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Major Article

Two decades of tuberculosis in a city in Northeastern Brazil: advances and challenges in time and space

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ABSTRACT

Introduction: This study presents two decades of epidemiological data on tuberculosis (TB), in order to understanding the disease profile and its spatiotemporal dynamics. **Methods**: This descriptive study was performed in the City of Olinda/Pernambuco, Brazil, from 1991-2010, and it analyzed new patients with TB living in the city. We used the χ^2-test with a p-value <0.05 to identify differences in trends. Incidence and cluster distribution were identified using spatial scan statistics. **Results**: In total, 6202 new cases were recorded during the two decades. The highest incidence occurred in 1995 (110 cases/100,000 inhabitants), and the lowest occurred in 2009 (65 cases/100,000 inhabitants) (β=-1.44; R^2=0.43; p=0.0018). The highest mortality occurred in 1998 (16 deaths/100,000 inhabitants), and the lowest occurred in 2008 (5 deaths/100,000 inhabitants) (β=-0.19; R^2=0.17; p=0.07). There was a male predominance (65%), and ages ranged from 20-49 years (65%). There was a substantial increase in the number of patients that were cured after treatment (60% to 67%; p<0.001) as well as those tested for HIV (1.9% to 58.5%; p<0.001). During the first decade, clusters with p-values <0.05 included 29% of the total notified cases, and in the second decade, that percentage was 12%. **Conclusions**: We observed a decreasing trend in incidence, which was significant, and mortality rates, which was not significant. The increased number of laboratory tests performed reflects advances in surveillance, and a reduction in the proportion of cases in primary clusters suggests, among other things, that the disease is spreading across the region.

Keywords: Tuberculosis. Epidemiological surveillance. Spatial analysis.

INTRODUCTION

Tuberculosis (TB) remains a major public health problem, affecting millions of people each year. In 2010, there were 8.8 million new cases worldwide and 1.5 million deaths. In the same year, Brazil registered 71,000 new cases and 4,800 deaths. At that time while TB incidence in Brazil was 37 cases/100,000 inhabitants, the state of Pernambuco had an incidence of 46 cases/100,000 inhabitants, the fourth highest incidence amongst Brazilian states. TB-associated mortality, which throughout Brazil was 2.4 deaths/100,000 inhabitants, in the State of Pernambuco reached 4 deaths/100,000 inhabitants[1] [2].

Within Brazil, metropolitan municipalities have conditions that potentiate a higher risk of TB infection, such as a high population density and large concentrations of poverty. The relationships between high rates of TB infection and socioeconomic and demographic determinants have been established both on individual (male, young adult) and population [high illiteracy or co-infection with human immunodeficiency virus (HIV)] levels, revealing some causes of high disease incidence[3] [4] [5] [6].

A tuberculosis surveillance system aligned to a territorial base would link occurrences of the disease to the space where it occurs, thus enabling a more appropriate response from health services[7] [8]. Despite the availability of geospatial analysis software, application of these technologies within services is still limited, particularly with regard to surveillance strategies, which would certainly benefit from information regarding the territory, conditions, and determinants of TB incidence in order to optimize resources and prioritize actions.

Olinda, a municipality within the metropolitan region of Recife in Pernambuco, is the focus of a study of endemic diseases, including TB[7] [8] [9] [10] [11]. TB was previously monitored there for a decade (1991-2000) in research studies using a geostatistical approach[7] [8].

The present study has made a rare contribution by extending the epidemiological analysis of TB in the residents of Olinda for a 20-year period in order to deepen our knowledge regarding the profile of the disease and its spatiotemporal dynamics.

This approach can thereby identify trends that may indicate what strategies and surveillance actions need to be maintained, optimized, or changed to control disease within the city.

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METHODS

This descriptive historical study was conducted in the City of Olinda from 1991 to 2010. In 2010, Olinda had 377,779 inhabitants and 9,296 inhabitants/km², the highest population density in northeast Brazil[12].

Olinda has three homogeneous areas with regard to quality of housing: 1) the coastal zone, which has urban infrastructure and vertical density; 2) the central area, a region with irregular water supply and low sewer/sanitation coverage; and 3) the west, with poor housing standards and poor urban infrastructure[13].

Reported cases were obtained from the National System for Notifiable Diseases [*Sistema de Informação de Agravos de Notificação* (SINAN)][14]. Data on mortality and resident population were obtained from the Mortality Information System [*Sistema de Informações sobre Mortalidade* (SIM)][15] and the Brazilian Institute of Geography and Statistics *Instituto Brasileiro de Geografia e Estatística* (IBGE)][12], respectively.

Incidence rates and mortality were calculated for each of the years studied. As recommended by the National Tuberculosis Control Programme [Programa Nacional de Controle da Tuberculose (PNCT)][16], incidence was calculated from new cases, excluding patients who defaulted or received prior treatment. In order to analyze trends, simple linear regression models ($y = \beta 0 + \beta 1t$) were used, in which TB rates and years were the dependent (y) and independent (t) variables, respectively. P values <0.05 were considered significant in the hypothesis test $\beta=0$.

Profiles of new patients with TB were described in five-year periods (1991-1995, 1996-2000, 2001-2005, and 2006-2010), according to years of schooling, race/color, clinical form, the proportion of TB and HIV coinfection, smear and sputum culture performance, HIV testing, and the situation at case closure. Race/color was categorized as black and non-black, with the former including black and dark-skinned patients and the latter including white and indigenous patients[17]. Tests were considered as having been performed when results were *positive* or *negative*, and those classified as *in progress* were presented in a separate category.

TB incidence and proportion were also calculated according to sex and age group. To calculate trends, χ^2 with a 5% significance level was used for the five-year analyses. Data analysis was conducted in Epiinfo7.

Tuberculosis spatial analysis was conducted in five-year periods by analyzing the annual mean incidence rates via census tracts and using scan statistics. For this technique, the residences of the new patients were georeferenced and aggregated by census tracts and five-year periods. The Poisson probability model was utilized to test the hypothesis that there was a homogeneous TB incidence within municipalities throughout all census tracts[18]. The scan statistic technique uses circular windows that correspond to a geographic area. In this study, the clusters included proportions less than or equal to 5% of the resident population[18].

The number of sectors that formed each cluster was identified, together with the number of observed and expected cases, the relative risk, the p-value, the proportion of cases in relation to the total that occurred within the municipality, and the percentage of the total municipality population who reside in the cluster. We also stratified clusters according to the p-value for testing the homogeneous spatial distribution hypothesis for TB incidence into those being less than or equal to 5%, those between 5% and 20%, and those greater than 20%. Spatial data analyses were performed with SatScan 9.3.1[18] and Terraview 4.2.2[19].

Ethical considerations

The research project that included this study was submitted for approval to the Research Ethics Committee at the Centro de Pesquisas Aggeu Magalhães (Number 33878514.4.0000.5190 - report 782312/2014).

RESULTS

Between 1991 and 2010, a total of 6,924 TB cases were reported, of which 6,202 (89.6%) were new cases, resulting in a mean total of 310 new cases/year (**Table 1**). During the study period, the highest incidence occurred in 1995 (110 cases/100,000 inhabitants) and the lowest incidence occurred in 2009 (65 cases/100,000 inhabitants). A reduction in incidence was described using the model $y = 99.9 - 1.44t$ ($R^2=0.43$; p=0.0018), i.e. 29 cases were avoided per 100,000 inhabitants during the twenty years analyzed, a decrease of only 1.7% or almost 100 cases per year (**Figure 1**). Mortality rates fluctuated, with the highest and lowest occurring in 1998 (16 deaths/100,000 inhabitants) and 2008 (5 deaths/100,000 inhabitants), respectively. Despite the decreasing trend, there was no statistical significance ($y = 11.5-0.19t$; $R^2=0.17$; p=0.07) (**Figure 1**).

Although reductions in incidence were observed in both sexes, males were the most affected throughout the period, during which the male/female ratio remained 2/1. Reductions in incidence were also observed for all age groups, but while over 60% of cases concerned patients between 20 and 49 years of age, patients older than 50 years were most affected, with a rate of 153.6 cases/100,000 inhabitants between 1996 and 2000 (**Table 2**). Disease among this group accounts 26.2% of cases. Other identified features, although hindered by the high proportion of missing records, included the high proportion of patients with less than 8 years of study, including those with no schooling (44%), as well as a predominance of cases within the black community (27%) (**Table 1**). The pulmonary form of this disease was detected in over 80% of patients. However, extrapulmonary form increased when the first and last five-year periods were compared [relative risk (RR) =1.33; $\chi^2=8.7$; p=0.003] (**Table 1**). During these two decades, the sputum smear test was performed in 70% of cases, and the sputum culture was performed increasingly, from 4.3% during the first five years to 7% between 2006 and 2010 ($\chi^2=15.0$; p=0.0001). The most significant development was related to HIV testing, which rose from 1.9% of patients being tested between 1991 and 1995

TABLE 1 - Operational and epidemiological characteristics of patients with tuberculosis in Olinda, Pernambuco State, from 1991 to 2010.

Operational and epidemiological characteristics	1991-1995		1996-2000		2001-2005		2006-2010		Total	
	n	%	n	%	n	%	n	%	n	%
Total number of cases	1,747	-	1,981	-	1,649	-	1,547	-	6,924	-
Type of entry										
new case	1,647	94.3	1,647	83.1	1,495	90.7	1,413	91.3	6,202	89.6
relapse	57	3.3	153	7.7	83	5	69	4.5	362	5.2
return after abandonment	43	2.4	181	9.2	71	4.3	65	4.2	360	5.2
Schooling (in years)*										
0	43	2.6	224	13.6	152	10.2	72	5.1	491	7.9
1–8	162	9.8	802	48.7	618	41.3	653	46.2	2,235	36
9–11	51	3.1	202	12.3	282	18.9	233	16.5	768	12.4
11 and over	9	0.6	64	3.9	95	6.3	89	6.3	257	4.1
not applicable	50	3	40	2.4	42	2.8	45	3.2	177	2.9
not informed	1,332	80.9	315	19.1	306	20.5	321	22.7	2,274	36.7
Raçe/color*										
black	-	-	155	9.4	638	42.7	899	63.6	1,692	27.3
non-black	-	-	99	6	343	22.9	407	28.8	849	13.7
not informed	1,647	100	1,393	84.6	514	34.4	107	7.6	3,661	59
Form of disease*										
pulmonary	1,478	89.7	1,392	84.5	1,225	81.9	1,170	82.8	5,265	84.9
extrapulmonary	167	10.1	202	12.3	213	14.3	185	13.1	767	12.4
pulmonary + extrapulmonary	1	0.1	46	2.8	57	3.8	58	4.1	162	2.6
not informed	1	0.1	7	0.4	-	-	-	-	8	0.1
Case result*										
cure	980	59.5	770	46.8	1,036	69.3	948	67.1	3,734	60.2
abandonment	200	12.1	178	10.8	129	8.7	133	9.4	640	10.3
death	107	6.5	196	11.9	171	11.4	154	10.9	628	10.1
others	360	21.9	503	30.5	159	10.6	178	12.6	1,200	19.4
Sputum smear*										
performed	1,233	74.9	1,059	64.3	1,008	67.4	1,013	71.7	4,313	69.5
positive	937		828		785		769		3,319	
negative	296		231		223		244		994	
not performed	412	25	520	31.6	487	32.6	400	28.3	1,819	29.4
not informed	2	0.1	68	4.1	-	-	-	-	70	1.1
Sputum culture*										
performed	70	4.3	51	3.1	68	4.5	99	7	288	4.6
positive	43		34		48		54		179	
negative	27		17		20		45		109	
performed – in progress	23	1.4	75	4.6	107	7.2	93	6.6	298	4.8
not performed	1,552	94.2	1,461	88.7	1,320	88.3	1,221	86.4	5,554	89.6
not informed	2	0.1	60	3.6	-	-	-	-	62	1
HIV Testing*										
performed	31	1.9	104	6.3	207	13.8	827	58.5	1,169	18.8
positive	29		54		93		155		331	
negative	2		50		114		672		838	
performed – in progress	2	0.1	84	5.1	225	15.1	251	17.8	562	9.1
not performed	1,611	97.8	1,384	84	1,063	71.1	335	23.7	4,393	70.8
not informed	3	0.2	75	4.6	-	-	-	-	78	1.3

HIV: human immunodeficiency virus. * Indicators calculated from the total of new cases notified during the five-year period.

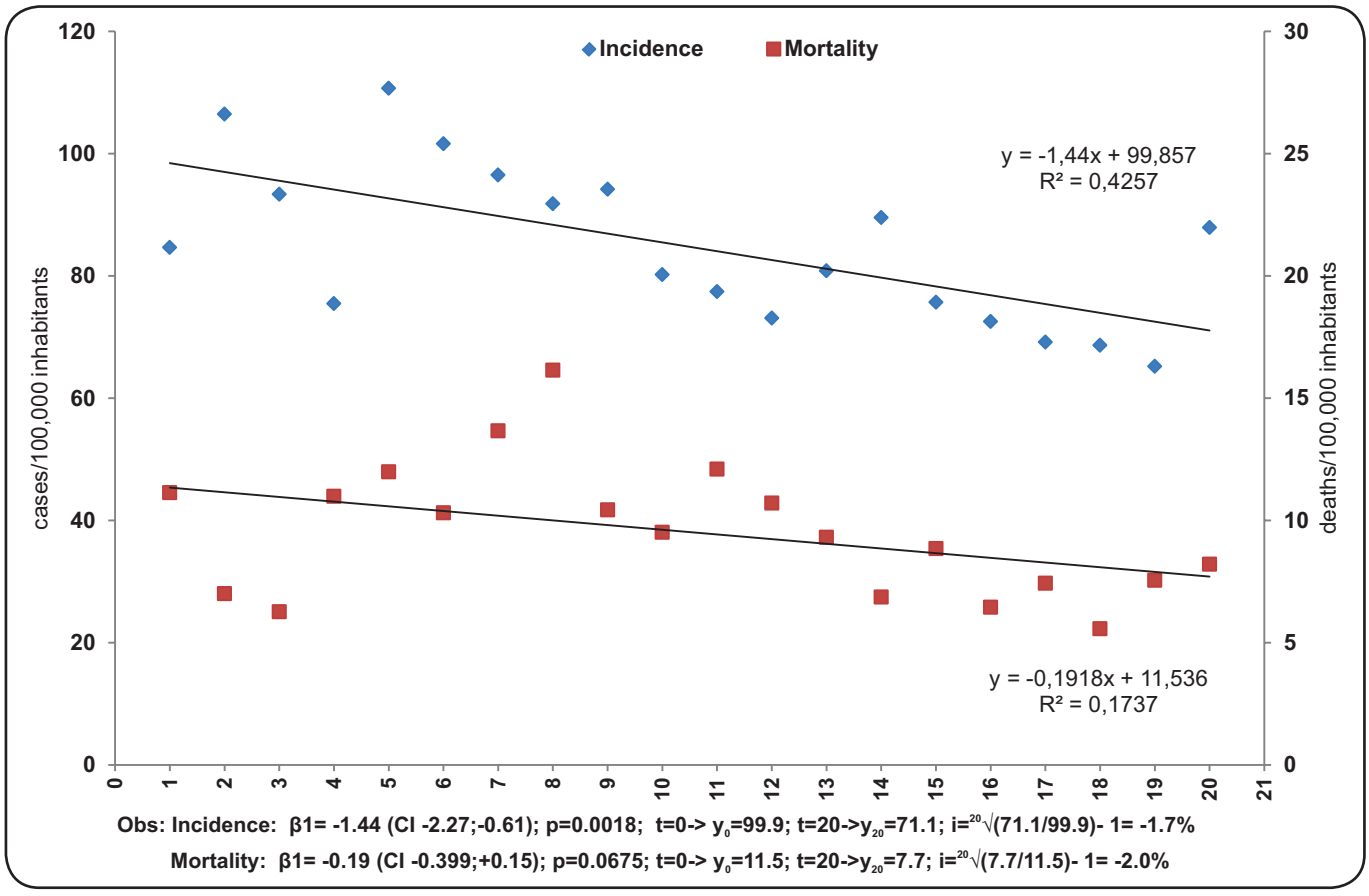

FIGURE 1- Incidence and mortality trends for tuberculosis in Olinda, Pernambuco State, from 1991 (t=1) to 2010 (t=20).

TABLE 2 - Distribution, incidence (cases/100,000 inhabitants), and relative risk of new TB cases according to patient age and sex in Olinda, Pernambuco State, from 1991 to 2010.

	1991-1995				1996-2000				2001-2005				2006-2010			
	n	%	incid	RR	n	%	incid	RR	n	%	incid	RR	n	%	incid	RR
Age group (years)																
<20	215	13.3	28.5	1.0	172	10.6	25.0	0.9	139	9.4	20.0	0.7	123	8.8	19.3	0.7
20–49	1,047	65.0	137.9	1.0	1,023	63.2	127.5	0.9	996	67.6	114.4	0.8	883	63.5	92.2	0.7
≥50	350	21.7	143.5	1.0	424	26.2	153.6	1.1	339	23.0	107.1	0.7	386	27.7	101.5	0.7
Sex																
male	1,078	65.5	130.4	1.0	1,008	61.2	121.5	0.9	976	65.3	110.9	0.9	906	64.1	98.6	0.8
female	569	34.5	61.1	1.0	639	38.8	68.3	1.1	519	34.7	51.9	0.8	507	35.9	48.0	0.8

TB: tuberculosis; **n:** number; %: percentage; **incid**: incidence; **RR:** relative risk.

to a total of 58.5% of cases reported during the last five years (RR=73.6; χ^2=1502 9; p<0.001) (**Table 1**). However, given the evolution of laboratory testing, there is an outstanding number of results classified as *in progress*, both for the sputum culture and HIV testing, which in the last five years reached 17.8% (**Table 1**).

Cure rates started at 59.5% in the first five-year period and reached 67.1% between 2006 and 2010 (RR=1.39; χ^2=63.0; p<0.001) and, over the same period, treatment abandonment was reduced from 12.1% to 9.4% (RR=0.75; χ^2=9.4; p=0.002) (**Table 1**). The model estimates an initial incidence of 99.9 cases / 100,000 inhabitants and a final incidence of 71.1 cases/100,000 inhabitants (**Figure 1**). With an average incidence of 86 cases/100,000 inhabitants, these three values guided the construction of spatial distribution categories. Rates

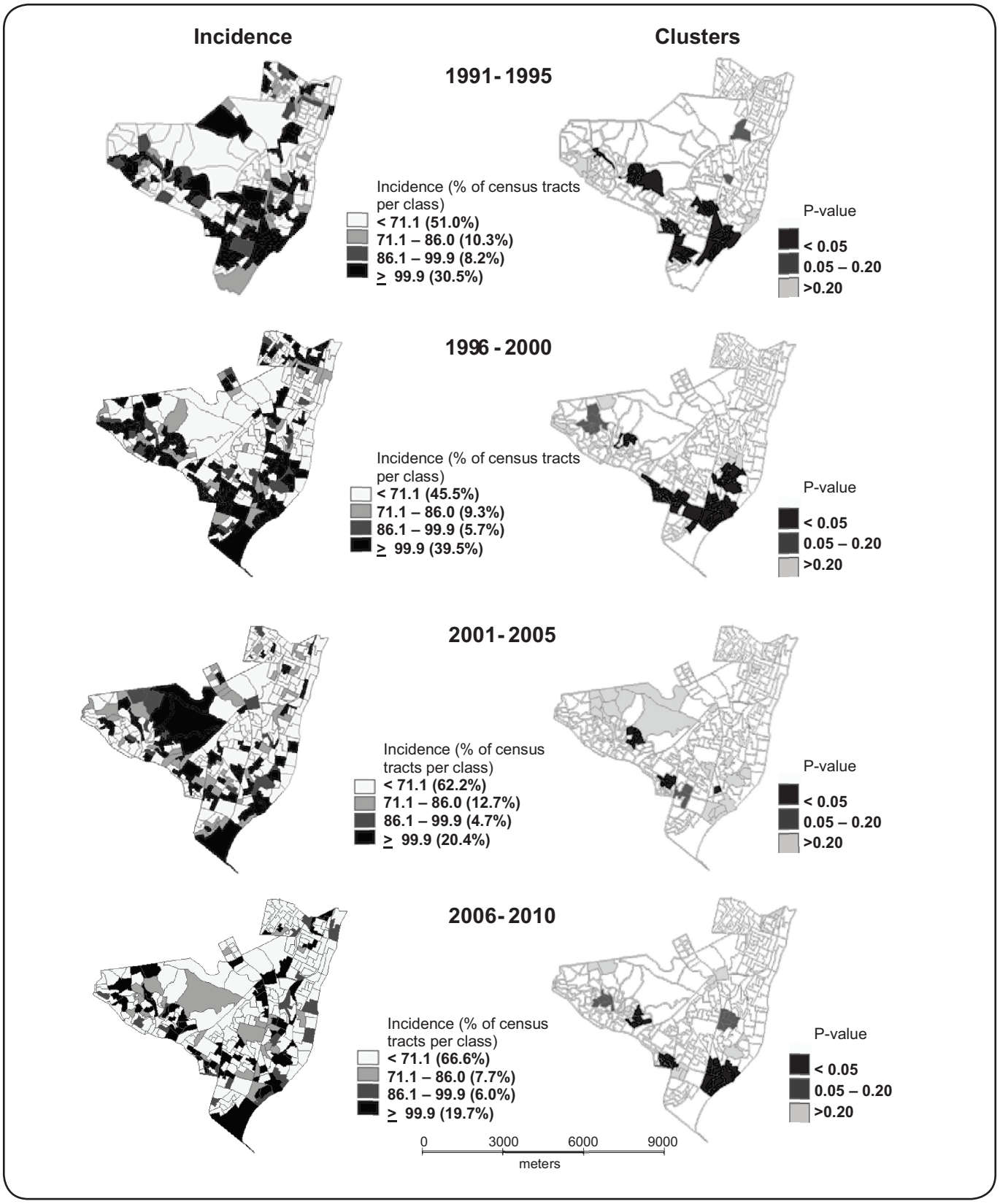

FIGURE 2 - Incidence (cases/100,000 inhabitants) and TB clusters according to residential census tracts in Olinda, Pernambuco State, from 1991 to 2010. **TB:** tuberculosis.

above 99.9 cases/100,000 inhabitants suggest that, over the study period, the sectors presented (or remained) in a situation similar to conditions observed in the early 1990s.

By comparing the four five-year periods, there was a significant reduction in the proportion of census tracts in which the incidence was higher than 99.9 cases/100,000 inhabitants, although with 6% of the confidence interval (CI) 86-99.9, suggesting the possibility of a homogeneous TB trend within the territory (**Figure 2**). Cluster analysis confirmed this hypothesis by demonstrating that in both five-year periods of the first decade almost 30% of cases were concentrated within the clusters with $p<0.05$, which had numbers of TB cases greater than would be expected if the spatial distribution was homogeneous. These values were significantly lower in the third and fourth five-year periods, suggesting a greater disease spread (**Figure 2** and **Table 3**).

TABLE 3 - Characteristics of TB clusters in Olinda, Perambuco State from 1991 to 2010.

Clusters	Number of sectors	Number of cases		RR	P value	Population (%)*	Cases (%)**
		observed	expected				
1991 to 1995							
1	8	112	44	2.7	$4.0x10^{-15}$	3.1	7.8
2	8	97	46	2.2	$1.8x10^{-8}$	3.2	6.8
3	3	45	18	2.5	$4.9x10^{-5}$	1.3	3.1
4	1	24	7	3.4	$3.1x10^{-4}$	0.5	1.7
5	7	77	46	1.7	0.009	3.2	5.4
6	5	55	30	1.9	0.018	2.1	3.8
7	1	21	8	2.7	0.055	0.6	1.5
8	1	14	4	3.1	0.122	0.3	1.0
9	4	34	18	1.9	0.290	1.3	2.4
10	2	17	7	2.4	0.439	0.5	1.2
11	5	48	30	1.6	0.509	2.1	3.4
12	1	11	5	2.2	0.995	0.3	0.8
1996 to 2000							
1	10	145	62	2.5	$1.0x10^{-17}$	3.7	8.6
2	4	71	25	2.9	$6.9x10^{-11}$	1.5	4.2
3	13	110	61	1.9	$7.0x10^{-6}$	3.6	6.6
4	8	75	41	1.9	0.001	2.4	4.5
5	8	99	59	1.7	0.001	3.5	5.9
6	7	72	45	1.6	0.074	2.7	4.3
7	1	18	7	2.5	0.320	0.4	1.1
8	1	18	7	2.5	0.330	0.4	1.1
9	1	16	6	2.5	0.480	0.4	1.0
10	4	40	24	1.7	0.688	1.4	2.4
11	1	14	6	2.4	0.787	0.3	0.8
12	1	10	4	2.8	0.899	0.2	0.6
13	2	20	11	1.8	0.998	0.7	1.2

continue....

TABLE 3 - Continuation.

Clusters	Number of sectors	Number of cases		RR	P value	Population (%)*	Cases (%)**
		observed	expected				
2001 to 2005							
1	5	58	23	2.6	$7.8x10^{-7}$	2.1	5.2
2	1	14	2	6.1	$1.6x10^{-4}$	0.2	1.2
3	4	35	15	2.4	0.007	1.3	3.1
4	4	35	17	2.1	0.059	1.5	3.1
5	1	15	5	2.8	0.319	0.5	1.3
6	7	44	27	1.7	0.590	2.4	3.9
7	1	15	6	2.5	0.638	0.5	1.3
8	5	29	17	1.8	0.876	1.5	2.6
9	3	19	10	1.9	0.990	0.9	1.7
10	1	7	2	3.0	0.993	0.2	0.6
11	1	7	2	3.0	0.993	0.2	0.6
12	2	17	9	1.9	0.999	0.8	1.5
13	2	13	6	2.0	0.999	0.6	1.2
14	3	21	12	1.7	0.999	1.1	1.9
2006 a 2010							
1	11	74	31	2.5	$1.2x10^{-7}$	2.9	6.8
2	8	63	29	2.3	$3.4x10^{-5}$	2.6	5.8
3	4	36	17	2.2	0.026	1.5	3.3
4	4	34	16	2.2	0.054	1.5	3.1
5	7	49	27	1.8	0.107	2.5	4.5
6	2	17	6	2.7	0.194	0.6	1.6
7	2	15	7	2.3	0.887	0.6	1.4
8	3	21	11	1.9	0.966	1.0	1.9
9	2	15	8	2.0	0.996	0.7	1.4
10	4	24	15	1.7	0.998	1.3	2.2
11	3	23	14	1.6	0.999	1.3	2.1
12	1	7	3	2.4	0.999	0.3	0.6

TB: tuberculosis; **RR:** relative risk. *Percentage of the total population in the city living in the cluster. **Percentage of the total number of cases in the city that occurred within the cluster.

DISCUSSION

The reduction in TB incidence in Olinda over two decades is in accordance with the behavior of the disease throughout Brazil as a whole[20]. Between 1990 and 2010, while there was a 3.2% decrease per year in incidence rate across the country[20], but in Olinda, this proportion was 1.7%. During the 20-year period analyzed, only about 100 cases have been avoided.

If we consider the country as a whole, the improvements observed through some tuberculosis indicators are in line with the advances made in healthcare management[21]. Municipalization, decentralization of actions and services, and strengthening of primary health care through the Family Health Strategy were some outstanding features of the 1990s. In the 2000s, TB was considered a priority in the National Policy of Primary Healthcare[22]. This was true at a federal level, with the creation of the Secretariat of Health Surveillance[23], and the PNCT underwent reforms that benefited the integration of support actions and epidemiological surveillance, especially within the states and municipalities.

With so many advances, the disconcerting question, *Why have strategies that have proved efficient for the country as a whole been unsuccessful in attaining the required magnitude of effects on TB indicators in the city of Olinda?* remains. The differences observed between Olinda and the rest of the country suggest that this improvement occurs with different intensities, possibly due to inequalities between municipalities and intramunicipal scales.

The TB situation within the municipality not only emphasizes the need to optimize the strategies already in place but also to adopt others that are able to harness data that go beyond those inherent to the health sector and may explain the occurrence of the disease, such as territory-based surveillance. This approach could provide support for planning and executing actions at different levels, thus positively influencing TB indicators.

There was an insignificant trend in mortality reduction. In 2010, mortality exceeded double the state and was more than three times the national average. However, these findings may not only be describing the poor prognosis in the city, as they may have been influenced by SIM quality improvement during the two decades analyzed[17] [24] [25]. This justification does not reduce the importance of implementing a mortality surveillance system that examines routine relationships between databases, home, and hospital; forms of a multidisciplinary technical group to discuss death and partnerships, such as civil society, and controls programs for sexually transmitted disease- acquired immunodeficiency syndrome (STD/AIDS) and viral hepatitis.

The higher proportion of male patients is consistent with findings in the current literature, with a possible cultural and social determination related to exposure[1] [26] [27] [28]. Biological factors should also be considered, since there are generally significant sexual differences between respiratory tract infection (RTI) development and outcomes[29]. Males appear to suffer from most commonly forms of RTI, and also they usually experience a more severe disease course with higher mortality rates[29] [30]. Being aware that only 5% to 10% of individuals who are exposed to *Mycobacterium tuberculosis* develop TB and that up to 70% of people who develop the disease are male[29], researchers should be encouraged to investigate in greater depth the manner in which genetic variations and steroid hormones, for example, differentially influence disease susceptibility between the sexes.

In terms of age, over 60% of cases involved patients who were between 20 and 49 years old, although there was a high incidence in those aged 50 years or older. Awareness that this population group is more sensitive to TB reactivation owing to lower immunity while they have higher occurrences of chronic diseases, the Tuberculosis Control Program needs to be linked to disease surveillance programs, health care programs for the elderly in order to minimize adverse outcomes. On the other hand, a reduction in cases involving patients who are less than 20 years old may indicate a reduction in active transmission and recent infection.

In the present study, 45% of patients reported that they received up to eight years of schooling, including the illiterate[25] [31] [32]. Low levels of education reflect a set of poor socioeconomic conditions that increase vulnerability to TB and consequently the increase disease incidence, while lowering adherence to treatment[32].

Information quality is directly related to the completeness of notification and monitoring tools. The present study revealed that the notification forms supplied to Sinan have become more thorough, now including variables such as race/color. This advancement, however, requires caution when interpreting data, since it is not possible to affirm, for example, that in Olinda there was an increase in notifications from the black community. It is probable that this increase was caused by improved registration, and not necessarily by a change in disease.

Tuberculosis can affect a number of organs and systems, with the pulmonary form, which in Brazil is detected in 85% of patients aged 15 years and over, being the most common. In Olinda, the mean ratio of this form is similar to that recorded for the entire country. More often than not, pulmonary bacillary TB are relevant to public health since they maintain the transmission chain of the disease[16].

High proportions of pulmonary TB in a community justify the need for the sputum smear – a simple and safe method that should be performed by all public health laboratories and authorized private laboratories. When performed properly, the test is able to detect between 60-80% of pulmonary TB cases[16]. Over the 20-year period, a mean 70% of patients notified during the five-year periods performed the test. Throughout all of Brazil, this ratio varied from 76.4% to 85.3%[16] [33] [34] [35].

Due to its importance, the sputum smear should be encouraged, along with other features, such as those offered by the GeneXpert system, which allows the simultaneous detection of *Mycobacterium tuberculosis* and rifampicin resistance testing using sputum[36]. A systematic review involving 18 studies and 10,224 biological specimens demonstrated that a single Xpert *Mycobacterium tuberculosis* (MTB) DNA and resistance to rifampicin (RIF) test detected 90.4% of pulmonary TB cases (98.7% smear-positive and 75% smear-negative)[37].

In pulmonary cases with negative sputum smears, sputum culture can increase bacteriological diagnosis of the disease by up to 30%[16]. Given this importance, there has been a modest increase in performing sputum culture performance from 4.3% to 7%.

During the two decades, HIV testing increased significantly. However, in 41.5% of the cases, tests were either not performed, or they were performed but results were still *in progress*. In Brazil, testing is still insubstantial, and in a number of localities the frequency of patients who do not undergo the test is over 80%[38]. The low proportion of HIV testing and culture may reflect difficulties in laboratory access, delays in receiving results, lost tests, or even a lack of updated information systems. Given the estimations in Olinda of patients coinfected with TB and HIV, both the efforts of professionals who serve patients and the validity of information are jeopardized due to these structural flaws.

In Brazil, TB is approximately 30 times more common in people living with HIV, compared to the incidence in the general population[39]. Hence, the Ministry of Health recommends that HIV testing be mandatory for patients with detected cases of TB, and vice versa[16], which is aimed at initiating immediate intervention. Clinical trials have shown that concomitant

treatment is able to reduce mortality by over 50%[40]. Thus, the high numbers of unperformed blood tests or of those still *in progress* jeopardizes the timely initiation of treatment and hinders the structuring of public health plans in order to prevent and reduce deaths from TB-HIV.

With regard to case outcomes, during the two decades, a cure rate of 60.2% was identified, reaching a maximum of 67.1% in the last five-year period, although the rate was still below the 85% recommended by PNCT[41]. Throughout the entire period, treatment abandonment and deaths remained at 10%. The abandonment of treatment not only affects the rising treatment costs, but it also affects mortality rates and disease recurrence, while facilitating the selection of resistant strains[42] [43].

However, similar to occurrences in other Brazilian cities[28] [34] [35], case outcome analysis is hampered by the high (19.3%) percentage of cases where circumstances at the end of treatment were classified as *ignored*, *transferred*, or *changed treatment*, thus suggesting failings in appropriate patient monitoring by the health team or insufficient flow of existing information.

In relation to the spatial analysis method used, it should be highlighted that the differential of this method lies in the manner with which it characterizes the relevant cluster according to the exposed population and the concentration of cases in relation to the total within the municipality. Contrary to misgivings concerning the use of grouping sectors with low incidence levels to generate clusters[44], this was not an issue in the present analysis.

The adopted cluster sizes grouped up to a maximum of 5% of the exposed population with the territory analysis characteristics, such as the distribution of cases and the exposed population. Demarcation of the problem based on census tracts has enabled us to view the heterogeneous distribution of the disease in urban areas, thus enabling intervention planning aimed at specific groups[9].

Although there has been a reduction in incidence in Olinda, it was nonetheless small. In addition to this, particularly when the first and second decades are compared, cluster spatial distribution reveals that, groups with statistical significance higher than p-value <0.05 accounted for a smaller proportion of cases and were composed of a smaller number of sectors. On the other hand, over the years, the cases were spread across the territory of Olinda, but, nonetheless, they still persisted in areas with greater social needs, an association that is widely described in the literature[4] [7] [8] [9] [10] [45] [46] [47] [48] [49]. Other factors may also have influenced this spreading, such as the common acquisition of the illness outside the home or the largest proportion of cases associated with reactivation, which was common for over 50 years. As described by Souza et al.[9], characteristics related to tuberculosis control programs, such as those in regions with households having more than one new case or retreatment cases may also be related to a greater number of cases in a given area.

In order to better understand how this spatial distribution develops, studies should be encouraged that, amongst other things, address two questions: 1) *Could primary care expansion in the City of Olinda, during the studied decades, have influenced higher TB detection levels?* and 2) *Could the apparent change in the disease distribution profile be related to a possible increase in TB/HIV coinfection?*

Finally, it is important to consider that there may be characteristics directly resulting from the disease control program associated with a higher TB incidence, such as cases of additional treatment and families with two or more affected persons in the same household[8]. This report reveals that the incorporation of mapping within routine health surveillance, along with periodic updates of the associated factors, may contribute to the organization of health services. On the other hand, it reinforces the greater responsibility that health services have to face with controlled actions that are able to impact disease incidence.

After a 20-year period, despite a reduction in incidence and a downward trend in mortality, TB rates in Olinda are higher than the mean rates of the state and the country as a whole. The low number of smear tests and sputum cultures indicate that the available technologies are underutilized. The high percentage of HIV tests *in progress* exemplifies the fragile feedback of the information system, and it hinders the estimates of TB-HIV co-infection in the city as well as planning based on the main instrument for decision making.

Analysis of the spatial distribution of cases demonstrated that relevant clusters remained in the same regions during the two decades, which not only indicates that these areas presented similar socioeconomic characteristics during the period, but it also indicates that the actions to control the disease need to be optimized and made more appropriate for this extremely vulnerable population group.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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