

CLINICAL- EPIDEMIOLOGICAL PROFILE OF PATIENTS WITH TUBERCULOSIS IN ALAGOAS

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Abstract: **Objective:** To evaluate the clinical-epidemiological profile of patients with tuberculosis in Alagoas. **Methods:** Observational study of historical analysis type. From January 2005 to December 2015, a survey was carried out of cases notified in the Information System for Notifiable Diseases and in reference centers for the treatment of tuberculosis in Alagoas. **Results:** 12,432 cases were reported, with a mean incidence of 35.7/100,000 inhabitants (31.8% reduction compared to the previous period). There was a predominance of males (61%), with 58.6% aged between 20 and 49 years, 69.4% brown and most with low education. The pulmonary form was predominant in 87.4% of the cases. The most frequent comorbidity was alcoholism (15.5%), followed by diabetes mellitus and human immunodeficiency virus infection, 7.8% and 5.3%, respectively. Cure occurred in 74.6% of cases and treatment was abandoned in 10.5%. Of the 127 patients referred to the reference centers, drug resistance was observed in 55.1% and adverse effects in 29.1%. There was a higher frequency of adverse effects in females under 40 years of age and of drug resistance in individuals under 40 years of age. **Conclusion:** The average incidence rate of tuberculosis in Alagoas, in the period, was 35.7/100 thousand inhabitants, representing a decrease of 31.8% in the last 10 years. The clinical-epidemiological profile was similar to that reported in the literature. In reference centers, patients with multidrug-resistant forms of tuberculosis or with adverse effects were predominantly referred. The analysis of cases of multidrug resistance and adverse effects requires a prospective study with an adequate sample.

Keywords: Tuberculosis, health profile, drug resistance, adverse effects, risk factors.

INTRODUCTION

Tuberculosis (TB) is recognized worldwide as a “neglected calamity”, affecting 9.9 million people worldwide, being the second cause of death among infectious and contagious diseases (1, 2). In Brazil, in 2021, 68,271 cases were diagnosed new, with an incidence rate of 32.0/100,000 inhabitants, according to the Notifiable Diseases Information System (SINAN). The state of Alagoas had an incidence of 22.1 cases/100,000 inhabitants, ranking second lowest incidence in the Northeast and the eighth in Brazil (3).

Brazil, in 2020, had a mortality rate of 2.1 deaths/100,000 inhabitants, likewise, the state of Alagoas also had the same mortality rate this year, ranking third in the Northeast and twelfth in the country. In the city of Maceió, 2.8 deaths/100,000 inhabitants were recorded, ranking twelfth among all the capitals in the country. Most deaths were found in metropolitan areas and hospital units (3).

Tuberculosis remains one of the main health problems to be faced globally, with social inequalities, migratory flows, deficiencies in the health system and cases of resistant tuberculosis contributing to this fact (4).

TB primarily affects males, young adults aged between 20 and 49 years, brown and with low education (5, 6, 7). The pulmonary form is the most frequent clinical and radiological presentation of TB, especially in immunocompetent patients (8). Some diseases contribute to the emergence of tuberculosis, especially infection by the human immunodeficiency virus (HIV), alcoholism and diabetes mellitus (DM) (9).

The reported cure rate with the use of drugs is greater than 90%, when using combinations of first-line anti-TB drugs: Rifampicin (R), Isoniazid (H), Pyrazinamide (Z) and Ethambutol (E); with correct and daily doses scheme, and use for a sufficient period of time

(intensive phase of 2 months with RHZE and 4 months of maintenance with RH) (10, 11).

The therapy is susceptible to resistance, being considered as monodrug resistant when resistance to a drug and polydrug resistant when there is resistance to two or more drugs, except for the association rifampicin and isoniazid. Individuals with tuberculosis who present a sensitivity test demonstrating bacillary resistance to at least R and H are considered multidrug-resistant (MDR-TB), and extensively resistant (XDR-TB) when they show resistance to rifampicin and isoniazid plus a fluoroquinolone and a second- rate drug line (amikacin, capreomycin, etc.), (8).

Anti-TB drugs have side effects, either by their own active principle or by its metabolites, with hepatotoxicity, gastrointestinal intolerance, skin reactions and allergies being considered the most important adverse effects (12). Hepatotoxicity is related to a higher rate of treatment abandonment, since it leads to an increase in the duration of treatment. therapy, higher number of hospitalizations and outpatient and home visits (13, 14).

Anti-TB drugs account for 3% of drug-induced liver diseases (DILI), which account for 30% of acute hepatitis cases and more than 50% of jaundice cases. In DILI, asymptomatic elevation of liver enzymes may occur in 20% of patients using isoniazid (15, 16). The incidence of hepatotoxicity by anti-TB drugs in the general population ranges from 2 to 28% (17). The lack of specificity of symptoms and the lack of monitoring of aminotransferases favor that liver injury is often underdiagnosed.

Risk factors related to the development of adverse effects by anti-TB drugs in the general population are: female gender, age over 40 years, malnutrition, slow acetylator patients, alcohol abuse, HIV infection, previous kidney and liver disease, mainly due to hepatitis B virus (HBV) and hepatitis C (HCV) (18,19,20). While the risk factors related to multidrug

resistance are: male gender, weight loss, previous and irregular treatments, alcoholism and smoking (21).

Given the data presented by Alagoas, with an incidence of 33.4 cases/100,000 inhabitants and mortality of 3.3 deaths/100,000, ranking second in the Northeast and fifth in the country, we propose to analyze the clinical-epidemiological profile of the cases notified of TB in Alagoas in referral centers, checking the reason for entry, the frequency of adverse effects of anti-TB and multidrug resistance drugs, and their relationship with risk factors.

METHODS

An observational study of the type of historical analysis was carried out, from January 2005 to December 2015, with data collection of notified cases of TB in Alagoas in SINAN and the cases treated in the following reference centers: "II Centro de Saúde Dr. Diógenes Juca Bernardes" in Maceió (AL), Hospital Universitário Professor Alberto Antunes (HUPAA) in Maceió (AL) and "Centro de Referência Integrado de Arapiraca" (CRIA) in Arapiraca (AL). The present study was approved by the Research Ethics Committee (CEP) of the State University of Health Sciences of Alagoas (UNCISAL), with the Certificate of Ethical Appreciation (CAAE): 57021716.0.0000.5011.

All TB cases reported on SINAN during the proposed period were included in this survey, as well as cases registered in reference centers, which had data properly completed in electronic medical records, available on a national reference site for TB (22). Patients with incomplete information were excluded.

The average incidence rate was calculated using the average of new TB cases notified on SINAN by the average of the estimated population, according to the Brazilian Institute of Geography and Statistics (IBGE) (23).

Socio-demographic characteristics were analyzed: gender, age, color and education; forms of clinical presentation in pulmonary and extrapulmonary, comorbidities (alcoholism, DM and HIV), in addition to the closure situation or outcome of the case. With regard to patients treated at reference centers, the reason for admission (adverse effects and drug resistance) and possible risk factors related to adverse effects and multidrug resistance were evaluated.

Data were tabulated and analyzed using a data spreadsheet program (Microsoft Excel2010) and, to enable the analysis of risk factors for adverse effects and multidrug resistance to anti-TB drugs, statistical analysis was performed using the BioEstat program, version 5.0, using Pearson's chi -square test, using a significance level (p) <0.05 .

RESULTS

During the analyzed period, 12432 new cases of TB were reported in the state of Alagoas (SINAN). The average incidence was 35.7 cases/100,000 inhabitants, the highest rate was observed in 2005 (41.4) and the lowest in 2015 (28.2), corresponding to a drop of 31.8%, as shown in figure 1.

Table 1 shows the clinical-epidemiological profile of the 12,432 TB cases evaluated. Most patients with TB in Alagoas were male (7642 cases; 61%), young adults (20-40 years old), corresponding to 7280 cases (58.6%) and brown (7865 cases; 69.4%). Low schooling was observed, consisting of illiterates (1582 cases; 19%) and incomplete/complete primary education (4986 cases; 60%).

The predominant clinical presentation of TB was the pulmonary form (10863 cases; 87.4%), followed by the extrapulmonary form (1569 cases; 12.6%).

The most frequent comorbidity was alcoholism (1933 patients; 15.5%), followed by diabetes mellitus (968 cases; 7.8%) and

HIV infection (661 cases; 5.3%).

As for the situation of closure or outcome, 9050 (74.6%) patients were considered cured, with 1296 (10.5%) cases of treatment abandonment (10.5%) and 987 transfers of patients being recorded, of which 127 (12.8%) for reference centers in the state.

Table 2 shows the reason for entry or referral of the 127 patients treated at the reference centers, with a predominance of drug resistance, 70/127 (55.1%) cases, with a pattern of multidrug resistance in 68.5% (48/70). Adverse effects accounted for 29.1% (37/127) of referrals, with a predominance of hepatotoxicity in 59.5% (22/37). Cases of non-TB mycobacteria (NTM), special scheme abandonment and others corresponded to the rest of the referrals (20 cases; 15.7%).

Table 3 shows the distribution of variables according to the effects adverse effects to anti-TB drugs, with a higher frequency of females and age below 40 years in individuals who had adverse effects (p) <0.05 . The other variables studied (alcoholism, DM and HIV) showed no significant difference.

Table 4 shows a higher frequency (p) <0.05 of cases of multidrug resistance in individuals younger than 40 years, which was not verified with other variables.

DISCUSSION

TB continues to deserve attention from society as a whole, as it still has all the criteria for prioritizing a public health problem, that is, of great magnitude, transcendence and vulnerability.

According to this research, the average incidence of TB in Alagoas was 35.7 cases/100,000 inhabitants, with a decrease of 31.8% during the period evaluated (2005-2015). Despite the average incidence remaining similar to the national one, its incidence in 2015 of 28.2/100,000 inhabitants is close to the recommended millennium development

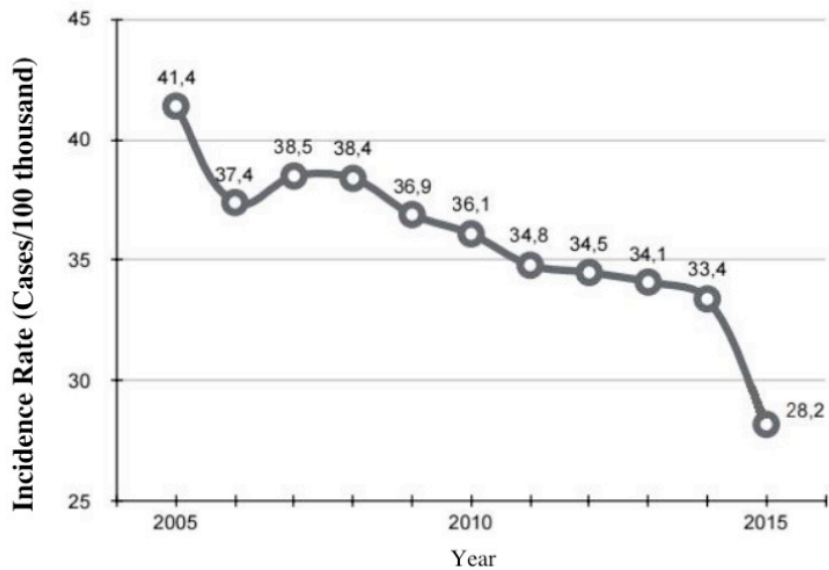


Figure 1. Distribution of the incidence rate according to the years evaluated.

Variables	n	%
Gender (n = 12432)		
Male	7642	61
Feminine	4790	39
Age Range (n = 12432)		
< 1	63	0.5
1 – 19	2773	22.3
20 – 49	7280	58.6
≥ 50	2316	18.6
Color (n = 11343)		
Brown	7865	69.4
White	1930	17.0
Black	1386	12.2
Yellow	114	1.0
Indigenous	48	0.4
Schooling (n = 8317)		
Illiterate	1582	19.0
Incomplete/complete primary Education	4986	60.0
Incomplete/complete high school	1382	16.6
Incomplete/Complete University Education	367	4.4
Clinical form (n = 12432)		
Pulmonary	10863	87.4
Extrapulmonary	1569	12.6
Comorbidities (n = 12432)		
Alcoholism	1933	15.5
Diabetes Mellitus	968	7.8
HIV infection ¹	661	5.3
Others	2132	17.2

Absent	6738	54.2
Termination situation (n = 12136)		
Cure	9050	74.6
Abandonment	1269	10.5
Transfer	987	8.1
Death from tuberculosis	416	3.4
Others	414	3.4

¹ HIV: Human Immunodeficiency Virus.

Table 1: Clinical-epidemiological profile of tuberculosis in Alagoas between 2005-2015

Reason for entry	n	%
Pharmacoresistance		
Multiresistance	48	68.6
Monoresistance	16	22.9
Polyresistance	5	7.1
Extensive resistance	1	1.4
Total	70	100
Adverse effects		
Hepatotoxicity	22	59.5
Gastrointestinal intolerance	6	16.2
Skin reaction	4	10.8
Allergy	3	8.1
Others	2	5.4
Total	37	100

Table 2: Distribution of reason for entering tuberculosis reference centers in Alagoas

Features	Adverse effects		Total (%)	P
	Yes (%)	No (%)		
Gender				
Male	17 (22.7)	58 (77.3)	75 (59)	0.04
Feminine	20 (38.5)	32 (61.5)	52 (41)	
Age				
< 40 years	20 (39.2)	31 (60.8)	51 (40.2)	0.04
≥ 40 years	17 (22.4)	59 (77.6)	76 (59.8)	
Alcoholism				
Yes	7 (31.8)	15 (68.2)	22 (17.3)	0.76
No	30 (28.6)	75 (71.4)	105 (82.7)	
HIV infection ¹				
Yes	6 (46.2)	7 (53.8)	13 (10.2)	0.15
No	31 (27.2)	83 (72.8)	114 (89.8)	

Diabetes Mellitus

Yes	3 (17.6)	14 (82.4)	17 (13.4)	0.26
No	34 (31)	76 (69)	110 (86.6)	
Total	37 (29.1)	90 (70.9)	127 (100)	

¹ HIV: Human Immunodeficiency Virus.

Table 3: Relationship between risk factors and adverse reactions to tuberculosis drugs.

Features	TBMR ¹		Total (%)	P
	Yes (%)	No (%)		
Gender				
Male	27 (36)	48 (76)	75 (59)	0.6
Feminine	21 (40.4)	31 (59.6)	52 (41)	
Age				
< 40 years	26 (51)	25 (49)	51 (40.2)	0.01
≥ 40 years	22 (29)	54 (71)	76 (59.8)	
Alcoholism				
Yes	6 (27.3)	16 (72.7)	22 (17.3)	0.2
No	42 (40)	63 (60)	105 (82.7)	
HIV infection				
Yes	4 (30.8)	9 (69.2)	13 (10.2)	0.5
No	44 (38.6)	70 (61.4)	114 (89.6)	
Diabetes Mellitus				
Yes	7 (41.2)	10 (58.8)	17 (13.4)	0.7
No	41 (37.3)	69 (62.7)	110 (86.6)	
Total	48 (37.8)	79 (62.2)	127 (100)	

¹ MDR TB: Multidrug-resistant Tuberculosis.

Table 4: Relationship between risk factors and multidrug-resistant tuberculosis.

goal of 25.6 cases/100,000 inhabitants (9).

The clinical-epidemiological profile of TB in the state of Alagoas was similar to that reported in the literature, demonstrating a predominance of males in 61% of TB cases, similar to the 60% reported in the Brazilian population, a fact attributed to biological factors and life habits (24, 25). There was a predominance of the age group from 20 to 49 years old (58.6%), as already described in 63% of the cases of tuberculosis (6). In our research, a predominance of brown people (69.4%) was observed, a result higher than the 45.2% of brown people verified in other surveys (3). However, our finding is similar to that reported by the IBGE, regarding the predominance of brown skin color in the population of Alagoas (67.7%) (23).

The low educational level of the population is directly related to a higher frequency of TB, probably contributing to non-adherence to treatment, being represented mainly by complete/incomplete primary education and illiteracy, present in 50.6% and 15.3% of cases, respectively (25, 26). These results are very close to the schooling profile found in our study, of 60% (complete/incomplete primary education) and 19% (illiterate). It is likely that this small difference is related to the low level of education in our region, especially in Alagoas, which has the highest illiteracy rate in the country (23).

The pulmonary form is the most frequent clinical and radiological presentation of TB, corresponding to 90% of cases (8). Our results confirm this data with 87.4% of this form of presentation of the disease. In the evaluation of comorbidities, a higher frequency of the association of TB/alcoholism was observed in our patients (15.5%), similar to that reported in the literature of 17.2% (10).

Regarding the closure situation, cure was observed in 74.6% of patients and abandonment in 10.5%, data that is consistent

with other studies, which reported cure in 73.1% and treatment abandonment in 11.2% of patients (9), thus reflecting the current status of TB treatment in our country. However, the goals recommended by the Ministry of Health are to achieve cure in at least 85% of patients with TB, keeping treatment abandonment at rates below 5% (27).

Referral to reference centers corresponded to drug resistance in 55.1% of cases, with multidrug resistance being observed in 68.5%, rates higher than other results, which showed 58.3% of drug resistance and 43.7% of multidrug resistance (28). It is possible that our results express the difficult management of patients with low sociocultural status associated with low adherence to treatment in reference centers, in addition to a reduced sample.

Adverse effects from the use of anti-TB drugs are described in 3 to 20% of cases (12) and were observed in our research in 29.1% of cases. Hepatotoxicity, considered the most important adverse reaction, due to its high morbidity and mortality and poor adherence to TB treatment (17), was observed in 59.5% of cases. Because it is a retrospective study, with a small sample (37 cases), we believe that this result is overestimated, which eventually justifies the discrepancy with other reports in the literature of 2 to 28% of hepatotoxicity (17).

When probable risk factors for adverse reactions to anti-TB drugs were analyzed, the female gender variable occurred in 54%, showing statistical significance, compatible with previous analyzes (29). This finding may be associated with hormonal oscillations in various phases of a woman's life, modifying the response to medications (30). Although in our study we observed that adverse reactions were more frequent in the age group below 40 years old, a higher frequency of these reactions in people over 40 years old is cited

in the literature (18). While age less than 40 years was related to multidrug resistance (29).

The analysis of our results allows us to conclude that the incidence of TB in Alagoas, despite an average of 35.7/100,000 inhabitants, presented a downward trend over the last 10 years of 31.8%. The clinical-epidemiological profile is similar to that reported in the literature.

Referrals to reference centers were predominantly patients with multidrug-resistant forms of TB or with adverse effects.

Safe analysis of cases of multidrug resistance and adverse effects, especially hepatotoxicity, requires a prospective study with an adequate sample from the primary

care units for patients with TB. The cure and abandonment goals recommended by the Ministry of Health have not yet been achieved, contributing to the high persistence of TB in our environment. Thus, greater articulation between TB control programs is needed, with the definition of strategies focused on social protection, aiming at the survival and quality of life of these patients.

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