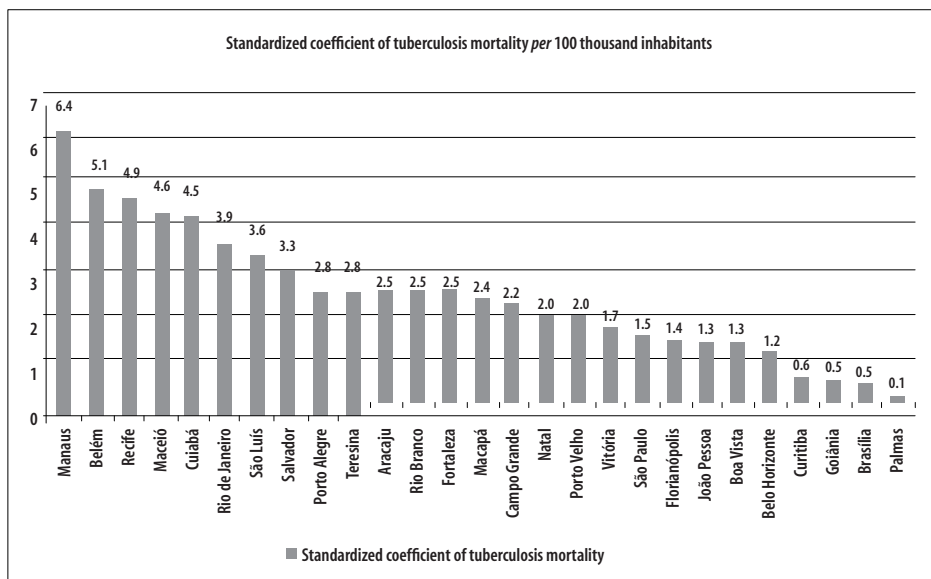


Figure 2 – Average standardized coefficient of tuberculosis mortality (per 100 thousand inhabitants) in Brazilian state capitals and the Federal District, 2008-2010

**Table 1 – Description of the explanatory variables of the study on tuberculosis mortality in Brazilian state capitals and the Federal District, 2008-2010**

Indicators	Average	Standard-deviation	Values: minimum; maximum
Gini Index	0.5	0.1	0.4;0.5
Proportion of poor individuals (%)	33.4	12.7	5.4;58.4
Proportion of poor black-skinned individuals (%)	27.9	9.1	13.0;42.6
Proportion of poor white-skinned individuals (%)	16.3	7.8	5.1;28.6
Human Development Index (HDI)	0.8	0.1	0.5;0.9
Unemployment rate (%)	8.3	2.5	4.6;12.7
Illiteracy rates (%)	4.9	2.5	1.9;11.3
Migration rates (%)	37.6	10.9	22.2;75.0
Proportion of black-skinned individuals (%)	56.6	17.1	14.1;79.5
III-defined causes of death	8.7	13.1	1.1;67.2
Coefficient of AIDS mortality ( <i>per 100,000 inhab.</i> )	18.3	12.8	4.5;70.5
Coefficient of hospitalizations due to tuberculosis ( <i>per 100,000 inhab.</i> )	14.9	7.0	2.1;36.9
Coefficient of HIV/tuberculosis co-infection ( <i>per 100,000 inhab.</i> )	5.2	4.9	0.8;24.4
Population coverage from the Family Health Strategy (%)	43.9	25.6	7.6;94.9
Population coverage from health community agents (%)	52.9	28.1	14.2;100.0
Number of physicians ( <i>per 1 thousand inhab.</i> )	2.5	1.0	1.2;4.9

**Table 2 – Pearson correlation between the coefficient of tuberculosis mortality and independent variables, in Brazilian state capitals and the Federal District, 2008-2010**

Indicators	r <sup>a</sup>	p-value
Gini Index	0.405	0.022
Proportion of poor individuals	0.383	0.048
Proportion of poor black-skinned individuals	0.527	0.005
Proportion of poor white-skinned individuals	0.246	0.020
Human Development Index (HDI)	-0.180	0.369
Unemployment rate	0.191	0.247
Illiteracy rates	0.147	0.121
Migration rates	0.663	0.000
Proportion of black-skinned individuals	0.269	0.458
III-defined causes of death	-0.247	0.214
Coefficient of AIDS mortality	-0.195	0.274
Coefficient of hospitalizations due to tuberculosis	0.191	0.224
Coefficient of HIV/tuberculosis co-infection	0.463	0.011
Population coverage from the Family Health Strategy	-0.388	0.080
Population coverage from health community agents	-0.381	0.079
Number of physicians	-0.277	0.162

a) r: Pearson correlation coefficient

To proceed to the analysis of tuberculosis mortality, the standardized rates per sex and age group were used. This analytical routing refers to the fact that young adult men are the group under greater risk of death due to tuberculosis.<sup>7-9</sup>

These findings corroborate to the current knowledge on tuberculosis epidemiology, which highlights some of the social groups most affected by the disease: individuals with low income, migrants and those who are HIV/tuberculosis co-infected.<sup>7</sup> The Gini index, which indicates differences in income distribution, contributed to analyze social inequalities which, associated with difficulties in accessing health services, decrease life quality, compromise people's health and can be a factor associated to tuberculosis mortality.<sup>15,16</sup>

The ecological association with social inequality which was observed in the current study is similar to national<sup>7-10</sup> and international<sup>12,17-20</sup> studies, through which we can observe that the risk of dying from tuberculosis increases significantly in scenarios where the social inequality results in the rise of poverty, the decrease of housing and food conditions and the precarious environment, working relations, health and education services available to the population.

This association is also observed at an individual scale. Individuals with low income and education level are

more vulnerable to the worsening of health conditions related to tuberculosis, to therapeutic flaw and to low treatment adherence.<sup>17</sup> These situations, when analyzed in the field of tuberculosis control, can be related to the insufficient knowledge on the disease, the little attention given to therapeutic adherence and to therapy costs for the patients, relatives and the health system.<sup>18</sup>

It is important to observe that these demands are covered by the Brazilian tuberculosis control programs, by the free distribution of medication and by the directly observed treatment short-course (DOTS); this latter is one of the main technical-organizational investments of the National Program for Tuberculosis Control, which suggests social rehabilitation, self-esteem improvement, professional training and tackling other social barriers.<sup>21</sup>

Another association with tuberculosis mortality found in this study is related to the group of poor black-skinned individuals, which instigates the discussion on social vulnerability and, in order to broaden the explanatory horizon, racism and its consequences for the black population in Brazil – a topic included in the debate on unfavorable outcomes in health.<sup>3</sup> In this sense, it is necessary to invest, in terms of quality and quantity, in intersectoral approaches in Education, Social Assistance, Justice and Health in order to achieve a better effect of actions in contexts of social inequity.<sup>3,18</sup>

**Table 3 – Multiple linear regression model between the coefficient of tuberculosis mortality and independent variables, in Brazilian state capitals and the Federal District, 2008-2010**

Indicators	Standardized Beta $\beta$ Coefficient	95%CI <sup>a</sup>	p-value
<b>Entry Model</b>			
Gini Index	0.341	17.487 (6.57;19.48)	0.011
Proportion of poor individuals	0.085	0.010 (-0.59;0.080)	0.755
Migration rates	0.528	0.077 (-0.13; 0.79)	0.007
Coefficient of HIV/tuberculosis co-infection	0.357	0.149 (-0.08;0.29)	0.087
Population coverage from the Family Health Strategy	-0.028	-0.008 (-0.09;0.05)	0.871
Population coverage from health community agents	0.011	0.036 (0.05;0.03)	0.851
Proportion of poor black-skinned individuals	0.451	0.078 (-0.144;0.301)	0.472
Proportion of poor white-skinned individuals	0.198	0.040 (-0.276;0.195)	0.726
<b>Final Model</b>			
Gini Index	0.454	21.149 (6.21;28.51)	0.001
Migration rates	0.537	0.780 (0.12;0.31)	0.002
Coefficient of HIV/tuberculosis co-infection	0.449	0.181 (0.05;0.28)	0.006
Proportion of poor black-skinned individuals	0.302	0.053 (-0.004;0.109)	0.065

a) 95%CI: 95% confidence interval

The literature demonstrates that migration processes contribute to worsening life condition in big urban areas, with two aspects to be considered. One of them refers to the fact that in these urban centers the government must take in migrants, many times without having the structure to respond to the new demands they represent.<sup>15,19-20</sup> Another aspect to be taken into consideration is related to the poor assistance of health services, which increases the possibility of irregularities and/or abandonment of medication treatment, situations related to the appearance of multidrug-resistant tuberculosis.<sup>17</sup>

In Brazil, from 1950 to 2010, the population resident in urban areas increased from 36 to 84%, as a consequence, mainly, from the disbanding of small rural properties, land loss for debt payment, the need to escape from inhospitable climate conditions, conflicting environments and violence contexts.<sup>22</sup> The relation between migration, poverty and lack of access to medical assistance given by Health Care is believed to act synergistically in the rise of chances of dying by tuberculosis.

At an individual scale, we can observe that migrants in poverty situation are more susceptible to become ill because they hardly ever have subsistence resources, whilst others live in a situation of poor households or on the streets, with fragile social support networks.<sup>10,24-25</sup> Besides that, we can also mention the access restrictions to primary health care units, which aim their assistance actions to the resident population of the municipality.<sup>20,26</sup>

In Barcelona, Spain, an increase in tuberculosis incidence has been observed since the 2000s, which was boosted by the strong immigration flow. In this scenario, managers have created specific health policies, such as the incorporation of agents who acted as translators and cultural mediators, monitoring households and hospitals.<sup>24</sup> In Malawi, one of the prioritized African countries by WHO for the implementation of tuberculosis control strategies, good results were reached with collective efforts for registering households, since many people did not access free treatment for not having this registration.<sup>20</sup>

In the Brazilian context, besides the internal migration flows, registered since 2005, there has been an increasing amount of Latin Americans and Africans entering the country.<sup>25</sup> A study conducted in the municipality of São Paulo, for the period from 1998 to 2008, presented high incidence of tuberculosis in areas where Bolivian migrants lived. The members of the Bolivian community had the same opportunities of

access and quality of health assistance as São Paulo's citizens, contributing to more favorable outcomes in the illness process.<sup>26</sup>

The association found between tuberculosis mortality and HIV/tuberculosis co-infection validates WHO data which indicate tuberculosis as the comorbidity that most determines the death of individuals with AIDS in Brazil.<sup>2</sup> Worldwide, in 2014, 1.2 million of the 6 million new tuberculosis cases occurred among people infected with HIV.<sup>1</sup>

One of the best known problems regarding HIV/tuberculosis co-infected mortality is that most people in this condition are not aware of their positive serology for HIV and, consequently, do not receive antiretroviral therapy (ART). A study conducted in Porto Alegre-RS, the Brazilian municipality and state capital with the highest incidence of HIV/tuberculosis co-infection, revealed that in 21.1% of new cases and in 20% of prevalent tuberculosis cases registered between 2007 and 2011, the test to detect HIV had not been done.<sup>11</sup>

Considering that the high prevalence of HIV is an important risk factor for tuberculosis,<sup>27</sup> it is evident that the mutual collaboration among the government programs responsible for preventing, treating and managing these diseases<sup>3,11,19</sup> may not be working well. Currently, these programs are proposed by the federal branch of the government, through the Department of STD, AIDS and Viral Hepatitis and the National Program for Tuberculosis Control, both from the Ministry of Health.

We did not observe any association between tuberculosis mortality and the coverage of the Family Health Strategy and the community health agents program. In this sense, the coverage of these strategies for health care is to be thought and allocated aiming to minimize limitations of geographical and functional access, continuing to improve the quality and resolution of the offered care. Possibly, this relation between the qualification of primary health care and the reduction of hospitalizations and deaths by tuberculosis in the country, is less sensible to the Public Health sector, although it is not less important in a short term.

Studies<sup>12,19</sup> of global relevance suggest that the decrease in tuberculosis incidence is more strongly related to biological, social and economic determinants, than to the performance of diagnosis, treatment and control programs. In Brazil, according to some authors,<sup>28</sup> the introduction of cash transfer programs to poorer populations, the existence of the Brazilian National

Health System – SUS – and social and environmental improvements are essential to the effectiveness of infectious diseases' control.

This issue was also discussed by authors that examined Colombia's tuberculosis control policy,<sup>29</sup> one of the 15 countries that, together with Brazil, answer for 73% of the notified cases of the disease in the Americas.<sup>30</sup> They observed that the dismantling of Colombia's national health system and the management privatization of their resources, since 1993, created a negative impact on the performance indicators from that country's Program for Tuberculosis Control.<sup>29</sup>

This study is susceptible to ecological fallacy, which is the causal relation inference between tuberculosis mortality in migrants, poor black-skinned, people in social inequality situation and HIV co-infected, nonetheless tuberculosis can lead to the death of individuals who do not belong to the groups that presented association with the outcome.

The analysis in this study should be improved in future researches, aiming to better understand the vulnerability of the social groups that are more affected by tuberculosis. Appropriate contributions may arise from approaches dedicated to social determinants

in health,<sup>4</sup> among which we can cite (i) the macro-structural determinants (poverty, income inequality, health service access) and (ii) proximal determinants, which focus on the illness, the severity of clinical pictures, the appropriate condition for diagnosis and treatment adherence.

In this perspective, we recommend, beyond macro-structural and proximal determinants, to also consider the analysis of illness paths<sup>3</sup> and therapeutic itineraries outlined by individuals affected by tuberculosis. Such analyses cover the cultural interferences and the social mediations and among the different matrices which can negatively impact, both in sickness and health care, competing to unfavorable outcomes.

### Authors' contributions

All authors contributed to the concept and design of the study, analysis and interpretation of data, writing and critical review of the intellectual content of the manuscript, have approved its final version and declared to be responsible for all aspects of the study, ensuring its accuracy and integrity.

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Received on 17/07/2015  
Approved on 13/09/2016