

Bronchiectasis: morbidity and mortality in Brazil and its impact on hospitalization rates

Bronquiectasias: morbilidad y mortalidad en Brasil y su impacto en las tasas de hospitalización

Dara Roberta Biatobock¹ , Milene da Silva Machado Paz² , Daniel Wenceslau Votto Olmedo^{1,2} , Edison Luiz Devos Barlem² , Daniela Fernandes Ramos^{1,2} 

¹ Universidade Federal do Rio Grande – FURG, Faculdade de Medicina, Laboratório de Desenvolvimento de Novos Fármacos (LADEFA). Rio Grande, RS, Brasil.

² Universidade Federal do Rio Grande – FURG, Faculdade de Medicina, Programa de Pós-graduação em Ciências da Saúde. Rio Grande, RS, Brasil.

Corresponding author: daniferamos@gmail.com

Abstract: Objective: To evaluate the morbidity and mortality of bronchiectasis, its interface with the maintenance of hospitalization rates and unsatisfactory prognostic outcomes, as well as the negative impact on Brazilian public health. **Methods:** The clinical and epidemiological information came from the IT department of the Brazilian Unified Health System - DataSus, from which the required data was filtered through the SUS - CID10 list of morbidities. Information was sought, in absolute numbers, regarding the hospitalization of bronchiectasis patients, such as gender, age, time and cost of hospitalization, care regime, and the number of deaths due to the disease. **Results:** From the variables found, it was noted that in the period from January 2008 to February 2020, around 24,087 bronchiectasis patients were hospitalized. 65% of the total number of hospitalizations due to the disease consisted of adults, with a large portion in the productive phase (between 20 and 79 years). 84% of the patients sought health units in an emergency mode and 47% used public services at the time of hospitalization. The Brazilian average length of stay in hospital was estimated at 8.1 days and the cost of the service was around R\$ 28 million in the twelve years analyzed. Besides, 698 deaths due to bronchiectasis



were recorded in Brazil. **Conclusions:** Diseases such as bronchiectasis are far from the adequate management that chronic lung diseases require. Despite the significant diagnostic evolution, the etiology and treatment of disease is still questionable, providing unsatisfactory quality of life for bronchiectasis patients.

Keywords: prognostic, infections, bronchiectasis, lung diseases.

Resumen: Objetivo: Evaluar la morbimortalidad de las bronquiectasias, su interface con el mantenimiento de las tasas de ingreso hospitalario y los resultados pronósticos insatisfactorios, y el impacto negativo en la salud pública brasileña. **Métodos:** Las informaciones clínicas y epidemiológicas provinieron del departamento de informática del Sistema Único de Salud de Brasil – DataSus, del cual se filtraron los datos requeridos a través de la lista de morbilidades del SUS – CID10. Se buscó información sobre la hospitalización de pacientes con bronquiectasias, como sexo, edad, tiempo y costo de la hospitalización, régimen de tratamiento y número de muertes a consecuencia de la enfermedad. **Resultados:** Se observó que de enero de 2008 a febrero de 2020 se hospitalizaron alrededor de 24.087 pacientes con bronquiectasias. El 65% eran adultos, con una gran porción en la fase productiva. El 84% de los pacientes buscó unidades de salud en modalidad de emergencia y el 47% acudió a los servicios públicos. El promedio brasileño de estancia hospitalaria fue estimado en 8,1 días, el costo del servicio rondaba los R\$ 28 millones y se registraron 698 muertes por bronquiectasias. **Conclusiones:** Enfermedades como las bronquiectasias están lejos del manejo adecuado que requieren las enfermedades pulmonares crónicas. A pesar de la importante evolución diagnóstica, la etiología y el tratamiento de la enfermedad siguen siendo cuestionables.

Palabras clave: pronóstico, infecciones bronquiectasias, enfermedades pulmonares.

1. INTRODUCTION

Hundreds of millions of people of all ages are affected by respiratory illnesses worldwide and more than 500 million of them live in developing countries. In addition to this, population aging is a crucial factor for the rise in prevalence and mortality from chronic non-communicable diseases. Another factor that predisposes to respiratory diseases is climate change, such as low air humidity, increased precipitation and sudden changes in temperature, which mainly affect extreme age groups, as well as the most vulnerable strata of the population, increasing hospitalization rates for Acute Respiratory Infections.

Respiratory diseases have been responsible for an enormous burden on global health, since they represent more than 10% of all years of life lost due to the unavailability of an active and productive life, causing the incapacity of these individuals and causing enormous economic impact and social. Respiratory diseases are five of the thirty most common causes of death, contributing to the death of 4 million people annually⁽¹⁾.

In this sense, bronchiectasis as a chronic respiratory disease has been neglected over the years. The impact of this disease, which causes airway obstruction, is highly variable with mortality rates ranging from 2 to 35%. In addition, considering that the diagnostic tools available detect only 50% of cases of bronchiectasis - 30-70% of which are classified as idiopathic in origin - and that studies on epidemiological evaluation and the origin of infections in bronchiectasis are scarce, there is urgent need research aimed at understanding the pathogenesis and reducing socioeconomic impact, which has been identified as significant in several countries around the world, especially in those where the disease has been identified as a pathology with an important impact on monetary costs and laborious handling in the health service⁽²⁾.

A recent study proposed that bronchiectasis would be classified as an emerging global epidemic, probably due to orphaned investments and research⁽³⁾. The heterogeneity of the disease-related to etiology, epidemiology, and mainly microbiology, has been highlighted by several authors, who highlight the scarcity of data in Asia, Africa, and South America. Also considering that Brazil is a country of continental dimensions and understanding its diverse socio-economic realities, the direct impact that this disease can generate on the availability and reality of national health services becomes evident.

Thus, identifying the Brazilian fragility about the information directly from the notification of health services, and the management of this chronic respiratory disease, this study aims to assess the morbidity and mortality of bronchiectasis, its interface with the maintenance of hospitalization rates, unsatisfactory prognostic outcomes, as well as the negative impact on public health in Brazil.

2. MATERIAL AND METHOD

This is an exploratory descriptive study with a qualitative approach, developed from April to June 2020, based on access to clinical and epidemiological information provided by the informatics department of the Brazilian Unified Health System ⁽⁴⁾, of the Secretariat of Strategic and Participative Management

of the Ministry of Health with the responsibility of collecting, processing and disseminating health information, filtered by the list of SUS morbidities - CID10, available at an electronic address in the public domain. For this reason, the study does not require submission to the Ethics Committee, as well as signing a Free and Informed Consent Form.

As variables for this temporal analysis, absolute data referring to sex and gender, as well as the number, time, and costs of hospitalizations for bronchiectasis were used; regime and type of health care used during hospitalization (public or private; elective or emergency, respectively) and deaths from the disease. This information was stratified by the Brazilian macro-region (North, Northeast, Midwest, South, and Southeast), to better visualize the distribution of the disease in the country, and at the national level. We also opted for the use of tools that facilitate the reading and understanding of the data, such as tables. The information was stored in a digital spreadsheet until the moment of its reading.

3. RESULTS AND DISCUSSION

In Brazil, according to the data available in DataSus, from January 2008 to February 2020, there were 24,087 patients hospitalized due to bronchiectasis. The temporal analysis allowed us to observe a trend in the reduction of the number of hospitalization since in 2008 a greater number of patients were admitted to the health services, followed by a progressive reduction in the years 2016, 2019, and 2020.

As shown in Table 2, the Northeast and Southeast regions of Brazil account for more than half of the hospitalization cases related to this pathology (8,246 *versus* 6,811 hospitalizations, in the Northeast and Southeast Regions, respectively).

In addition, the outcomes appear to be associated with a more advanced age group, between 50 and 79 years, in which there was a greater number of hospitalizations for the disease (8,742 cases), with the female hospitalization cases (12,136) slightly higher than the male (11,951) in Brazil, as well as in the North (1,585), Northeast (4,242) and South (1,601) Regions (Table1).

Despite the heterogeneity of the disease, some studies have already identified similar clinical and prognostic characteristics, such as exacerbations, which have been shown to interfere negatively in the course of bronchiectasis⁽⁵⁾. The acute lack of control of symptoms can lead the patient to seek health services in an emergency mode.

Table 1. Sociodemographic and clinical characteristics attributed to the patient with bronchiectasis from January 2008 to February 2020, stratified by geographic macro-region, presented in absolute numbers

	Brazil	North	Northeast	Southeast	South	Midwest
Hospitalization x Gender						
Male	11,951	1,464	4,004	3,479	1,513	1,492
Female	12,136	1,585	4,242	3,333	1,601	1,375
Hospitalization x Age						
0-19 years	4,829	709	1,628	1,453	454	585
20-49 years	7,050	910	2,556	1,824	1,081	679
50-79 years	8,742	992	2,915	2,414	1,243	1,178
>80 years	1,650	179	577	448	150	296
Kind of service						
Elective	3,874	456	1,215	1,280	762	161
Urgency	20,211	2,593	7,030	5,530	2,352	2,706
Others	2	0	1	1	0	0
Regime of service						
Public	11,408	1,553	4,339	2,999	1,001	1,516
Private	6,734	330	1,785	2,355	1,367	897
Not registered	5,945	1,166	2,122	1,457	746	454

Source: Authors.

According to the registration of the Brazilian platform, 84% (20,211/24,087) of patients with the disease sought health units in emergency mode during the period studied, with emphasis on the Northeast Region, which received almost 35% (7,030/20,211) of patients in these conditions. Also, 47% (11,408/24,087) of bronchiectasis patients resorted to public services at the time of admission, of which 4,339 patients were hospitalized in these conditions also in the Northeast Region, in which unfavorable conditions are part of the socio-economic reality.

In the face of failure in clinical treatment, exacerbations become frequent,

increasing the chances of hospitalization of this patient⁽⁶⁾. In the DataSus records, the national average stays in the hospital for bronchiectasis is 8.1 days of hospitalization, so that the Southeast Region stands out for presenting a value higher than the Brazilian index with 9.1 days of hospitalization. In Brazil, the costs of institutionalizing the patient with bronchiectasis totaled approximately R\$ 28,133,489.13 in the period, with emphasis again on the Southeast region, which alone invested around 35% (R\$ 9,896,684.49) in the hospitalization of these patients (Table 2).

Research published in 2018 and developed with 1470 bronchiectasis patients from Spain and Latin America used tools to better assess the severity and prognosis of the disease: the *Exacerbation in the previous year, FEV1, Age, Colonization, Extension and Dyspnea* (E- FACED), and the *Bronchiectasis Severity Index* (BSI), establishing predictive values concerning mortality, hospital admissions, exacerbations and quality of life⁽⁷⁾.

Although these are methods that are unable to predict the evolution of the patient in the course of bronchiectasis, they are extremely relevant because of the number of deaths due to the disease. In Brazil, 698 deaths were registered during the more than 12 years studied, with emphasis on the Northeast Region, which represents almost 33% of the total deaths (228/698), followed by the Southeast Region with 30% of deaths (212/698) (Table 2).

The long period of hospitalization increases the chances of secondary infections, reflecting an increase in hospital costs, with a direct impact on the worsening of the clinical condition and possibly on mortality rates. Therefore, the Northeast and Southeast regions stand out, with an increase of more than half in hospitalizations, expenses and number of deaths from the disease in Brazil.

In the past, bronchiectasis - especially those not associated with cystic fibrosis - were considered an "orphan disease"⁽⁸⁾ that is, of the unknown clinical condition and, therefore, under-diagnosed. Today, although it is commonly part of the diagnostic hypothesis in medical practice and represents about 2.9% (698/24,087) in the list of deaths and hospitalizations due to bronchiectasis, this is a chronic disease still neglected and of questionable therapy.

There is, in the theoretical framework, no consistent justification for the high rate of 2008, but it is known that in the same year the Spanish Society of Pulmonology (SEPAR) developed initial guidelines on the diagnosis of bronchiectasis and that, only in 2010, would be published the first international guideline including treatment of the disease.

Table 2. Data regarding hospitalization of bronchiectasis patients and deaths due to the disease, categorized by Brazilian macro-region, presented in absolute numbers for the period from January 2008 to February 2020

Bronchiectasis	
Hospitalization (n)	
Brazil	24,087
North	3,049
Northeast	8,246
Southeast	6,811
South	3,114
Midwest	2,867
Length of Stay (Days)+	
Brazil	8.1
North	7.9
Northeast	7.8
Southeast	9.1
South	9.0
Midwest	5.8
Hospital Expenses (R\$)	
Brazil	28,133,489.13
North	2,398,029.65
Northeast	8,982,235.85
Southeast	9,896,684.49
South	4,857,409.14
Midwest	1,999,130.00
Deaths (n)	
Brazil	698
North	107
Northeast	228
Southeast	212
South	93
Midwest	58

Source: authors.

Although the gold standard for diagnosis has been computed tomography of the chest since the mid-1990s⁽⁹⁾, many countries did not have extensive access to this tool or even specialist professionals capable of correctly identifying the disease.

Thus, with scientific advances and the improvement of treatment and evaluation as we know it today, the possibility of false-positive results in that period is inferred, which could reflect on the hospitalization rates for the disease over the years.

The low pharmacological therapeutic diversity of years ago may have a direct influence on frequent episodes of exacerbation and, consequently, on the demand for hospitalization. It is considered, then, that the fall in years by achievers - except for the year 2020, which presents low rates due to data not yet released in the DataSus database - was due to the better diagnostic conditions and the expansion of the therapeutic possibility, mainly in the use of antibiotics, as well as in the facilitated treatment of associated diseases.

A study carried out with adult patients in the United Kingdom from 2004 to 2013 revealed that the incidence and prevalence associated with non-cystic fibrosis bronchiectasis have increased annually in all age groups, emphasizing that in the female gender both parameters have increased⁽¹⁰⁾.

The Brazilian platform, in which there is no individual record for each subdivision of bronchiectasis, highlights advanced age groups as those most affected by the disease, a group that is clinically known for presenting common episodes of exacerbation and, which may present significant pulmonary impairment, due to habits such as smoking, as well as acquired associated comorbidities.

Given the service regime, identified in this study as responsible for 47% of cases destined for the public sector, it is possible to outline a justifiable scenario in relation to the Brazilian per capita income, made available by the Brazilian Institute of Geography and Statistics, through which the disparity between federative units. The Northeast Region, previously highlighted in this study as the largest user of the public system in cases of hospitalization for bronchiectasis, is also the one with the second-worst household income per capita in the country, according to the agency in 2019, with Piauí and Maranhão being the states with the lowest average monthly income (R\$ 1,280 and R\$ 1,287 respectively)⁽¹¹⁾.

Regarding the prolonged period of institutionalization of these patients, as

already mentioned in this study - the length of hospital stay for bronchiectasis is 8.1 days in Brazil -, it can be inferred that its occurrence is due to the need for intravenous antibiotic therapy. The literature also points to infections by *Pseudomonas aeruginosa*, which often acquires persistence (chronicity), resulting in greater attention in the care of these patients. The length of hospital stay and antibiotic therapy are variables currently used to outline the prognosis, associated with colonization by *P. aeruginosa*, which are proportional to the morbidity of the bronchiectasis patient⁽¹²⁾.

Cole's "vicious cycle" model has been the most accepted to establish an evolution of bronchiectasis, in which, after inefficient mucociliary release, the persistence of microorganisms in the synobronchial tree and, consequently, microbial colonization, so that the association between infection airway obstruction and peribronchial fibrosis can further increase the time and cost of hospitalization for these patients, as well as compromising their quality of life^(13,14). In developing countries such as Brazil, bronchiectasis has been frequently linked to post-infectious causes, such as severe respiratory infections in childhood, recurrent pneumonia in the elderly, and cases of tuberculosis⁽¹⁵⁾.

In this context, we could be underestimating the costs of hospitalization during the study period, since the maintenance of this "vicious cycle", through pulmonary infections, in addition to contributing to the high morbidity of these patients, could be reflected in one of the three mechanisms involved independently, leaving bronchiectasis as a secondary factor in these scenarios. If this is true and considering that hospitalization costs associated with tuberculosis and pneumonia are approximately 10 and 270 times higher than those related to bronchiectasis, we would have an even greater increase in public spending and private.

The Brazilian Consensus on Non-Fibrocystic Bronchiectasis highlights that, in addition to hospital admissions and their duration, factors such as age, chronic infection by *P. aeruginosa*, and exacerbations have directly reflected in the rising costs of treating bronchiectasis patients.

The same document points out that studies have invested in the identification of the individual, congenital and sociodemographic characteristics common to these patients, which support the hypothesis currently best accepted to explain its origin and development. As already exposed in this study, the slightly higher incidence of disease involvement in women may signal specificity of bronchiectasis, or else, despite being linked to the fact that in recent years the Brazilian population was mostly composed of women, as disclosed by IBGE in

2019: 48.3% men and 51.7% women⁽¹⁶⁾.

In 2016, a study in which seven European cohorts were included, comprising 1,612 patients, revealing a mortality rate of up to 35.1%, based on the BSI and FACED (F: volumen espiratorio forzado en 1 s [FEV1]; A: edad ; C: colonización crónica por *Pseudomonas aeruginosa* ; E: extensión radiológica [número de lóbulos pulmonares afectados], y D: disnea) scores. In 2018, a multicenter observational study of a cohort of 651 bronchiectasis patients involving six teaching centers in Latin America, to establish a relationship between the combination of two exacerbations or one hospitalization per year and the number of deaths due to the disease, finding mortality of 14.6% (95/651) in the sample⁽¹⁷⁾.

In an analysis of morbidity and mortality in the period from 2003 to 2013, the Ministry of Health pointed out a reduction in hospitalization rates (44%) and mortality (3%) due to chronic respiratory diseases (CKD) in Brazil⁽¹⁸⁾, suggesting that the country is walking for health promotion. However, it is noted that diseases such as bronchiectasis are far from the ideal management that chronic lung diseases require.

4. CONCLUSION

Over the years, there has been a significant diagnostic evolution, but the etiology and therapy have not yet been definitively established, making the quality of life of the bronchiectatic patient, until this moment, unsatisfactory.

Adherence to the treatment of a chronic disease is influenced by the socioeconomic reality observed in each location. The heterogeneity of our results, ranging from the most populous Macroregion of Brazil (Southeast Region) to one of the most socio-economically vulnerable (Northeast Region), reveals that access to health services and the availability of regular follow-ups can be essential factors for proper treatment and complete.

Training of professionals reflected directly in the improvement of the assistance provided. Bronchiectasis patients, aware of their condition, diagnosis and therapy, will hardly not adhere to treatment and professional recommendations, such as the case of immunization by the pneumococcal vaccine, required for this group upon medical request and, in most cases, not performed due to unfamiliarity.

Aiming at a satisfactory prognostic outcome, the aim is to reduce the hospitalization rates for the disease, through appropriate therapy, in

which there is control of exacerbations and, consequently, a decrease in hospitalization and medication costs, positively impacting the Brazilian health service and providing a significant improvement in the patient's quality of life.

Finally, we highlight that the main limitations of this study are associated with the use of secondary information in the public domain, which could present gaps, inconsistencies and incomplete data.

ACKNOWLEDGEMENTS

This study was supported by the Nucleus for the Development of New Drugs - NUDEFA, the Nucleus for Research in Medical Microbiology - NUPEMM, the Faculty of Medicine of the Federal University of Rio Grande - FURG and the National Council for Scientific and Technological Development - CNPQ.

AUTHORS CONTRIBUTION

DRB, MSMP and DWVO worked on the conception and design, analysis and interpretation of data and writing of the article. ELDB and DFR worked on the critical review and approval of the version to be published.

DECLARATION OF INTERESTS

There are no interests to declare.

REFERENCES

1. Forum of International Respiratory Societies. The Global Impact of Respiratory Disease. Forum of International Respiratory Societies; 2017.
2. Pereira MC, et al. Brazilian consensus on non-cystic fibrosis bronchiectasis. *J. Bras. Pneumol.* 2019. doi: 10.1590/1806-3713/e20190122
3. Chotirmall SH, Chalmers JD. Bronchiectasis: An emerging global epidemic. *BMC Pulm. Med.* 2018;8:2-4.
4. DataSus. Departamento de Informática do Sistema Único de Saúde do Brasil; 2020.
5. Martinez-Garcia MÁ, et al. Prognostic Value of Frequent Exacerbations in Bronchiectasis: The Relationship With Disease Severity. *Arch. Bronconeumol.* 2019;55:81-87.

6. Menéndez R. et al. Factors associated with hospitalization in bronchiectasis exacerbations: A one-year follow-up study. *Respir. Res.* 2017;18:1-8.
7. De La Rosa Carrillo, D. et al. The annual prognostic ability of FACED and E-FACED scores to predict mortality in patients with bronchiectasis. *ERJ Open Res.* 2018;4:00139-02017.
8. Barker Alan F, Bardana Jr EJ. Bronchiectasis: Update of an Orphan Disease. *Am. Rev. Respir. Dis.* 1988;137:969-978.
9. Tiddens HAW, Meerburg JJ, van der Eerden MM, Ciet P. The radiological diagnosis of bronchiectasis: What's in a name? *Eur. Respir. Rev.* 2020;29:1-9.
10. Quint JK, et al. Changes in the incidence, prevalence and mortality of bronchiectasis in the UK from 2004 to 2013: A population-based cohort study. *Eur. Respir. J.* 2016;7:186-193.
11. IBGE - Instituto Brasileiro de Geografia e Estatística. Síntese de Indicadores Sociais. 2020. Available in: <https://www.ibge.gov.br/estatisticas/sociais/saude/9221-sintese-de-indicadores-sociais.html?=&t=o-que-e>
12. Da Silva Filho LVR F, et al. Pseudomonas aeruginosa infection in patients with cystic fibrosis: Scientific evidence regarding clinical impact, diagnosis, and treatment. *J. Bras. Pneumol.* 2013;39:495-512.
13. Sahuquillo-Arce J, Méndez R, Hernández-Cabezas A, Menéndez R. Non-cystic fibrosis bronchiectasis: The long road to multidrug resistant bacteria. *Community Acquir. Infect.* 2016. doi: 10.4103/2225-6482.198491.
14. McShane PJ, Naureckas ET, Tino G, Strek ME. Non-cystic fibrosis bronchiectasis. *Am. J. Respir. Crit. Care Med.* 2013;88:647-656.
15. Redondo M, Keyt H, Dhar R, Chalmers JD. Global impact of bronchiectasis and cystic fibrosis. *Breathe.* 2016;12, 222-235.
16. IBGE - Instituto Brasileiro de Geografia e Estatística. Pesquisa Nacional por Amostra de Domicílios Contínua. 2020. Available in: <https://www.ibge.gov.br/estatisticas/multidominio/cultura-recreacao-e-esporte/17270-pnad-continua.html?=&t=o-que-e>
17. De La Rosa D, et al. Annual direct medical costs of bronchiectasis treatment. *Chron. Respir. Dis.* 2016;13:361-371.

18. Boccolini CS. Morbimortalidade por doenças crônicas no Brasil: Situação Atual e Futura. Fundação Oswaldo Cruz , 2016.