

# Non-cystic fibrosis bronchiectasis in an endemic area of pulmonary tuberculosis, Belém do Pará - Brazil - 2019

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Bronquiectasias por fibrosis no quística en una zona endémica de tuberculosis pulmonar, Belém Do Pará - Brasil - 2019

## RESUMO

Objetivos: Descrever o perfil clínico-epidemiológico de pacientes com bronquiectasia não fibrocística atendidos em ambulatório especializado em Belém-PA, área com altas taxas de tuberculose pulmonar. Método: O estudo avaliou 100 prontuários, incluiu 53, atendidos em 2019, sendo avaliadas características sociodemográficas e clínicas. Resultados: mulheres, de procedentes da capital, com início dos sintomas na idade adulta, cuja principal etiologia é pós-tuberculose. Os sintomas mais prevalentes são tosse, expectoração e dispnéia. Radiologicamente o comprometimento difuso e bilateral, e as principais classificações morfológicas: cilíndrico e sacular. As medicações mais utilizadas: beta-2 agonista de longa duração e acetilcisteína. Segundo o escore de gravidade E-FACED, a maioria dos pacientes foram classificados como doença leve. Conclusão: mulheres com antecedente de tuberculose pulmonar, com tosse e expectoração persistentes devem ser investigadas para doença bronquiectásica.

**DESCRIPTORES:** Bronquiectasia; pneumologia; tuberculose; tosse.

## ABSTRACT

Objectives: Describe the clinical and epidemiological features of non-cystic fibrosis bronchiectasis patients treated at a specialized health-service in Belém-PA, an area with high rates of pulmonary tuberculosis. Method: The study evaluated 100 medical records, including 53, attended in 2019, with sociodemographic and clinical characteristics. Results: women from the capital, with onset of symptoms in adulthood, whose main etiology is post-tuberculosis. The most prevalent symptoms are cough, sputum and dyspnea. Radiologically, diffuse and bilateral involvement, and the main morphological classifications: cylindrical and saccular. The most used medications: long-acting beta-2 agonist and acetylcysteine. According to the E-FACED severity score, most patients were classified as mild disease. Conclusion: women with a history of pulmonary tuberculosis, with persistent cough and sputum should be investigated for bronchiectasis.

**DESCRIPTORS:** Bronchiectasis; Pneumology; tuberculosis; cough

## RESUMEN

Objetivos: Conocer el perfil clínico-epidemiológico de los pacientes con bronquiectasias no fibroquísticas atendidos en un ambulatorio especializado en Belém-PA, zona con altos taxones de tuberculosis pulmonar. Método: Estudié 100 historias clínicas, incluidas 53, atendidas en 2019, mostrando características sociodemográficas y clínicas. Resultados: las mujeres, de la ciudad capital, iniciaron con dos síntomas en un adulto, cuya principal etiología fue la post-tuberculosis. Los síntomas más prevalentes son tos, expectoración y disnea. Compromiso radiológico o difuso y bilateral, y las principales clasificaciones morfológicas: cilíndrica y sacular. Los medicamentos más utilizados: agonista beta-2 y acetilcisteína. Segunda puntuación de gravedad o E-FACED, como máximo dos pacientes se clasificaron como enfermedad leve. Conclusión: las mujeres con antecedentes de tuberculosis pulmonar, tos persistente y expectoración deben ser investigadas por bronquiectasias.

**DESCRIPTORES:** Bronquiectasias; neumología; tuberculosa; tos.

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**INTRODUCTION**

**B**ronchiectasis is a chronic, heterogeneous clinical condition of variable severity characterized by an abnormal and permanent dilation of the airways, whose etiologies can be of congenital or acquired origin.<sup>1</sup> The main classification divides: those of cystic fibrosis patients and those of other causes (Non-cystic fibrosis). The post-infectious and secondary cause of tuberculosis in Brazil is the main cause, resulting in chronic bronchial dilatation, with a peculiar clinical picture and compromised quality of life.<sup>2</sup>

The state of Pará, in 2019, had the highest incidence of tuberculosis cases notified and monitored in Primary Care.<sup>3</sup> Unlike what happens in the northern health region of Espírito Santo, which between 2018 and 2019 presented an incidence coefficient lower than the national average.<sup>4</sup> In 2020, 4913 new cases of tuberculosis were confirmed in the state, of which 4221 were pulmonary.<sup>5</sup>

Respiratory symptoms with persistent cough and large amounts of sputum, sometimes hemoptysis and recurrent infections, plus high-resolution computed tomography (HRCT) scans of the chest confirm the diagnosis, thus enabling early intervention and preservation of the pulmonary function.<sup>6,7</sup>

Monitoring through spirometry with a bronchodilator test, in addition to evaluating the microbiota present in the airway of patients, are important for monitoring and scoring systems are proposed, thus estimating the severity of the patients. Among them, we have the so-called: E-FACED, which assesses the percentage (%) of predicted forced expiratory volume in one second (FEV-1), age, colonization by *Pseudomonas aeruginosa*, extent of im-

**The post-infectious and secondary cause of tuberculosis in Brazil is the main cause, resulting in chronic bronchial dilatation, with a peculiar clinical picture and compromised quality of life**

pairment on HRCT, the dyspnea scale and presence of exacerbations.<sup>8</sup>

Treatment must be individualized according to clinical and etiological particularities, and drug therapy includes: antimicrobials, bronchodilators and mucoactive substances; and respiratory physiotherapy with maneuvers to clear this secretion is of paramount importance. Vaccination against influenza and pneumococcus, use of osmotic agents are also mainstays of treatment. From a surgical point of view, lung resections in localized and refractory disease, and even lung transplantation, may be considered.<sup>1</sup>

The lack of studies on the subject in the state and the high burden of pulmonary infections (especially tuberculosis) in the region, calls attention to the need to describe the profile of patients with bronchiectasis in the region, their main etiologies, in addition to their clinical-epidemiological behavior. In this way, promoting academic knowledge on the subject, aiming to improve the quality of life of patients and reduce hospitalizations.

The objective of the research was to trace the clinical and epidemiological profile of patients with non-cystic fibrosis bronchiectasis treated at a specialized outpatient clinic at a university hospital in Belém-PA.

**METHODS**

Cross-sectional and retrospective study of appointments performed in 2019, which included patients over 18 years of age, with a diagnosis confirmed by high-resolution computed tomography (HRCT), and patients diagnosed with cystic fibrosis were excluded. Data collection started after approval by the Ethics Committee and was carried out based on electronic medical records of patients treated at the outpatient

clinic specializing in bronchiectasis. Data Use Commitment Terms (TCUD) have been completed.

Socio-demographic and clinical characteristics were evaluated, such as: period of onset of symptoms, probable etiology, signs and symptoms and tomographic alterations. The number of exacerbations, need for hospitalization, pulmonary colonization proven by sputum culture, degree of dyspnea by the modified dyspnea scale – Medical Research Council (mMRC) and severity assessment by the E-FACED score, in addition to the proposed treatment, were described.

The sample characterization information was calculated and entered into a spreadsheet created in the Microsoft® Office Excel® 2016 software. In the application of Descriptive Statistics, tables and graphs were built to present the results and position measurements were calculated as arithmetic mean and standard deviation.

Statistical analysis was performed using the G and Chi-Square Adherence Tests for univariate tables. Descriptive and analytical statistics were performed using BioEstat® 5.4 software. For decision making, the significance level  $\alpha = 0.05$  or 5% was adopted, indicating the significant values with an asterisk (\*).

**RESULTS**

One hundred medical records were analyzed, including 53 in the research, as the rest had insufficient data. Table 1 describes the epidemiological profile of patients.

The onset of symptoms predominantly started in adulthood ( $p < 0.0001$ ), and the etiology is probably more frequent after respiratory infection ( $p = 0.004$ ), especially after pulmonary tuberculosis. The other probable etiologies were described in Table 2, however it is important to emphasize that in some patients there was suspicion of two etiologies at the same time, due to history and clinical picture. Symptoms were described in Table 2, and cough was statistically significant ( $p = 0.006$ ).

Of the 53 patients studied, 40 (75.47%)

Table 1: Epidemiological data of patients with non-cystic fibrosis bronchiectasis undergoing therapeutic follow-up at a University Hospital of Belém-PA, 2019

Variables	Frequency	% (N = 53)	p-value
Gender			0.0001*
Female*	41	77,4%	
Male	12	22,6%	
Age group			0.0133*
< 30	4	7,5%	
30 to 39	6	11,3%	
40 to 49	11	20,8%	
50 to 59*	12	22,6%	
> = 60*	20	37,7%	
Minimum / Average / Maximum	21 / 53.8 / 80	0.0060*	
Origin			
Metropolitan region	37	69,8%	
Interior	16	30,2%	

\*Chi-Square Adherence Test

Table 2: Profile of patients with non-cystic fibrosis bronchiectasis undergoing therapeutic follow-up at the pulmonology clinic of a University Hospital in Belém-Pará, 2019.

Variables	Frequency	% (N=53)	p-value
Onset of symptoms			< 0.0001*
Childhood	8	15,1%	
Adulthood *	45	84,9%	
Post respiratory infection:*			0.0004*
Tuberculosis	40	75,5%	
Other respiratory infections	7	13,2%	
Etiology			
Genetics	7	13,2%	
Asthma	6	11,3%	
Idiopathic	3	5,7%	
COPD	1	1,9%	
GERD	1	1,9%	
Toxic substance	1	1,9%	

Symptoms	Cough*	37	69,8%	0,0060*
	Expectoration	31	58,5%	
	Dyspnea	28	52,8%	
	Hemoptysis	8	15,1%	
	Hemoptoic	7	13,2%	
	Chest pain	5	9,4%	
	Wheezing	1	1,9%	

Chi-Square test adhesion. Note: COPD (Chronic Obstructive Pulmonary Disease) / GERD (GastroEsophageal Reflux Disease).

Table 3: Assessment of the number of exacerbations and need for hospital admission of patients treated at a University Hospital in Belém-PA, in 2019.

Variables	Frequency	%(N=53)	p-value
Exacerbation	23	43,4%	-----
No	30	56,6%	
Yes, once a year	21	39,60%	
Yes, twice a year	2	3,8%	
Hospitalization in the last year			< 0.0001*
Yes	6	11,3%	
No*	47	88,7%	

\*Chi-Square test

Table 4: Severity rating scale for non-cystic fibrosis bronchiectasis in follow-up at the pulmonology outpatient clinic of a University Hospital in Belém-Pará, 2019

Variables	Frequency	%(N = 53)	p-value
E-FACED escore			
Light*	43	81,1%	< 0.0001*
Moderated	10	18,9%	
Severe	0	0,0%	

\*Chi-Square test adhesion  
Note: E-FACED – Bronchiectasis severity rating scale.

were non-smokers, 10 (18.87%) were active smokers, with an average smoking load of 19.73 packs/year and standard deviation of about 24.31 packs /year ( $p < 0.00010$ ) and the rest (3; 5.7%), passive smokers.

Regarding bacteria isolated in sputum culture, *Pseudomonas aeruginosa* was found in 8 patients (15.10%), followed by *Klebsiella pneumoniae* in 9.40% (5) and *Staphylococcus aureus* in 3.80% (2). As for the extent of pulmonary involvement on CT, most of it was diffuse, with more

than two lobes affected in 49.1% (26) of the patients ( $p = 0.0004$ ). When analyzing the tomographic morphological aspects and considering that there were concomitant findings, 47.2% (25) of the sample had cylindrical bronchiectasis, 43.4% (23) of the saccular type, followed by 24.5% (13) of the varicose type. Pulmonary function assessed by spirometry showed that 32 (60.4%) patients had  $FEV1 > 50\%$ , and the rest (21; 39.6%) had  $FEV1 < 50\%$ .

Regarding drug treatment, 62.3%

(33) of the patients were using long-acting B2 agonist bronchodilator (LABA) ( $p = 0.0214$ ), 49.1% (26) of mucoactive agents such as acetylcysteine, 34% (18) inhaled corticosteroids and 24.5% (13) used systemic antibiotics due to exacerbations. Among the non-pharmacological treatments, 15.1% (8) of the patients underwent respiratory physiotherapy. Surgical treatment, lobectomy, was observed in 5.70% (3) of the study population. Table 3 shows the number of exacerbations and hospital admissions for the disease.

The degree of dyspnea classified by the mMRC showed that 64.2% (34) was said to be degree zero ( $p < 0.0001$ ). The classification of patients according to the criteria of severity and prognosis provided by the E-FACED score showed a result of 81.1% (43) as classified as having mild bronchiectasis (Table 4).

## DISCUSSION

For some decades, bronchiectasis disease was considered an orphan disease due to the scarcity of studies and public-private policies on the subject. However, with the increase in the number of cases around the world, it is taking a robust statistical shape led by the European registry (EMBARC).<sup>9</sup>

Women in the sample in question, as well as in a reference hospital in São Paulo, are the most affected. 8 With the onset of symptoms in adulthood, and the imprecise assessment of the mean age, they are repeated in other cohorts around the world, such as in a tertiary hospital in Pakistan, 10 in which the majority of patients had the onset of symptoms over the age of sixty years, and another in Morocco, 11 in which the age of onset of symptoms was 48 years of age.

A multicenter cohort study in Europe and India, 12 found that about 41.7% of 2195 patients had tuberculosis as the main probable cause of bronchiectasis, as well as Oliveira et al. 13 among those cases of post-infectious origin, tuberculosis was the main one involved. Clinically, cough is the most cited symptom, followed by expecto-

ration and dyspnea. It is noteworthy that the hodgepodge of symptoms is common similar to the registry data from the University Hospital of Basketn in Adana-Turkey, 14 where most patients had cough, sputum and dyspnea, respectively, as the main symptoms.

The radiological pattern most observed in this study is the diffuse and bilateral one, with involvement of more than two lung lobes, that is, of severe extension on HRCT scans. A Pakistani study shows a different result, showing that 41.8% of patients have focal lung injury, and only 20.4% have diffuse bilateral injury. 15

The predominant tomographic morphological type was the cylindrical shape, followed by the saccular pattern, which diverges from those found by Tejada et al., 16 in which the prevalent morphology was mainly saccular, followed by varicose and cylindrical pattern.

This study showed that most patients, 75.47%, do not have a history of smoking. As in a study by Martinez-Garcia et al, 14 who analyzed 1912 patients with bronchiectasis in which 58.4% were non-smokers.

There was a statistically significant

proportion of patients undergoing drug therapy, especially LABA, and there was an expressive use of mucolytics such as N-acetylcysteine by the sample. The use of oral antibiotics was used in cases of exacerbation by secondary infections. Since this drug therapy is similar to that found by Dhar et al, 12 and the one proposed by the Brazilian Consensus on Non-Fibrocystic Bronchiectasis. 2

Pulmonary rehabilitation is recommended in all current guidelines and analysis of treatment protocols as a factor that improves the quality of life of patients and should be encouraged. Surgical treatment was strongly recommended by the 2017 European consensus, 17 for patients with focal impairment, whose clinical treatment was unsuccessful.

In a prospective cohort study of 608 patients, it showed that the majority (363) had at least one exacerbation over a year, 18 130 of these were hospitalized. Contrary to what was seen in this research, 56.6% of the sample did not show exacerbation recorded in 2019.

Regarding dyspnea assessed by the mMRC scale, most patients in this study were classified as grade zero, that is,

dyspnea after intense exercise, similar to the study by Clamers et al. 19 When analyzing the E-FACED score, most respondents were classified as mild, followed by moderate cases, similar to the result of a multicenter observational study of a historical cohort, 20 in which 60.5% of the patients were classified as having mild bronchiectasis by the same score, 30% and 8.6% as having moderate and severe, respectively.

## CONCLUSION

Thus, it is concluded that a history of pulmonary tuberculosis is an important predictor of bronchiectasis and in regions where the prevalence of tuberculosis is high, bronchiectasis should be investigated in patients with persistent symptoms such as coughing and pulmonary hypersecretion. Drug therapy shows benefit in terms of disease prognosis, as according to the E-FACED severity and prognosis score, most patients were classified as having mild bronchiectasis. It is expected that this cohort of patients will be evaluated in the future with a larger number of participants, over a longer period of time and with more adequate control of the variables involved.

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