

Tuberculosis, HIV, and poverty: temporal trends in Brazil, the Americas, and worldwide*

Tuberculose, HIV e pobreza: tendência temporal no Brasil, Américas e mundo

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Abstract

Objective: To analyze the temporal trends of the incidence and prevalence of tuberculosis, with and without HIV co-infection, as well as of the associated mortality, in Brazil, the Americas, and worldwide. **Methods:** We collected data related to tuberculosis, with and without HIV co-infection, between 1990 and 2010, in Brazil, the Americas, and worldwide. Temporal trends were estimated by linear regression. **Results:** We identified a trend toward a decrease in tuberculosis prevalence and mortality, and that trend was more pronounced in Brazil and the Americas than worldwide. There was also a trend toward an increase in the incidence of tuberculosis/HIV co-infection, as well as in the rates of detection of new cases of active and latent tuberculosis. The incidence of tuberculosis was found to trend downward in Brazil, whereas it trended upward worldwide. Tuberculosis incidence rates correlated positively with poverty rates and with HIV incidence rates. **Conclusions:** Social inequality and the advent of AIDS are the major factors that aggravate the current situation of tuberculosis. In this context, methodical approaches to the assessment of surveillance activities are welcome, because they will identify situations in which the reported tuberculosis data do not reflect the true incidence of this disease.

Keywords: Tuberculosis/epidemiology; HIV; Socioeconomic factors.

Resumo

Objetivo: Analisar a tendência temporal das taxas de prevalência, incidência e mortalidade por tuberculose, associada ou não com HIV, no Brasil, nas Américas e no mundo. **Métodos:** Foram coletados os dados relacionados à tuberculose, com e sem coinfeção por HIV, entre 1990 e 2010, no Brasil, nas Américas e no mundo. As tendências foram estimadas por regressão linear. **Resultados:** Foi identificada uma tendência de redução nas taxas de prevalência e mortalidade de tuberculose, que foi maior no Brasil e nas Américas que no mundo. Houve uma tendência crescente na incidência da coinfeção tuberculose/HIV e nas taxas de detecção de casos de tuberculose ativa e latente. Houve uma tendência de redução da incidência de tuberculose no Brasil, mas de aumento dessa no mundo. Houve uma correlação direta das taxas de incidência de tuberculose com as taxas de pobreza e as taxas de incidência de HIV. **Conclusões:** Desigualdades sociais e o advento da AIDS são os principais fatores que agravam a atual situação da tuberculose. Nesse contexto, abordagens metodológicas para a avaliação das ações de vigilância da tuberculose são bem-vindas, pois essas indicarão situações de dados de notificação da tuberculose que não reflitam a verdadeira incidência dessa doença.

Descritores: Tuberculose/epidemiologia; HIV; Fatores socioeconômicos.

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Introduction

Tuberculosis is a public health problem worldwide, being known as “the neglected calamity”⁽¹⁾ and remaining unresolved in the 21st century.⁽²⁾

It was estimated that 11% of all adults with tuberculosis in 2001 were co-infected with HIV or had AIDS.⁽³⁾ The World Health Organization (WHO) estimated that 14% of the 72% of tuberculosis patients tested for HIV in 2009 were found to be HIV-positive.⁽⁴⁾ In mortality surveillance systems, co-infection rates have been reported to be as high as 51% in Rio de Janeiro, Brazil.⁽⁵⁾

The increase in the rates of tuberculosis/HIV co-infection poses challenges that prevent the reduction in the incidence of both infections, and these challenges have been well documented in recent years. The increase in the overall prevalence of HIV has serious implications for tuberculosis control programs, particularly in countries in which the prevalence of tuberculosis is high. In addition to contributing to an increase in the number of tuberculosis cases, HIV has been a major factor responsible for increased mortality among co-infected patients.⁽⁶⁾

Since the 1980s, HIV has been a major factor contributing to the resurgence of tuberculosis in developed and developing countries alike.^(7,8) The virus has altered the balance between human beings and Koch’s bacillus, as well as having a noticeable impact on the epidemiology, natural history, and clinical evolution of tuberculosis.^(9,10) Co-infection with tuberculosis/HIV results in higher mortality rates than does HIV infection alone.⁽⁵⁻⁸⁾ Antituberculosis drug resistance and an increased risk of transmission have also emerged as problems due to noncompliance with the tuberculosis treatment.⁽⁷⁾ Because of impaired immune response, HIV-infected patients are at increased risk of reactivation of latent tuberculosis infection, and AIDS is a strong risk factor for death in patients with tuberculosis. In co-infected patients, mortality is commonly related to delayed diagnosis, because some HIV-infected individuals postpone seeking health care in order to avoid receiving an AIDS diagnosis.⁽¹¹⁾

In addition to tuberculosis/HIV co-infection, poverty is a major reason why tuberculosis remains a public health problem. Tuberculosis and poverty have a bidirectional relationship, which means that poverty can lead to poor health status and vice versa. Individuals with poor health status

have limited job opportunities, and this can lead to poverty, therefore creating a vicious cycle that tends to worsen. The severity and negative impact of tuberculosis are inversely proportional to the Human Development Index, and the uneven distribution of the disease is influenced by several factors, such as landmass, uncontrolled population growth, and the concentration of people living on the outskirts of cities and towns. The last two factors have long been an unsolved problem. The relationship between poverty and tuberculosis is well documented, as are the risks related to socioeconomic indicators, such as population clusters, poverty, and unemployment. However, no effective solution has been found. Although many investments are being made, they focus on tuberculosis treatment rather than prevention. Although there are measures for the prevention and control of tuberculosis, innovative and effective strategies, such as the directly observed treatment, short-course (DOTS) strategy, are still unavailable to most of the population, which is due to a lack of funding and political involvement.⁽¹²⁾ Therefore, we posed the following question: what are the trends in tuberculosis incidence, prevalence, and mortality in Brazil, the Americas, and worldwide? In an attempt to answer that question, we conducted the present study, the objective of which was to analyze the temporal trends in the incidence and prevalence of tuberculosis, as well as in the mortality of tuberculosis patients, with and without HIV co-infection, in Brazil, the Americas, and worldwide.⁽¹³⁾

Methods

This was an ecological study examining data on the incidence of, prevalence of, and mortality from tuberculosis, with and without HIV co-infection, collected by the WHO between 1990 and 2010. The data were divided among the populations of Brazil, the Americas, and the world, and the tuberculosis incidence, prevalence, and mortality rates were calculated for each of those populations in the period.⁽⁶⁾

Initially, scatter plots were drawn for the incidence of, prevalence of, and mortality from tuberculosis, with and without HIV co-infection, in order to visualize the relationship among them. The modeling process was then initiated. Tuberculosis incidence, prevalence, and mortality

constituted the dependent variable (y), whereas years constituted the independent variable (x). In order to study the trends, we chose to estimate regression models. The advantages of estimating trends using polynomial regression models include the great statistical power of such models, as well as the fact that they are easy to construct and interpret.⁽¹²⁾ In order to avoid collinearity among the terms of the regression equation, we used the centered variable. The first model tested was the simple linear regression model ($y = \beta_0 + \beta_1 x$). Subsequently, higher-order models were tested: a second-order or parabolic model ($y = \beta_0 + \beta_1 x + \beta_2 x^2$); a third-order model ($y = \beta_0 + \beta_1 x + \beta_2 x^2 + \beta_3 x^3$); and an exponential model ($y = e^{\beta_0 + \beta_1 x}$).

The best model was the model that showed the highest coefficient of determination (R^2), together with statistical significance (lowest value of p) and unbiased residuals. When two models were statistically similar for the same location, we chose the simpler model, i.e., the lower-order model. A trend was considered significant when its estimated model showed a value of $p < 0.05$. For the statistical analyses, we used the Statistical Package for the Social Sciences, version 19.0 (SPSS Inc., Chicago, IL, USA). Finally, in order to calculate the average annual percent change in tuberculosis incidence, prevalence, and mortality, we used the Joinpoint Regression Program (Statistical Methodology and Applications Branch and Data Modeling Branch, Surveillance Research Program, National Cancer Institute, Rockville, MD, USA).

Results

Among tuberculosis patients without HIV co-infection, there was a trend toward a decrease in the overall incidence and prevalence of tuberculosis, as well as in the overall mortality from tuberculosis, in Brazil and the Americas. Between 1990 and 2010, there was a reduction in tuberculosis incidence, prevalence, and mortality over the years in the three populations studied (Table 1). There was an 11.4% reduction in the incidence of tuberculosis worldwide; in Brazil and the Americas, the incidence of tuberculosis was reduced by 48.8% and 50.0%, respectively. The prevalence of tuberculosis in Brazil, the Americas, and worldwide was reduced by 58.9%, 60.8%, and 24.6%, respectively. The mortality from tuberculosis in Brazil, the Americas, and worldwide was reduced by 70.8%, 70.7%, and 40.0%, respectively.

Table 1 shows, for the 20-year historical series, the estimated annual percent change in tuberculosis incidence, prevalence, and mortality for the populations studied. The trend toward a decrease in tuberculosis incidence, prevalence, and mortality was more pronounced in the Americas and in Brazil than worldwide.

Table 2 shows the secular trends in the estimated incidence and prevalence of tuberculosis, as well as in the estimated mortality from tuberculosis, in Brazil, the Americas, and worldwide in the 1990-2010 period. The trend toward a decrease in the overall prevalence of tuberculosis was more pronounced in the world population than in the Brazilian population, as well as being more pronounced in the Brazilian population

Table 1 – Percent change in tuberculosis incidence, prevalence, and mortality in Brazil, the Americas, and worldwide, 1990-2010.

Rates	Locations	n/100,000 population		Mean rate in the study period	Cumulative change %	AAPC	95% CI	p
		1990	2010					
Incidence	Americas	58	29	42.00	-50.0	-3.5	-3.5 to 3.4	< 0.001
	World	144	128	139.05	-11.4	-0.4	-0.5 to 0.3	0.006
	Brazil	84	43	61.48	-48.8	-3.2	-3.3 to 3.2	< 0.001
Prevalence	Americas	92	36	58.67	-60.8	-4.4	-4.6 to 4.3	0.007
	World	236	178	234.52	-24.6	-1.9	-2.3 to 1.5	0.04
	Brazil	116	47	77.05	-59.5	-4.3	-4.5 to 4.0	< 0.001
Mortality	Americas	7.5	2.2	4.22	-70.7	-5.6	-5.8 to 5.3	0.002
	World	25	15	21.24	-40.0	-2.4	-2.7 to 2.0	0.03
	Brazil	8.9	2.6	5.11	-70.8	-5.5	-5.8 to 5.2	0.002

AAPC: average annual percent change. Source: World Health Organization, 2011.⁽⁶⁾

than in the population of the Americas; the trend toward a decrease in the estimated mortality from tuberculosis (all forms of tuberculosis, except for tuberculosis/HIV co-infection) per 100,000 population was more pronounced in the world population than in the Brazilian population, as well as being more pronounced in the Brazilian population than in the population of the Americas; the trend toward a decrease in the estimated incidence of tuberculosis (all forms) per 100,000 population was more pronounced in Brazil and the Americas, the estimated incidence of all forms of tuberculosis having slightly increased worldwide; the estimated incidence (new cases with positive sputum smears) per 100,000 population decreased in Brazil and the Americas, having increased worldwide; the upward trend in tuberculosis/HIV co-infection was more pronounced in the world population than in the population of the Americas, as well as being more pronounced in the Americas than in Brazil; the trend toward an increase in the rates of detection of new cases (all forms) was more pronounced in the Americas than in Brazil, as well as being more pronounced in Brazil than in the world; finally, the trend toward an increase in the rates of detection of new cases (with positive sputum smears) was more pronounced in the Americas than in the world, as well as being more pronounced in the world than in Brazil.

Figures 1 and 2 show the correlation between tuberculosis/HIV co-infection and poverty for the world, as well as showing the incidence of tuberculosis in the countries. There is a direct correlation between tuberculosis/HIV co-infection and poverty, Pearson's correlation coefficients ranging from 0.58 to 0.80, respectively, for

the proportion of the population living below the poverty line (an economic indicator that is widely used in order to assess the development of countries) and the prevalence of HIV-positive patients in the population.

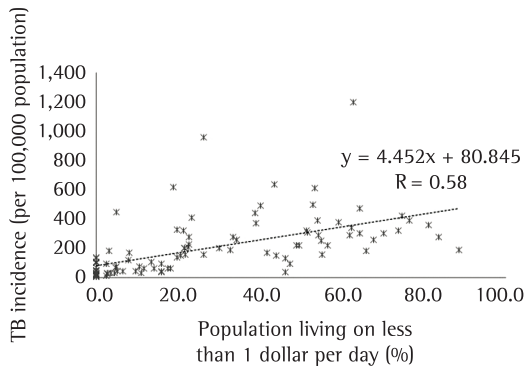


Figure 1 - Correlation between the proportion of the population living in poverty and the incidence of tuberculosis (TB) worldwide, 2010. Source: World Health Organization, 2011.⁽⁶⁾

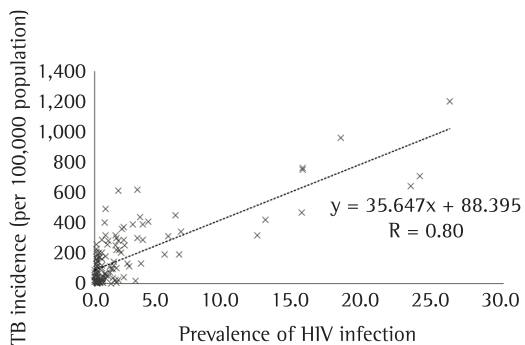


Figure 2 - Correlation between the prevalence of HIV infection and the incidence of tuberculosis (TB) worldwide, 2010. Source: World Health Organization, 2011.⁽⁶⁾

Table 2 - Secular trends in the estimated incidence of, prevalence of, and mortality from tuberculosis in Brazil, the Americas, and worldwide, 1990-2010.

Trends	Brazil		Americas		World	
	Linear model	R ²	Linear model	R ²	Linear model	R ²
Prevalence of TB ^{abc}	y = -3.29x + 113.28	0.98	y = -2.64x + 87.76	0.96	y = -4.25x + 281.27	0.87
Mortality from TB ^{acd}	y = -0.28x + 8.27	0.95	y = -0.24x + 6.85	0.94	y = -0.49x + 26.62	0.94
Incidence ^{abc}	y = -2.01x + 83.50	0.99	y = -1.47x + 58.18	0.98	y = -0.55x + 145.15	0.68
Incidence ^{acc}	y = -1.16x + 47.24	0.99	y = -0.78x + 31.26	0.98	y = 0.49x + 56.33	0.90
TB/HIV co-infection, % ^{b,c}	y = 0.23x + 15.42	0.17	y = 43.86x + 378.25	< 0.01	y = 73.91x + 197	0.96
Rates of detection of cases, % ^b	y = 1.03x + 66.27	0.56	y = 1.24x + 55.54	0.63	y = 0.53x + 44.61	0.26
Rates of detection of cases, % ^c	y = 0.84x + 65.08	0.57	y = 3.60x + 23.04	0.57	y = 3.18x + 5.61	0.87

TB: tuberculosis. ^aPer 100,000 population. ^bAll forms. ^cEstimation. ^dAll forms, except for TB/HIV co-infection. ^eNew cases with positive sputum smears. Source: World Health Organization, 2011.⁽⁶⁾

Discussion

The results shown in Table 1 reveal that there was a significant decrease in the prevalence of tuberculosis in Brazil, the Americas, and worldwide; however, the estimated incidence of the disease per 100,000 population decreased noticeably in Brazil and the Americas but not worldwide.⁽¹⁴⁾

In general, the indicators of tuberculosis and tuberculosis/HIV co-infection assessment are consistent with the rates in Brazil and the Americas but not necessarily with the overall rates, highlighting the significant contribution of Brazil to the rates of the continent and the small contribution of the Americas to the overall rates, possibly influenced more strongly by pockets of poverty in Africa and in countries that are more densely populated, such as China, India, and Russia.⁽¹⁵⁾

Regarding the incidence of tuberculosis without HIV co-infection, the ninth WHO report shows a decrease in the number of cases worldwide, at a rate of 1% per year; in Brazil, the rate of decline is 3% per year for smear-positive cases and for all tuberculosis cases. The exception is the African continent, where the number of HIV cases is extremely high.⁽¹⁾

Regarding the data presented in Table 2, in all cases, the best descriptive model was the linear model, which revealed a relatively stable and homogeneous trend, as ratified by the (mostly) high coefficients of determination (R^2).

We found a downward trend in the estimated prevalence of all forms of tuberculosis, with a more significant reduction in the overall rates. The trend toward a decrease in the estimated mortality from tuberculosis (without HIV co-infection) was most pronounced in Brazil. Regarding the incidence of tuberculosis (bacillary forms and all forms of tuberculosis), we found a downward trend in Brazil and the Americas and an upward trend worldwide, other world territories, such as Africa, having been found to contribute to the global burden of disease.

We found an upward trend in the proportion of tuberculosis/HIV co-infection cases in Brazil, the Americas, and worldwide, the overall rates being particularly high. This constitutes further evidence of the contribution of other continents to the global burden of disease, as well as reflecting the impact that HIV infection and AIDS have on the occurrence of tuberculosis cases worldwide. Finally, the trend in the indicators of health care

quality suggests an improvement in the sensitivity of health care systems in screening for cases of tuberculosis (active or latent), reflecting an improved performance of health care facilities in establishing diagnosis for early treatment and possible cure.

Tuberculosis surveillance is aimed at identifying tuberculosis cases in the population, allowing the adoption of measures to interrupt the transmission of the disease to susceptible individuals. However, the cases that are diagnosed at and reported by health care facilities possibly represent only a proportion of the actual number of tuberculosis cases.⁽¹⁶⁾

The detection of new cases has increased over time. This contributes to early treatment, which in turn contributes to downward trends in tuberculosis incidence, prevalence, and mortality. However, other measures must be adopted in order to achieve the goals established by the WHO.

The estimation of the number of tuberculosis cases in a given population has been a challenge to epidemiologists and tuberculosis control planners. Current indirect methods of estimation depend on the accuracy of other tuberculosis-related data, such as the number of individuals infected with *Mycobacterium tuberculosis* and the number of deaths. Such data depend on the effective functioning of health care systems.⁽¹⁶⁾ Because studies of tuberculosis prevalence are costly and methodologically complex, few such studies have been conducted. In this context, methodical approaches to the assessment of tuberculosis surveillance activities are welcome because they can identify situations in which the reported incidence of tuberculosis differs from the true incidence of the disease.⁽¹⁷⁾

With regard to tuberculosis treatment, many challenges are encountered, such as improving treatment adherence, making the DOTS strategy more widely available (with quality control), decentralizing the programs, increasing access to treatment, and expanding the coverage of the program to the entire network of primary health care clinics. Therefore, the WHO has set some resolution goals: to detect 70% of the estimated cases; to cure 85% of the reported cases; and to reduce treatment noncompliance to less than 5%. In addition, one of the millennium goals set by the WHO is to reduce tuberculosis prevalence and mortality by half by 2015, by means of the Stop TB Strategy.⁽¹²⁾

The increase in the rates of tuberculosis/HIV co-infection poses challenges that prevent the reduction in the incidence of both infections.⁽¹³⁾ Data show that immunocompetent individuals infected with *M. tuberculosis* have a 10% chance of developing the disease over the course of their lifetime; among HIV-infected individuals without therapeutic intervention, that chance is approximately 10% per year.⁽⁹⁾ Annual data indicate that the mortality rates are higher in HIV-positive patients who are co-infected with tuberculosis than in those who are not. Infection with HIV is currently a major risk factor for developing tuberculosis.⁽¹⁵⁾

Tuberculosis and AIDS are diseases of such magnitude that they are not confined by biological barriers, constituting a serious social problem. Individuals become vulnerable when they assume that they are not at risk and therefore neglect self-care; in addition, limited access to health care increases patient vulnerability.⁽¹⁸⁾

The epidemiological aspects of the association between tuberculosis and AIDS represent a major challenge, given the difficulties in coordinating tuberculosis and AIDS control measures. These measures are performed under separate programs, which do not coordinate efforts and which adopt control policies at different levels of health care.

Nearly all health indicators confirm the association between disease and low socioeconomic status. Respiratory and infectious diseases are two groups of diseases specifically reported as being effects of deprivation. Tuberculosis, in particular, has historically been associated with high poverty rates. The decline in the number of reported cases of tuberculosis, which began after the advent of effective chemotherapy, might have been due to the reduction in overpopulation and the improvement in nutritional and social status.⁽¹³⁾

Tuberculosis has traditionally been a disease of the poor. However, because poverty is multifaceted, it is difficult to assess that. Moreover, poverty levels are relative to the wealth of society as a whole. The poverty and deprivation indices used range from extremely simple indices to extremely complex indices.⁽¹⁹⁾

Exactly how poverty can directly cause tuberculosis remains unclear. Poverty probably results in very poor nutrition, which probably makes the immune system more vulnerable to invasion by organisms, such as *M. tuberculosis*.⁽²⁰⁾

Protein malnutrition is associated with changes in immune functions mediated by T cells, and animal studies have shown that BCG vaccination is less effective in protein-deficient animals than in normally nourished animals. Therefore, wherever there is social deprivation, particularly in areas with poor housing, high unemployment rates, and low income, there should be an increased awareness of the possibility of diagnosing tuberculosis.⁽²¹⁾

It should be noted that the worsening of social and economic conditions results in significant degradation of living conditions, increasing the vulnerability of individuals and, consequently, the risk of tuberculosis/HIV co-infection.⁽²²⁾ In this sense, national planning for the restructuring of health care systems is as important as funding, leading to integrated health care systems and decentralized care in order to improve treatment adherence. The global health issues discussed in the last decade by governments, donor organizations, and national leaders should not be forgotten at this important stage of the combined pandemic (and, in particular, of the combined pandemic associated with poverty).

There is a lack of communication between AIDS programs and tuberculosis programs. More often than not, co-infected patients remain unidentified until death; this highlights a failure of the health care system to detect, diagnose, and treat these related diseases.⁽⁸⁾ Therefore, efforts to prevent and control tuberculosis/HIV co-infection in impoverished populations, who have limited access to health care, are unlikely to succeed without an integrated approach that seeks to reduce the underlying social inequalities for which Brazil has been known.

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