Revista O Mundo da Saúde

DOI: 10.15343/0104-7809.202347e13912022I

Effect of COVID-19 Pandemic on New Cases of Tuberculosis in Brazil: A Temporal and Spatial Analysis

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Abstract

This study aimed to analyze, through the spatial and temporal patterns, the effect of the COVID-19 pandemic in the detection of new cases of tuberculosis in Brazil. This is an ecological study, which adopted the average rate of detection of new cases of tuberculosis in the pre-pandemic (2016 to 2019) and pandemic (2020) periods. The spatial analysis was calculated using the percent variation of detection in Brazilian regions and states and the risk ratio between smoother detection rates through the local Bayesian empirical method for municipalities. The temporal trend analysis was performed through Joinpoint regression, with the month of detection as the unit of analysis. A reduction of the tuberculosis detection rate was observed in all Brazilian regions and in 81.5% of states. Approximately 60.0% of municipalities showed stabilization or a decrease in detection rates. Time analysis revealed that all regions had, since 2016, a trend of increased case detection and that, especially in the first half of 2020, a strong decreasing rate was identified. Changing the organization of healthcare services imposed by pandemic may have influenced the under-reporting of cases and consequent reduction of tuberculosis detection rates.

Keywords: Tuberculosis. COVID-19 Pandemic. Spatial analysis. Epidemiological monitoring.

INTRODUCTION

Tuberculosis is a transmissible infectious disease caused by *mycobacterium tuberculosis bacillus*, propagated when people infected expel the bacillus through the air, by coughing or sneezing. It is a disease of chronic evolution that hits the lungs but can also affect other places. Most infected people do not show symptoms of the disease, but when the individual develops some fragility of the immune system or is malnourished, there is a manifestation of persistent cough, sputum or presence of blood when coughing, weight loss, chest pain, fever, and asthenia, which may evolve to death if not treated[1]. Tuberculosis is curable and avoidable, and treatment is essential to reduce the transmission of the disease in the community[1].

In 2019 it was estimated that ten million people got sick by tuberculosis worldwide and that 1.2 million died from the disease[2]. Brazil is among the 30 countries with the highest load of the disease and in 2020 recorded 66,819 new cases, which represents a detection rate of 31.6 cases per 100,000

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inhabitants[3]. In order to influence this magnitude, the World Health Organization (WHO) approved, in the World Health Assembly of 2014, the END TB strategy, which proposes a radical change of the paradigm in the fight against tuberculosis, with the aim of eliminating the disease as a Public Health problem by reducing cases by 90% and reduce deaths by 95% by 2035, compared to 2015, also eliminating the economic impact for families affected by the disease[4].

Although a series of efforts were underway, with goals to control this endemic, the COVID-19 pandemic influenced epidemiological behavior of numerous diseases. The overload of healthcare systems has interfered strongly in the prevention, control, and monitoring actions of tuberculosis. In Brazil, the National Tuberculosis Control Program (NTCP) identified the reduction in the total notifications of the disease at the three levels of healthcare and a reduction in the use of rapid test cartridges for tuberculosis compared to 2019[3]. Economic impacts from the pandemic also interfered with important indicators, because with the increase in unemployment and accentuation of poverty and social inequality, factors such as malnutrition and difficult access to healthcare services accentuate the propagation of tuberculosis and its aggravation[2].

Time and spatial series analyses can contribute to the management of health policies by assisting in the identification of health demands and services in a given geographical space, activity planning, and evaluation of healthcare services[5]. Historically, tuberculosis has been analyzed mainly in the spatial context, but considering the changes in the organization of healthcare services imposed during the pandemic period, it is necessary to carry out spatial time studies that can signal possible behavioral changes in the occurrence of the disease. Thus, this article aimed to analyze, through the spatial and temporal pattern, the effect of COVID-19 pandemic on the detection of new cases of tuberculosis in Brazil.

METHODOLOGY

This is an ecological, descriptive, retrospective, quantitative study that used data on the distribution of new cases of tuberculosis in the 5,570 Brazilian municipalities among the pre-pandemic (2016 to 2019) and pandemic (2020) periods. As a data source, the National Tuberculosis Database of the National Disease Notification System was used. Population data were obtained by the population estimates of the Brazilian Institute of Geography and Statistics (IBGE) regarding the study analysis period. For Brazilian regions and their respective states, tuberculosis detection rates (new cases of TB / 100,000 inhabitants) were calculated in the pre-pandemic and pandemic periods. Subsequently, the percentage variation of the detection rate was calculated by the difference between the average detection rates in the pandemic and pre-pandemic periods divided by the pre-pandemic average detection rate multiplied by 100.

Time series analysis was performed through Joinpoint Regression, capable of identifying significant trends or moments when a significant change in a trend occurs over time. As described by Gonçalves[6], this model tests if a temporal line with multiple segments is statistically suitable to describe the temporal evolution of data compared to a line with fewer segments or is straight. The regression model allows you to identify not

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only the trend of a stationary, increasing, or decreasing indicator, but also points to where there is a modification in this trend, as well as its variation[6].

The calculation of monthly change of detection rates in the study period according to the English Monthly Percent Change (MPC) was used, starting from the regression model for inflection points. MPC analysis uses inflection points according to an algorithm that tests if one line is significantly different than another and can be straight or with fewer segments.

To this end, the Joinpoint Regression Program Statistical Program version 4.9.0.1 (2022) according to Kim *et al.* (2000) was used[7]. The trends were considered stationary when the P value ≥ 0.05 and increasing or decreasing when the variation was positive or negative, respectively, and P <0.05. A maximum of three inflection points were considered in the analysis for the periods and the best models were eligible through Bayesian Information Criterion (BIC).

Regarding spatial standards, considering the municipal scale analysis, it is known that brute detection rates with small populations may be influenced by random fluctuations due to small numbers. Gross rates may be equal to zero, which does not mean that there is no associated risk, but rather of oscillations of a temporal window that was not long enough[8]. The small denominator can also generate a large variability in estimates. To overcome these methodological limitations, the local empirical Bayesian estimator was adopted, useful for mitigating estimates of calculated coefficients for small (or underreported) geographical areas, eliminating random fluctuations not associated with risk[9].

Finally, the spatial dynamics of new cases of tuberculosis during the pandemic was presented by calculating the risk ratio (RR) between the detection rates in the previous period and during the pandemic, based on Bayesian detection rates for the municipalities. The software used were TerraView 4.2, QGIS 2.18, and spreadsheets. The cartographic foundation of Brazil, according to each municipality, was made available by IBGE.

This study used data from secondary public domains in which the identification of individuals is not possible; therefore, the authorization of the Research Ethics Committee was waived.

RESULTS

In Brazil, in the pre-pandemic period analyzed, an annual average of 92,089 new cases of tuberculosis were reported, representing a detection rate of 44.2 new cases / 100,000 inhabitants. By 2020, a reduction in detected cases (n = 86.166) was observed and consequently the detection (40.7 new cases/ 100,000 inhabitants).

The reduction in the detection rate was perceived in all Brazilian macroregions, ranging from 2.1% in the northern region to 10.6% in the northeastern region (Table 1). The southern region stands out for its decreased detection rates in all its states, and Santa Catarina was the state with the highest percent variation with a decreasing tendency (-26.6%) (Table 1).

Even during the pandemic, the country presented, in more than 25% of its municipalities, a detection rate of 25 cases/ 100 thousand inhabitants (Figure 1b). However, approximately 60% of Brazilian municipalities (n = 3,290) had stabilized trends or a decrease in tuberculosis detection rates. It is noteworthy

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that the decline in detections was identified in 2,051 municipalities (36.9%) (Figure 1c).

The temporal trend analysis through Jointpoint regression revealed that Brazil presented, from January 2016 until the beginning of 2020, a significant trend of increased detection of new tuberculosis cases (Table 2). Similar behavior was observed in all Brazilian regions, with the exception of the northern and southern regions, which, as early as August and October 2019, respectively, began a decreasing tendency that remained until December 2020 (Table 2).

It is possible to observe, during the pandemic period analyzed, that the Northeast, Midwest, and Southeast regions suffered an abrupt decrease in detections during the first half of 2020 and then a subsequent increasing trend, which was significant only in the northeastern region (Table 2).

Table 1 - Detection rate (DR) of tuberculosis and percent variation, according to region and state of residence. Brazil, 2016 to 2020.

Region/State	Average DR (2016 to 2019)	DR 2020	Variation (%)
Northern region	57.6	56.4	-2.1
Rondonia	42.5	33.6	-20.8
Acre	58.3	67.8	16.2
Amazonas	90.6	84.1	-7.2
Roraima	42.8	52.8	23.4
Para	55.9	56.6	1.2
Amapa	36.4	37.7	3.7
Tocantins	13.7	13.0	-5.2
Northeastern region	42.6	38.1	-10.6
Maranhao	36.4	35.3	-3.1
Piaui	25.6	23.1	-10.0
Ceara	48.2	41.5	-13.9
Rio Grande do Norte	40.3	46,6	15.8
Paraiba	34.8	28.1	-19.3
Pernambuco	62.2	57.3	-7.9
Alagoas	38.6	31.1	-19.5
Sergipe	40.1	37.5	-6.3
Bahia	37.4	30.8	-17.5
Southeastern region	47.7	43.6	-8.6
Minas Gerais	19.9	18.7	-6.0
Espirito Santo	35.2	43.6	24.0
Rio de Janeiro	83.8	77.1	-8.0
Sao Paulo	48.0	42.5	-11.5
Southern region	39.0	35.9	-8.0
Parana	22.6	22.5	-0.8
Santa Catarina	31.9	23.4	-26.6
Rio Grande do Sul	59.8	57.3	-4.2
Midwestern region	27.2	25.0	-8.1
Mato Grosso do Sul	47.1	47.7	1.4
Mato Grosso	42.6	36.3	-14.8
Goias	16.7	15.4	-7.5
Distrito Federal	15.6	13.5	-13.6

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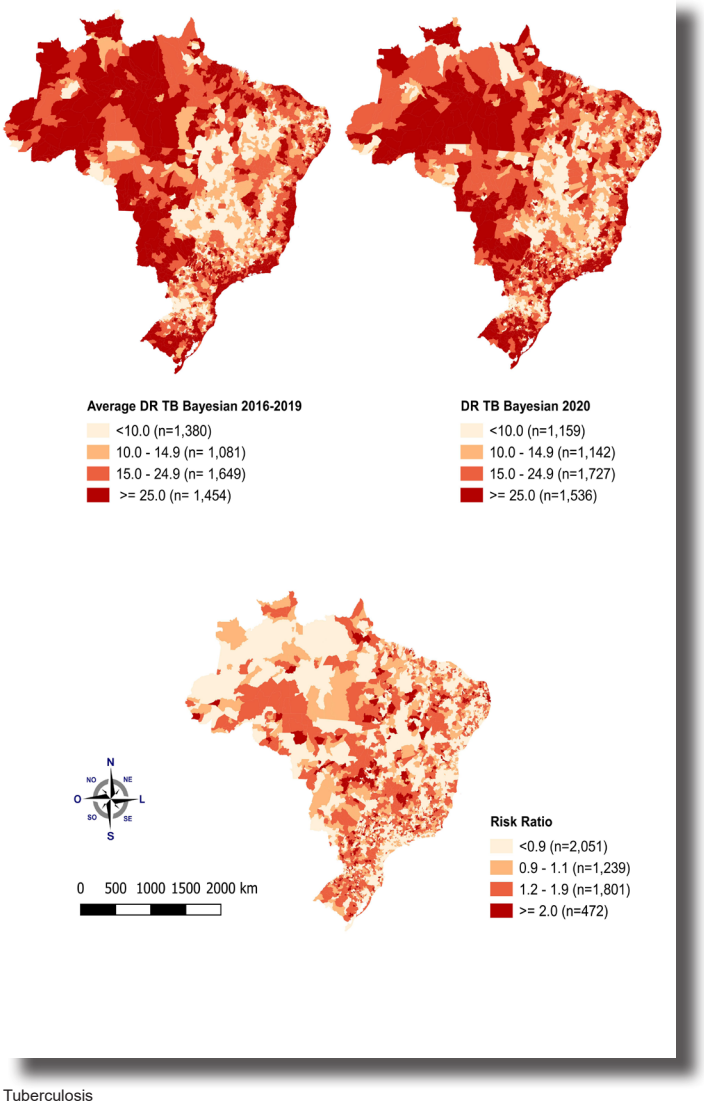
Figure 1 - Tuberculosis detection rate (cases/100 thousand inhabitants) according to city of residence, Brazil. (A) 2016-2019 (B) 2020 (C) Risk Ratio.



Note: DR - Detection Rate. TB - Tuberculosis

Table 2 - Tuberculosis Detection Rate Trend, according to model Joinpoint. Brazil and Regions, 2016 to 2020.

	1st Trend				2nd Trend				3rd Trend			
Region	Period		WPC	95%CI	Period		WPC	95%CI	Period		WPC	95%CI
North	Jan/16	Aug/19	0.5*	(0.3 ; 0.8)	Aug/19	Dec/20	-1.2*	(-2.3 ; -0.1)	-	-		-
Northeast	Jan/16	Feb/20	0.2*	(0.1 ; 0.4)	Feb/20	May/20	-11.0	(-28.5 ; 11.7)	May/20	Dec/20	4.0*	(0.9 ; 7.2)
Midwest	Jan/16	Mar/20	0.3*	(0.1 ; 0.5)	Mar/20	Jun/20	-11.0	(-33.8 ; 20.5)	Jun/20	Dec/20	4.3	(-1.0 ; 9.8)
Southeast	Jan/16	Jan/20	0.2*	(0.1 ; 0.4)	Jan/20	May/20	-6.2	(-16.9 ; 5.8)	May/20	Dec/20	2.4	(-0.8 ; 5.7)
South	Jan/16	Oct/19	0.3*	(0.1 ; 0.5)	Oct/19	Dec/20	-2.0*	(-3.1 ; -0.9)	-		-	-
Brazil	Jan/16	Jan/20	0.3*	(0.1 ; 0.4)	Jan/20	May/20	-6.4	(-16.1 ; 4.3)	May/20	Dec/20	2.2	(-0.7 ; 5.2)

Note: MPC: Monthly Percent Change ; 95% CI: 95% confidence interval; * P <0.05.

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DISCUSSION

The Pan American Health Organization estimates that non-pharmacological prevention measures used in the COVID-19 pandemic may have helped reduce the transmission of other respiratory diseases[10]. The Stop TB Partnership suggests that social distancing and use of face masks would be able to reduce 10% of tuberculosis rates in countries with high disease burden[11,12]. However, it is recognized that COVID-19 pandemic has severely impacted social, economic, and sanitary areas, especially compromising the performance of the healthcare system in facing public health problems in the country, including tuberculosis.

In this context, the reduction in the number of new cases of tuberculosis in Brazil, during the analyzed period, suggests a possible underreporting of cases. One of the points to be considered is that tuberculosis health services have turned to meet COVID-19 needs, impacting negatively on early diagnosis, treating new cases of tuberculosis, and, in medium and long terms, in the increase of strains resistant to medicines[13,14,15].

In a period prior to the pandemic, it was already recognized that the advances in regional policies focused on healthcare prioritized regional, intergovernmental negotiation strategies, investment, planning, and expansion of the care network to face health inequalities. However, limitations arising from the sectoral logic of politics and the healthcare system were also already occurring, as well as regional inequalities, in which the reduction in the detection of new cases of tuberculosis in the country were already influenced[16,17].

From the behavior observed in Brazil and other countries, the WHO identified the standards of case detection, and performed estimates considering increased mortality due to the reduction of the detection rate[18]. It is estimated that by 2026 there would be an increase of up to 20% in the number of deaths from tuberculosis due to barriers in access to diagnosis and proper care, building upon the pandemic period[19].

It is suggestive that to achieve the global strategy goals for ending TB in the national territory by 2035 was compromised due to the negative effect of the pandemic on tuberculosis services, represented here by reduced detection rates - in addition to the heterogeneous form that this trend was given. In addition, the NTCP presented a decrease in latent investigation of the disease in asymptomatic adults and adolescents in contact with individuals with active tuberculosis, which may lead to delays in the diagnosis and treatment of new cases[20].

CONCLUSION

The present study demonstrated changes in the temporal space patterns of tuberculosis over the time of analysis, strongly impacted during the COVID-19 pandemic. To minimize the COVID-19 pandemic's effect on tuberculosis, effort and articulation between different government levels, educational institutions, and the population will be required, as well as the encouragement for the use of virtual and digital healthcare technologies to support adhesion, early treatment, monitoring, counseling, and follow-up of individuals.

Studies that investigate the relationship between epidemiological indicators of tuberculosis and social determinants in the pandemic and post-pandemic scenario should be encouraged. These analyses can support the implementation of strategies that strengthen the adoption of social protection measures, specifically in municipalities with greater reductions in detection and/or those with worsening performance indicators combined with low economic development and social inequality.

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DOI: 10.15343/0104-7809.202347e13912022I

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Conceptualization: Hentringer, IMB; Ribeiro, JAM; Barrett, IJB; Silva, APSC. Methodology: Hentringer, IMB; Silva, APSC. Validation: Hentringer, IMB; Ribeiro, JAM; Barrett, IJB; Silva, APSC. Statistical analysis: Silva, APSC. Formal analysis: Hentringer, IMB; Ribeiro, JAM; Barrett, IJB; Silva, APSC. Research: Hentringer, IMB; Ribeiro, JAM; Barrett, IJB; Silva, APSC. Resources: Hentringer, IMB; Ribeiro, JAM; Barrett, IJB; Silva, APSC. Original draft preparation: Hentringer, IMB; Ribeiro, JAM; Barrett, IJB; Silva, APSC. Writing-reviewing and editing: Hentringer, IMB; Ribeiro, JAM; Barrett, IJB; Silva, APSC. Visualization: Hentringer, IMB; Ribeiro, JAM; Barrett, IJB; Silva, APSC. Supervision: Silva, APSC. Project management: Hentringer, IMB; Silva, APSC

All authors read and agreed with the published version of the manuscript.

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Received: 30 september 2022.
Accepted: 10 march 2023.
Published: 23 may 2023.