Tuberculosis in Northeastern Brasil (2001-2016): trend, clinical profile, and prevalence of risk factors and associated comorbidities

INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by any of the seven species that make up the Mycobacterium tuberculosis complex; however, the most important sanitary wise is M. tuberculosis. Transmission occurs from the inhalation of particles from the airways of bacillary individuals.1,2

SUMMARY

OBJECTIVE: To describe the temporal trend, clinical profile, and the prevalence of risk factors and associated comorbidities in new cases of tuberculosis in the Northeast (2001-2016).

METHODS: A prevalence study involving all tuberculosis cases registered in Northeast Brasil, 2001-2016. Data were obtained from the National System of Notification of Disorders. For statistical analysis, the inflection point regression model and descriptive statistics were used.

RESULTS: 331,245 cases of tuberculosis were reported. The overall incidence rate decreased from 44.84/100,000 inhabitants (2001) to 30.92/100,000 inhabitants (2016), with a decreasing trend (AAPC: -2.3; p<0.001). The profile was characterized by men (73.53%), age 20-59 years (73.56%), pulmonary tuberculosis (86.37%), positive smear microscopy (54.78%). The main risk factors and comorbidities were: AIDS (4.64%), HIV (12.10%), Diabetes mellitus (5.46%), alcohol (11.63%), institutionalized, (4.31%) and deprived of liberty (2.30%).

CONCLUSIONS: Even with a reduced incidence, tuberculosis represents a real public health problem in the Northeast region. The profile was characterized by a male population, in economically-active age, lung smear-positive pulmonary presentation, and the risk factors and comorbidities of Aids, TB/HIV co-infection, diabetes mellitus, alcohol consumption, institutionalized and deprived of freedom reflect the complexity of the challenges in facing the disease.

KEYWORDS: Tuberculosis. Epidemiology. Risk factors.
TB is one of the top ten causes of death from a single infectious agent throughout the world. In 2018, 77,788 new cases of the disease were reported in Brazil, with an incidence of 34.8/100,000 inhabitants. In that same year, the Northeast ranked second regarding the number of cases (26.20% n=19,075) and third in incidence coefficient (33.1/100,000 inhabitants)3.

Whereas the epidemiological context, the Ministry of Health drew up the National Plan for the End of Tuberculosis as a Public Health Problem, with goals to, by 2035, reduce the incidence coefficient to less than 10/100,000 inhabitants and the TB mortality coefficient to less than 1/100,000 inhabitants34, and have no families affected by TB expenses that surpass citizens’ socioeconomic condition. The national plan defines strategies divided into three main groups: i) prevention and integrated care focused on individuals with TB; ii) bold policies and support system; and (iii) intensification of research and innovation4.

Based on the above, the objective of this study was to describe the temporal trend, clinical profile, and prevalence of associated risk factors and comorbidities in new cases of tuberculosis in the Northeast (2001-2016).

METHODS
Study design, population, and period
This is a prevalence study involving all TB cases recorded in the period of 2001-2016 in Northeastern Brasil.

Study locale
The study was conducted in the Northeast region of Brasil, which is composed by nine states (Maranhão, Piauí, Ceará, Rio Grande do Norte, Paraíba, Pernambuco, Alagoas, Sergipe, and Bahia) and has a population of 56.9 million inhabitants, corresponding to 27.62% of the Brazilian population5.

Study variables and collection procedures
We included in the study an epidemiological indicator (coefficient of incidence per 100,000 inhabitants) and 18 variables (age, clinical presentation, 1st of sputum bacilloscopy, 2nd sputum bacilloscopy, sputum culture, rapid TB test, outcome status, AIDS, alcoholism, diabetes mellitus, mental illness, illicit drugs, smoking, HIV testing, institutionalization, population deprived of liberty - PDL, homeless population, and health professional).

The data related to TB cases were extracted from the Brazilian Case Registry Database (Sistema de Informações de Agravos de Notificação) and the population data were extracted from IBGE.

Statistical treatment
The statistical treatment was completed in two stages. In the first stage, we carried out the analysis of the temporal trend using a joinpoint regression model6. The trends were sorted as ascending, descending, or stationary. We calculated the annual percent change (APC) and the average annual percent change (AAPC) with a confidence interval of 95% (95% CI) and a significance level of 5%. The analysis was made using the Joinpoint regression program (version 4.6.0.0, National Cancer Institute, Bethesda, MD, USA). In the second stage, a descriptive analysis was completed (absolute and relative frequencies) of the clinical variables and comorbidities.

Ethical aspects
The present study used secondary data in the public domain, for which reason the appreciation by the Human Research Ethics Committee was dismissed.

RESULTS
Trend analysis
The incidence of TB in the Brazilian Northeast dropped from 44.8/100,000 in 2001 to 30.9/100,000 in 2016. The regression model showed two distinct temporal behaviors: the first was stationary between 2001-2004 (APC: 0.54%; p=0.7), and the second was of decline between 2004 and 2016 (APC: -2.99%; p<0.001). This reduction was also observed in the analysis according to sex. In men, the incidence was reduced from 55.8/100,000 in 2001 to 41.9/100,000 in 2016, with two distinct temporal behaviors: stationary between 2001-2005 (APC: 0.01%; p=1.0), and in decline from 2005 (APC: -2.37%; p<0.001). In women, the incidence was reduced from 33.9/100,000 to 20.3/100,000, with a stationary trend in 2001-2004 (APC: 0.45%; p=0.8), and in decline from 2004 (APC: -4.18%; p<0.001). (Figure 1).

Clinical profile, risk factors, and prevalence of associated comorbidities
Out of the 331,245 TB cases registered in the Brazilian Northeast, the profile was characterized by males
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(63.53%; n=210,454), age between 20 and 59 years (73.56%; n=243,670) and pulmonary clinical presentation (86.37%; n=286,080). A total of 54.78% (n=181,469) of cases was positive in the 1st sputum bacilloscopy, 17.90% (n=59,307) in the 2nd sputum bacilloscopy, and 5.92% (n=19,601) in culture. In addition, 5.22% (n=346) of individuals who underwent the molecular rapid test presented resistance to rifampicin. The cure rate was 70.66% (Table 1).

Regarding the risk factors and comorbidities, the following stood out: Aids (4.64%; n=15,372), alcoholism (11.63%; n=38,516), diabetes mellitus (5.46%; n=18,077), mental illness (1.87%; n=6,197), illicit drugs (0.86%; n=2,858), and smoking (1.80%; n=5,962); 43.93% (n=145,506) of individuals were tested for HIV, with a rate of 12.10% of seroreacting (n=17,602), considering only those who were tested, and 5.31% considering all the cases. Of the total, 4.31% were institutionalized, and prisons stood out (2.30%; n=7,628) (Table 2).

DISCUSSION

The study showed important nuances of TB in the Brazilian Northeast. Even in the face of the difficulties in combating TB, the temporal analysis showed a significant decrease in the incidence of the disease in the Northeast region during the period studied, following the same pattern of reduction observed in Brazil. It is possible to associate this reduction to the Brazilian government’s efforts in combating the disease, most prominently the strengthening of tuberculosis control programs in municipalities and states, and the greater coverage of the actions of the Family Health Strategy in recent years.

In the state of Piauí, the actions carried out by the Family Health Strategy, whose coverage reached 98.7% in 2016, and the decentralization of TB control actions in Primary Care may result in greater access to diagnosis and treatment, and, consequently, in reducing the transmission of the disease. Similar advances were also observed in Paraíba: in 2007, the priority municipalities already had 95% of the healthcare units with the TB control program implemented, and of these, 55% already used the strategy of supervised treatment.

Even with significant advances, many problems still prevent the consolidation of TB control programs. In 2018, for example, the cure rate in Paraíba was 55.5% and the abandonment rate was 10.4%, which shows that the state is still far from achieving the goals recommended by the WHO. A similar context is also observed in the neighboring state of Pernambuco, in which the cure rate was 73.3% and the abandonment rate was 9.3%. This scenario shows that it is still necessary to strengthen the actions for combating TB in the Northeast.

In addition to the magnitude of the disease, it is necessary to reflect on the clinical profile and the prevalence of risk factors and associated comorbidities. In this study, 63.53% of the cases were in men, which is similar to the findings of other investigations, in which this population was approximately twice as affected. The resistance in looking for assistance in health services as well as less access to these services by this population are conditions that hinder the early
TABLE 1. SOCIODEMOGRAPHIC AND CLINICAL CHARACTERIZATION OF NEW CASES OF TUBERCULOSIS IN RESIDENTS OF THE NORTHEAST REGION, BRASIL, 2001-2016.

| Variables | Ignored n=90 (0.03%) | Male n=210454 (63.53%) | Female n=120701 (36.44%) | Total n = 331245 (100%) |
|-----------|----------------------|------------------------|--------------------------|-------------------------|
|           | n | %    | n | %    | n | %    | n | %    |
| **Age range** |               |                       |                          |                         |
| 0-10       | 5  | 5.55 | 4317 | 2.05 | 3520 | 2.92 | 7842 | 2.37 |
| 10-19      | 6  | 6.66 | 14692 | 6.98 | 12845 | 10.64 | 27543 | 8.31 |
| 20-59      | 69 | 76.68 | 158336 | 75.24 | 85265 | 70.64 | 243670 | 73.56 |
| 60 or more | 10 | 11.11 | 33028 | 15.69 | 19031 | 15.77 | 52069 | 15.72 |
| Blank      | -  | -    | 81  | 0.04 | 40  | 0.03 | 121  | 0.04 |
| **Presentation** |         |          |                  |                         |
| Pulmonary  | 72 | 80.00 | 183654 | 87.27 | 102354 | 84.80 | 286080 | 86.37 |
| Extrapulmonary | 13 | 14.44 | 22111 | 10.55 | 16138 | 13.37 | 38362 | 11.58 |
| Pulmonary + extrapulmonary | 5 | 5.56 | 4515 | 2.15 | 2183 | 1.81 | 6703 | 2.02 |
| Blank      | -  | -    | 74  | 0.03 | 26  | 0.02 | 100  | 0.03 |
| **1st Bacilloscopy- sputum** |     |          |                  |                         |
| Positive   | 52 | 57.78 | 118375 | 56.25 | 63042 | 52.23 | 181469 | 54.78 |
| Negative   | 16 | 17.78 | 43984 | 20.90 | 26058 | 21.59 | 70058 | 21.15 |
| Not performed | 22 | 24.44 | 47129 | 22.39 | 31032 | 25.71 | 78161 | 23.60 |
| Does not apply | - | - | 895 | 0.43 | 542 | 0.45 | 1437 | 0.44 |
| Blank      | -  | -    | 71  | 0.03 | 27  | 0.02 | 98   | 0.03 |
| **2nd Bacilloscopy- sputum** |     |          |                  |                         |
| Positive   | 5  | 5.55 | 39100 | 18.58 | 20202 | 16.74 | 59307 | 17.90 |
| Negative   | 1  | 1.11 | 19364 | 9.20  | 11585 | 9.60  | 30950 | 9.34  |
| Not performed | 6 | 6.67 | 36767 | 17.47 | 21347 | 17.68 | 58107 | 17.55 |
| Blank      | 78 | 86.67 | 115223 | 54.75 | 67567 | 55.98 | 182868 | 55.21 |
| **Sputum culture** |     |          |                  |                         |
| Positive   | 4  | 4.44 | 12728 | 6.05  | 6869  | 5.70  | 19601 | 5.92  |
| Negative   | 4  | 4.44 | 7610  | 3.62  | 4288  | 3.55  | 11902 | 3.59  |
| Ongoing    | 7  | 7.78 | 11382 | 5.41  | 6819  | 5.65  | 18208 | 5.50  |
| Not performed | 75 | 83.34 | 178663 | 84.89 | 102697 | 85.08 | 281435 | 84.96 |
| Blank      | -  | -    | 71  | 0.03 | 28  | 0.02 | 99   | 0.03 |
| **Rapid TB test** |     |          |                  |                         |
| Detectable sensitive to rifampicin | 1 | 1.11 | 3211 | 1.53  | 1262  | 1.05  | 4474  | 1.35  |
| Detectable resistant to rifampicin | - | - | 226 | 0.11  | 120  | 0.10  | 346   | 0.10  |
| Not detectable | - | - | 515 | 0.24  | 286  | 0.24  | 801   | 0.24  |
| Inconclusive | - | - | 656 | 0.31  | 352  | 0.29  | 1008  | 0.30  |
| Not performed | 1 | 1.11 | 20251 | 9.62  | 10579 | 8.76  | 30831 | 9.31  |
| Blank      | 88 | 97.78 | 185995 | 88.19 | 108102 | 89.56 | 293785 | 88.70 |
| **Outcome** |                  |                  |                          |                         |
| Cure       | 53 | 58.89 | 144541 | 68.70 | 89470 | 74.12 | 234064 | 70.66 |
| Abandonment | 7 | 7.78 | 21140 | 10.04 | 9039  | 7.49  | 30186 | 9.11  |
| Death from tuberculosis | - | - | 5304 | 2.52  | 2038  | 1.69  | 7342  | 2.22  |
| Death from other causes | 4 | 4.44 | 9699 | 4.61  | 4255  | 3.52  | 13958 | 4.21  |
| Transfer   | 15 | 16.67 | 22103 | 10.50 | 11485 | 9.52  | 33603 | 10.15 |
| DR-TB      | 2  | 2.22 | 555  | 0.26  | 314   | 0.26  | 871   | 0.26  |
| Change of scheme | - | - | 230 | 0.11  | 153  | 0.13  | 383   | 0.12  |
| Failure    | -  | -    | 31  | 0.01 | 15   | 0.01  | 46    | 0.01  |
| Primary abandonment | - | - | 112 | 0.05 | 55    | 0.05  | 167   | 0.05  |
| Blank      | 9  | 10.00 | 6739 | 3.20  | 3877  | 3.21  | 10625 | 3.21  |
| **Total**  | 90 | 100  | 210454 | 100   | 120701 | 100   | 331245 | 100   |

Legend: TB: Tuberculosis; DR-TB: Drug-Resistant tuberculosis.
| Variables                  | Ignored n=90 (0.03%) | Male n=210454 (63.53%) | Female n=120701 (36.44%) | Total n=331245 (100%) |
|----------------------------|----------------------|------------------------|--------------------------|-----------------------|
|                            | n       | %      | n       | %      | n       | %      | n       | %      |
| AIDS                       |         |        |         |        |         |        |         |        |
| Yes                        | 5       | 5.56   | 10816   | 5.14   | 4551    | 3.77   | 15372   | 4.64   |
| No                         | 10      | 11.11  | 86630   | 41.16  | 49165   | 40.73  | 135805  | 41.00  |
| Blank                      | 75      | 83.33  | 113008  | 53.70  | 66985   | 55.50  | 180068  | 54.36  |
| Alcoholism                 |         |        |         |        |         |        |         |        |
| Yes                        | -       | -      | 34029   | 16.17  | 4487    | 3.72   | 38516   | 11.63  |
| No                         | 15      | 16.67  | 84639   | 40.22  | 56892   | 47.13  | 141546  | 42.73  |
| Blank                      | 75      | 83.33  | 91786   | 43.61  | 59322   | 49.15  | 151183  | 47.36  |
| Diabetes mellitus          |         |        |         |        |         |        |         |        |
| Yes                        | 2       | 2.22   | 10654   | 5.06   | 7421    | 6.15   | 18077   | 5.46   |
| No                         | 14      | 15.56  | 101018  | 48.00  | 54469   | 45.13  | 155501  | 46.94  |
| Blank                      | 74      | 85.56  | 98782   | 46.49  | 58811   | 48.72  | 157667  | 47.60  |
| Mental Illness             |         |        |         |        |         |        |         |        |
| Yes                        | 1       | 1.11   | 4130    | 2.00   | 2066    | 1.71   | 6197    | 1.87   |
| No                         | 12      | 13.33  | 106287  | 50.50  | 58633   | 48.58  | 164932  | 49.79  |
| Blank                      | 77      | 85.56  | 100037  | 47.50  | 60002   | 49.71  | 160116  | 47.34  |
| Illicit drugs              |         |        |         |        |         |        |         |        |
| Yes                        | -       | -      | 2447    | 1.16   | 411     | 0.34   | 2858    | 0.86   |
| No                         | 2       | 2.22   | 21909   | 10.41  | 12167   | 10.08  | 34078   | 10.29  |
| Blank                      | 88      | 97.78  | 185096  | 88.43  | 108123  | 89.58  | 294309  | 88.55  |
| Smoking                    |         |        |         |        |         |        |         |        |
| Yes                        | -       | -      | 4779    | 2.27   | 1183    | 0.98   | 5962    | 1.80   |
| No                         | 2       | 2.22   | 19854   | 9.43   | 11478   | 9.51   | 31334   | 9.46   |
| Blank                      | 88      | 97.78  | 185821  | 88.30  | 108040  | 89.51  | 293949  | 88.74  |
| HIV test                   |         |        |         |        |         |        |         |        |
| Positive                   | 5       | 5.55   | 12455   | 5.92   | 5142    | 4.26   | 17602   | 5.31   |
| Negative                   | 7       | 7.78   | 63259   | 30.06  | 34169   | 28.31  | 97435   | 29.41  |
| Ongoing                    | 5       | 5.56   | 19940   | 9.47   | 10524   | 8.72   | 30469   | 9.20   |
| Not performed              | 73      | 81.11  | 114729  | 54.52  | 70839   | 58.69  | 185641  | 56.05  |
| Blank                      | -       | -      | 71      | 0.03   | 27      | 0.02   | 98      | 0.03   |
| Institutionalized          |         |        |         |        |         |        |         |        |
| No                         | 10      | 11.11  | 83662   | 39.75  | 48987   | 40.59  | 132659  | 40.05  |
| Prison                     | -       | -      | 6607    | 3.14   | 1021    | 0.85   | 7628    | 2.30   |
| Care home                  | -       | -      | 155     | 0.07   | 63      | 0.05   | 218     | 0.07   |
| Orphanage                  | -       | -      | 285     | 0.14   | 149     | 0.12   | 434     | 0.13   |
| Psychiatric Hospital       | -       | -      | 318     | 0.15   | 99      | 0.08   | 417     | 0.12   |
| Others                     | -       | -      | 3565    | 1.70   | 1990    | 1.65   | 5555    | 1.68   |
| Blank                      | 80      | 88.89  | 115862  | 55.05  | 68392   | 56.66  | 184334  | 55.65  |
| PDL                        |         |        |         |        |         |        |         |        |
| Yes                        | -       | -      | 2657    | 1.26   | 166     | 0.14   | 2823    | 0.85   |
| No                         | 3       | 3.33   | 21214   | 10.08  | 11754   | 9.74   | 32971   | 9.95   |
| Blank                      | 87      | 96.67  | 185838  | 88.66  | 108781  | 90.12  | 295451  | 89.20  |
| Homeless Pop.              |         |        |         |        |         |        |         |        |
| Yes                        | -       | -      | 432     | 0.20   | 160     | 0.13   | 592     | 0.18   |
| No                         | 2       | 2.22   | 23023   | 10.94  | 11658   | 9.66   | 34683   | 10.47  |
| Blank                      | 88      | 97.78  | 186999  | 88.86  | 108883  | 90.21  | 295994  | 89.36  |
| Total                      | 90      | 100    | 210454  | 100    | 120701  | 100    | 331245  | 100    |

Legend: AIDS: Acquired immunodeficiency syndrome; HIV: Human immunodeficiency virus; PDL: Population deprived of liberty; Homeless pop.: Homeless population; Health prof.: Health professionals.
diagnosis of the disease. In addition, men are more exposed to factors that may compromise immunity, such as illicit drugs, smoking, and chronic diseases, such as diabetes mellitus and HIV.

The involvement of the economically active population is another issue that deserves attention. Similar results were observed in Rio de Janeiro (44% of the cases), Mato Grosso do Sul (49.9%) and Rio Grande do Sul (near 50%). The start of treatment requires temporary removal from work, which may, to a greater or lesser degree, compromise the economic situation of households.

In addition, the treatment of TB impacts the economy of the country itself since it requires specific human resources for the program, in addition to operational costs. In 2018 alone, the total cost of TB in Brazil was US$ 57 million.

The predominance of the pulmonary presentation (86.37%) and bacillary cases (54.78%) is also in line with the literature. It is estimated that a person with positive bacilloscopy infects from 10 to 15 people over the period of one year. It is important to emphasize that the percentage of bacillary individuals may be even higher since 23.60% of the cases did not undergo this exam.

Associated with this, the rates of cure (70.66%) and abandonment (9.11%) represent additional challenges for TB control. Low percentages of cure and high rates of treatment abandonment have been observed throughout the country. The complexity of this process is justified by the existence of multiple factors, among which those of personal nature stand out, such as the use of alcohol, illicit drugs, and smoking, as do those related to the availability and quality of services offered to the patients, as already discussed. We must highlight that the minimum cure rate recommended must be greater than or equal to 85% and the maximum abandonment rate is 5%.

In addition to these factors, the TB/HIV coinfection also deserves mention. In this study, 12.10% of individuals tested were reactive for HIV, similar to what was observed in other states of the country. Research carried out with the Brazilian population has shown that the cure is lower for patients with HIV (50.74% in HIV-positive patients and 71.10% in HIV-negative patients); in contrast, the abandonment rate is higher in this population (13.60% in coinfected patients and 9.52% in patients with TB only). It is noteworthy that 56.04% of the patients did not undergo HIV testing, which shows the magnitude of the challenge in combating the disease since the strategy recommends HIV testing in 100% of the TB cases diagnosed.

Even considering all the methodological care, the present study has limitations: (i) a large number of variables without information, particularly those representing risk factors and associated comorbidities; ii) use of secondary data from health information systems that may not express the reality; and (iii) the quality of the information, which has often been questioned, mainly due to the weaknesses faced by health monitoring services in smaller municipalities.

Finally, the study showed consistent evidence on the maintenance of the tuberculosis chain of transmission in the Northeast and the magnitude of the challenges to be faced. The epidemiological characterization and identification of risk factors and comorbidities represent an important step to the development of strategies that can help in the process of combating the disease.

Author’s Contribution
All authors participated in the development of the concept, planning of the study, data collection and analysis, discussion of the results, scientific writing, as well as in the review and approval of the final version of the work.
CONCLUSÕES: Mesmo com redução da incidência, a tuberculose representa um real problema de saúde pública na região Nordeste. O perfil caracterizado pela população masculina, idade economicamente ativa, forma pulmonar com baciloscopia positiva e os fatores e comorbidade Aids, coinfecção TB/HIV, diabetes mellitus, consumo de álcool, institucionalizados e privados de liberdade refletem a complexidade dos desafios para o enfrentamento à doença.

PALAVRAS-CHAVE: Tuberculose. Epidemiologia. Fatores de risco.

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