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

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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%). The cure rate was 70.66% and the abandonment rate was 9.11%.

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.

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].

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 Brasil, 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 inhabitants[3,4], 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 innovation[4].

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 population[5].

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 model[6]. 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 44,84/100,000 in 2001 to 30.92/100,000 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 55.81/100,000 in 2001 to 41,98/100,000 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 33,97/100,000 to 20,30/100.000, 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).
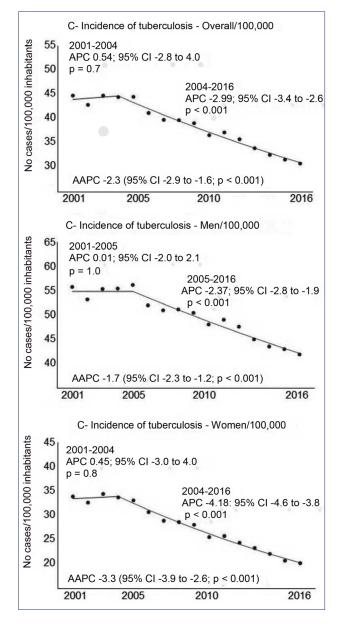
Clinical profile, risk factors, and prevalence of associated comorbidities
Out of the 331,245 TB cases registered in the Brazilian Northeast, the profile was characterized by males

(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 Brasil[7]. 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[3], and the greater coverage of the actions of the Family Health Strategy in recent years[8].

In the state of Piaui, the actions carried out by the Family Health Strategy, whose coverage reached 98.7% in 2016[7], 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[8]. 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[9].

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[3]. 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%[3]. This scenario shows that it is still necessary to strengthen the actions for combating TB in the Northeast[10,11].

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[12-14]. 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

FIGURE 1

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	22211	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	78183	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	58120	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	185595	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.

TABLE 2. RISK FACTORS AND COMORBIDITIES ASSOCIATED WITH 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	%
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	45.64
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	82.22	98782	46.94	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	48.34
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	186098	88.43	108123	89.58	294309	88.85
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	186583	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	295970	89.35
Health prof.								
Yes	-	-	178	0.08	257	0.21	435	0.13
No	2	2.22	23256	11.05	11558	9.58	34816	10.51
Blank	88	97.78	187020	88.87	108886	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 ppulation; Health prof.: Health professionals.

diagnosis of the disease[13.15]. 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[12.13].

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)[16], Mato Grosso do Sul (49.9%)[17], and Rio Grande do Sul (near 50%)[18]. The start of treatment requires temporary removal from work, which may, to a greater or lesser degree, compromise the economic situation of households[19].

In addition, the treatment of TB impacts the economy of the country itself[20] since it requires specific human resources for the program, in addition to operational costs[21]. In 2018 alone, the total cost of TB in Brasil was US$ 57 million[2].

The predominance of the pulmonary presentation (86.37%) and bacillary cases (54.78%) is also in line with the literature[12,16-18].]It is estimated that a person with positive bacilloscopy infects from 10 to 15 people over the period of one year[21]. 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[16.18]. 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[13,19,22], illicit drugs[22], and smoking[23], as do those related to the availability and quality of services offered to the patients, as already discussed[24]. We must highlight that the minimum cure rate recommended must be greater than or equal to 85% and the maximum abandonment rate is 5%[4].

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[16.17]. 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)[14]. 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.

RESUMO

OBJETIVO: *Descrever a tendência temporal, o perfil clínico e a prevalência de fatores de risco e comorbidades associadas em casos novos de tuberculose no Nordeste (2001-2016).*

MÉTODOS: *Estudo de prevalência envolvendo todos os casos de tuberculose registrados no Nordeste do Brasil, no período 2001-2016. Os dados foram obtidos do Sistema de Nacional de Agravos de Notificação. Para a análise estatística, empregaram-se o modelo de regressão por pontos de inflexão e a estatística descritiva.*

RESULTADOS: *Foram notificados 331.245 casos de tuberculose. A taxa de incidência geral reduziu de 44,84/100.000 habitantes (2001) para 30,92/100.000 habitantes (2016), com tendência decrescente (AAPC: −2,3; p<0,001). O perfil foi caracterizado por homens (73,53%), idade 20-59 anos (73,56%), tuberculose pulmonar (86,37%), baciloscopia positiva (54,78%). Os principais fatores de risco e comorbidade foram: Aids (4,64%), HIV (12,10%), Diabetes mellitus (5,46%), álcool (11,63%), institucionalizados (4,31%) e população privada de liberdade (2,30%). A taxa de cura foi 70,66% e a de abandono, 9,11%.*

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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