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Determining factors of non-fibrocystic bronchiectasis in patients from southern Brazil: pilot study

Fatores determinantes das bronquiectasias não fibrocísticas em pacientes do sul do Brasil: estudo piloto

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ABSTRACT

Introduction: Bronchiectasis is a chronic respiratory disease that is largely related to inflammatory processes, irreversible dilation of the bronchi and the presence of recurrent lung infections. Furthermore, the disease presents a wide geographic, prevalence and etiological variability, driving the need for local assessments that aim to understand the disease and its behavior in different regions of the world.

Objective: To carry out a first approach to the prevalence profile of the disease in the extreme south of Brazil.

Method: Census study evaluating the clinical, sociodemographic profile and prevalence of bronchiectasis in patients treated at a regional reference pulmonology outpatient clinic.

Result: Of the 95 patients eligible for the study, 21 were classified as bronchiectatic through tomographic diagnosis. The majority of patients were women (67%), caucasian (86%), and aged between 61 and 80 years (62%). Regarding the diseases and symptoms reported by patients, a considerable presence of post-tuberculosis patients (40%) could be identified. Furthermore, the performance of pneumococcal vaccination was also a variable that showed a significant difference, where 55% of diagnosed patients did not undergo vaccination.

Conclusion: This study allows the development of a population-based study, guiding health policies that favor the monitoring and quality of life of these patients.

KEYWORDS: Bronchiectasis. Tuberculosis exacerbation. Prognosis. Infection.

Central Message

Bronchiectasis is considered a chronic respiratory syndrome that occurs after permanent dilation of the bronchi. Non-cystic fibrosis bronchiectasis is associated with the occurrence of symptoms such as cough, daily sputum production and development of recurrent respiratory infections.[1] Therefore, the clinical part of bronchiectasis is the result of different genetic factors and acquired medical conditions, containing a high index of clinical and epidemiological heterogeneity

Perspective

This study allows the development of a population-based study, guiding health policies that favor the monitoring and quality of life of these patients.

RESUMO

Introdução: A bronquiectasia é uma doença respiratória crônica que está amplamente relacionada a processos inflamatórios, dilatação irreversível dos brônquios e presença de infecções pulmonares recorrentes. Além disso, a doença apresenta ampla variabilidade geográfica, prevalente e etiológica, impulsionando a necessidade de avaliações locais que visem compreender a doença e seu comportamento em diferentes regiões do mundo.

Objetivo: Realizar uma primeira abordagem do perfil de prevalência da doença no extremo sul do Brasil.

Método: Estudo censitário avaliando o perfil clínico, sociodemográfico e a prevalência de bronquiectasias em pacientes atendidos em um ambulatório de pneumologia de referência regional.

Resultado: Dos 95 pacientes elegíveis para o estudo, 21 foram classificados como bronquiectásicos por meio do diagnóstico tomográfico. A maioria dos pacientes era do sexo feminino (67%), caucasiana (86%) e com idade entre 61 e 80 anos (62%). Em relação às doenças e sintomas relatados pelos pacientes, foi possível identificar uma presença considerável de pacientes pós-tuberculose (40%). Além disso, a realização da vacinação pneumocócica também foi uma variável que apresentou diferença significativa, onde 55% dos pacientes diagnosticados não realizaram a vacinação.

Conclusão: Este estudo permite o desenvolvimento de um estudo de base populacional, orientando políticas de saúde que favoreçam o acompanhamento e a qualidade de vida desses pacientes.

PALAVRAS-CHAVE: Bronquiectasias. Exacerbação da tuberculose. Prognóstico. Infeção.

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INTRODUCTION

Bronchiectasis is considered a chronic respiratory syndrome that occurs after permanent dilation of the bronchi. Non-cystic fibrosis bronchiectasis is associated with the occurrence of symptoms such as cough, daily sputum production and development of recurrent respiratory infections.[1] Therefore, the clinical part of bronchiectasis is the result of different genetic factors and acquired medical conditions, containing a high index of clinical and epidemiological heterogeneity.[2] Furthermore, bronchiectasis has a considerable impact on the social and health sectors, due to the increasing cases of hospitalizations and mortality.[3,4]

In the current scenario, especially non-cystic fibrosis, the conditions and epidemiological factors of the disease are still partially unknown, as most of the published studies were developed with cross-sectional and retrospective designs, making it difficult to understand the syndrome.[5,6] This is a worrying fact, because contrary to epidemiological reports that highlighted bronchiectasis as a rare disease, a longitudinal study from the United Kingdom, based on primary care data, showed an increase in the annual incidence of the disease between 2004 and 2013.[7]

The prevalence of bronchiectasis has progressively increased, being related to the development and availability of diagnostic tools in different clinical contexts.[8,9] Furthermore, some authors have proposed that there is a strong relationship between the host microbiota and chronic lung diseases, such as bronchiectasis.[10,11] This relationship has also been highlighted, as patients who present greater exacerbation were associated with the microbial diversity existing in the lower airways and consequently were inclined towards a worse clinical evolution.[12-15]

Geographic variability, clinical characteristics, epidemiological profiles of incidence and prevalence of the disease are also considered an aggravating factor in the compression of its distribution[16], therefore, local data are necessary to assist in the development and prioritization of public policies. Furthermore, the coexistence of bronchiectasis and other diseases such as asthma, chronic obstructive pulmonary disease (COPD) and non-chronic obstructive pulmonary disease, ends up making an accurate epidemiological design difficult[3] negatively influencing patient survival.[17]

In the Brazilian scenario, few studies have been described with this population[18-21] and no one on the prevalence of non-cystic fibrosis bronchiectasis in Brazilians. On the other hand, a recent study established important relationships between the disease and outcomes such as mortality and increased hospitalization rates in different Brazilian regions.[22] Therefore, considering the high rates of respiratory infections in the country, it is even more necessary[23] to collect these data in order to help improve the assessment of the development and progression of bronchiectasis.

This fact demonstrates the importance of prevalence studies on the syndrome, seeking to identify clinical aspects and differences between populations. Based on the above, a pilot and census study was conducted, which aimed to describe the clinical and sociodemographic profile and prevalence of bronchiectasis in patients at a regional reference pulmonology outpatient clinic located in the extreme south of Brazil.

METHOD

Study design and population

The study was conducted using a longitudinal design with census sampling consisting of a sample size of 95 participants. All patients treated at the pulmonology outpatient clinic of the Dr. Miguel Riet Corrêa Jr. University Hospital, located in the city of Rio Grande (Southern of Brazil), during the period evaluated participated in the study (from July to August 2018). For the survey of bronchiectasis, the diagnosis of bronchiectasis obtained through the results reported in the medical records and confirmed by imaging tests with a tomographic report were considered. Stable patients, over 18 years of age, treated at the pulmonology outpatient clinic during the study period were eligible. Patients diagnosed with cystic fibrosis and patients who presented exacerbation at the time of collection were excluded.

Instruments and data collection

The collection of socioeconomic, demographic and clinical data was performed through a semi-structured questionnaire containing open and closed questions, and radiological information presented in the participant's medical records. The pilot study followed all ethical precepts and was submitted for analysis and approval by the Ethics Committee in Research in the Health Area ofthe Federal University of Rio Grande, nº 23116.006049-2018-10.

Respiratory sample collection and processing

Respiratory samples were collected from all patients included in the study at the time of the interview, using an oropharyngeal swab. For bacterial identification, smears were prepared from the samples of each participant and subsequently stained using the Gram method, differentiating the microorganisms according to their morpho-staining characteristics (Gram positive or Gram negative), classified according to their morphology and arrangement.

Statistical analysis

After the questionnaire was applied, the data were coded and double-entered using EPIDATA 3.1 software. After entering the data, the data were cross-checked and typing errors were corrected. The data from the medical records were entered directly

using Excel 16.0 software. Stata 13.0 software was used for statistical analysis. First, the frequencies of the study variables were analyzed, and then a categorization was performed. Thus, a bivariate analysis was generated through the chi-square test with a significance level of 95%, with p≤0.05 being considered significant. Bivariate (crude) and multivariate (adjusted) Poisson regression was performed only with bronchiectasis patients, in order to assess factors associated with the outcome. Thus, the independent variables that constituted the model theory for determining risk and protection were primary (socioeconomic and demographic conditions): sex, skin color, age, income in quartiles, education; secondary (health conditions and lifestyle habits): smoking, asthma, COPD, emphysema, gastroesophageal reflux, pneumococcal vaccine; and tertiary (symptoms related to the outcome): dyspnea, productive cough, antibiotic use in the last 12 months, having had tuberculosis in life, colonization, and affected lobes. All statistical analyses were performed in the software with a significance level of 5%.

RESULT

The prevalence of bronchiectasis in the study population during the period evaluated was 22%. Most participants were female (68%), white (80%) and had incomplete elementary education (55%). The mean age of the population was 60 ± 16 years (Table 1). The mean income presented was U$ 523 (standard deviation ± 462), representing 2.22 minimum wages for the year 2019. Most of the patients treated during the study period reported being former smokers (52%) and never having consumed alcohol (55%).

Among the participants with bronchiectasis, 67% were women (14/21), with white skin color (18/21) and an average age of 65 years. The average income of bronchiectasis patients was U$ 507 and incomplete elementary education (52%) was the level of education presented by most participants; however, none of the socioeconomic variables showed statistical difference (p>0.05, Table 2).

Most participants were former smokers (67%) and had not been vaccinated against pneumococcal vaccine (55%). Regarding the use of antibiotics in the last 12 months, there was a 91% prevalence among the participants. Considering the comorbidities most frequently associated with bronchiectasis, it is possible to see that 53% of the population did not report gastroesophageal reflux and 52% did not have asthma. On the other hand, most of the population had dyspnea (76%), COPD (60%) and had a productive cough (90%). The prevalence between the presence or absence of a diagnosis of tuberculosis during life showed a statistical difference between the groups (p=0.002), with most participants never being diagnosed with tuberculosis (60%, Table 3).

TABLE 1 — Characterization of the sample through the sociodemographic profile, health conditions and lifestyle of patients treated at the pulmonology outpatient clinic of the Miguel Riet Corrêa Jr. University Hospital from July 3, 2018 to August 1, 2018.

	n	%
Bronchiectasis		
No	74	77.9
Yes	21	22.1
Gender		
Male	30	31.6
Female	65	68.4
Race/Ethnicity		
White	76	80
Black	5	5.2
Other	7	7.4
No Information	7	7.4
Age		
18-40	10	10.7
41-60	30	32.3
61-80	49	52.7
>80	4	4.3
Income (quartiles)		
1 (< U$ 234)	27	28.7
2 (U$ 234 – 492)	28	29.8
3 (U$ 492 – 862)	20	21.3
4 (>U$ 862)	19	20.21
Education		
Never studied	8	8.4
Completed Elementary	7	7.4
Incomplete Elementary	52	54.8
Completed High School	12	12.6
Incomplete High School	10	10.5
Completed Higher Education	2	2.1
Incomplete Higher Education	3	3.2
Postgraduate	1	1
Smoking		
Never	29	31.5
Ex-smoker	48	52.2
Smoker	15	16.3
Alcoholism		
Never	52	54.7
Ex-alcoholic	22	23.1
Alcoholic	21	22.1

Regarding the number of affected lobes, there was a significant difference in the study population (p=0.0001), with 65% having no more than 2 affected lobes. Considering the respiratory samples it was identified that most of them contained colonization by gram-positive cocci (65%), followed by a mixed colonization between gram-positive cocci and gram-negative bacilli (25%). In addition, lung function data were available for only 15 of the 21 bronchiectasis patients, and from the available data, 53% of the patients presented altered lung function.

In the bivariate and multivariate analyses related to socioeconomic and demographic factors, only the variables skin color and sex demonstrated a significant association (Table 4). It was observed that being male and white skin color have a prevalence ratio of 1.^{04} and 1.^{4,} respectively, for the development of the outcome: presence of bronchiectasis.

TABLE 2 — Sociodemographic profile, health conditions and lifestyle of participants diagnosed with bronchiectasis included in the study (n=21)

Variables	n	%	p*
Gender			
Male	7	33.3	0.84
Female	14	66.7	
Race/Ethnicity			
White	18	85.7	
Black	0	0	0.15
Other	3	14.3	
No Information	0	0	
Age			
18-40	1	4.8	
41-60	5	23.8	0.3
61-80	13	61.,9	
>80	2	9.5	
Income (quartiles)			
1 (<U$ 234)	6	30	
2 (U$ 234 – 492)	5	25	0.5
3 (U$ 492 – 862)	3	15	
4 (>U$ 862)	6	30	
Education			
Never studied	1	4.8	
Completed elementary	2	9.5	
Incomplete elementary	11	52.4	
Completed high school	3	14.3	0.65
Incomplete high school	2	9.5	
Completed higher education	0	0	
Incomplete higher education	2	9.5	
Postgraduate	0	0	

**p value determined using Pearson's chi-square test with 95% statistical significance*

TABLE 3 — Profile of health conditions assessed in the 21 bronchiectasis patients included in the study

Variables	n	%	*p
Smoking			
Never	6	28.6	0.18
Ex-smoker	14	66.6	
Smoker	1	4.8	
Asthma			
Yes	10	47.6	0.2
No	11	52.4	
COPD			
Yes	12	60	0.09
No	8	40	
Gastroesophageal reflux			
Yes	9	47,4	0.8
No	10	52,6	
Pneumococcal vaccine			
Yes	9	45	0.05
No	11	55	
Dyspnea			
Yes	16	76.2	0.4
No	5	23.8	
Productive cough			
Yes	19	90.5	0.5
No	2	9.5	
Use of ATB 12 months			
Yes	17	90.9	0.8
No	4	19.1	
Tuberculosis in life			
Yes	8	40	0.002
No	12	60	
Bacterial Colonization			
Gram + Cocci	13	65	
Gram - Bacilli	2	10	0.4
Mixed	5	25	
>2 affected lobes			
Yes	7	35	0.001
No	13	65	

**p value determined by Pearson's chi-square test with 95% statistical significance. The comparison between the population within each variable was performed. COPD: Chronic obstructive pulmonary disease; ATB: antibiotic; G+: Gram positive; G-: Gram negative.*

TABLE 4 — Poisson regression analysis of risk and protective factors associated with the outcome (diagnosis of bronchiectasis)

Levels	Variable	Bivariate	Multivariate
		PR (IC95%)	PR (IC95%)
1º	Gender	p=0.94	p=0.043
	Female	1	1
	Male	0.717 (0.312; 1.643)	0.962 (0.416; 2.222)
	Race/Ethnicity	p=0.239	p=0.001
	White	1.432 (0.909; 2.257)	1.399 (1.214;1.612)
	Black	1	1
2 º	Pneumococcal vaccine	p=0.063	p=0.005
	Yes	1	1
	No	1.936 (0.940; 3.989)	1.708 (1.172; 2.487)
3 º	Tuberculosis in life	p=0.005	p=0.840
	Yes	1	1
	No	0.734 (0.432; 0.926)	1.024 (0.810; 1.294)
	>2 affected lobes	p=0.001	p=0.001
	Yes	1	1
	No	0.481 (0.435; 0.531)	0.468 (0.428; 0.511)
	Productive cough	p=0.001	p=0.001
	Yes	1	1
	No	0.557 (0.432; 0.769)	0.541 (0.407; 0.719)

Significance level of 5% / PR=Prevalence ratio/CI=95% confidence interval

Regarding the 2nd level of the model, only the pneumococcal vaccination variable demonstrated statistical significance, where it was possible to observe that not having been vaccinated is also a risk factor related to the outcome, being 70% higher compared to patients who were vaccinated. Regarding the 3rd level of the model, the lifetime tuberculosis variable presented statistical significance only in the bivariate analysis, demonstrating that other variables can influence this relationship.

The presence of more than 2 affected lobes demonstrated a significant difference in the bivariate and multivariate analysis (p=0.001), demonstrating a protection factor of 53% when the patient does not have more than two affected lobes. The presence of the symptom productive cough was also a variable that presented statistical significance, in which not having a productive cough demonstrated to be a protection factor of 46% with a p value of 0.001.

DISCUSSION

Studies on bronchiectasis are highly relevant for improving human health, but despite this, there are few studies that evaluate the epidemiology and prevalence of bronchiectasis in different regions, especially in Latin America. Based on this, in the present study, it was possible to identify a higher prevalence of bronchiectasis in women, caucasians, with low levels of education and of advanced age. Furthermore, being female, having white skin color, not having been vaccinated against pneumococcus, having a history of tuberculosis, having more than two affected lobes and presenting symptoms of productive cough became risk factors for the development of bronchiectasis under the conditions of the present study. On the other hand, in a recent study, based on access to secondary data on bronchiectasis available in the Brazilian Unified Health System, in 2022,[22] it was shown that the type of access to the health system (public or private) and per capita

income are factors strongly linked to the number of deaths and hospital admissions, which varies according to the Brazilian macro-region.

In Latin America, the etiology of bronchiectasis is largely related to infection and is therefore impacted by the high rates of infectious diseases on the continente.[16] Endemic diseases in different regions and countries, such as tuberculosis, whooping cough, and measles, can greatly influence the prevalence of the disease. The high rates of pneumonia and tuberculosis in childhood are also factors that may contribute to the prevalence and incidence of bronchiectasis in the countries that make up Latin America. In addition, other factors related to developing countries, such as low adherence to vaccination, influence the predisposition of the population to infectious diseases already related to bronchiectasis.[16,24]

The present study identified a greater predominance of the disease associated with risk factors for females, as already highlighted in other studies conducted in different countries.[10,13-15,25] Studies conducted with Brazilian populations also identified females as a factor related to the disease.[18-21] In contrast to the present study, a cohort study conducted in Catalonia (northeastern Spain)6 identified a higher prevalence of males. Such discrepancies may be related to the geographic, social and etiological variability of the disease, demonstrating the importance of evaluating bronchiectasis in different regions.

This geographic variability of the disease was also discussed recently in the Brazilian scenario, with emphasis on the Southern macro-region, which had one of the lowest mortality rates caused by bronchiectasis and its complications between 2008 and 2020. Furthermore, evaluating the data available in the IT department of the Brazilian Unified Health System (DataSus), over 12 years, the prevalence rate of the disease in this region was the second lowest (approximately 13%)[22], even below that evidenced in this study in the extreme south of the country (22%).

Another important factor, but with a wide variation among the data already available in the literature, is the average age of bronchiectasis patients. In studies conducted within Brazilian territory, the average age of patients ranged from 50-75 years.[18,19,21] The age range of these patients, in addition to being associated with direct clinical prognostic outcomes, appears to impact the increased frequency of mutagenic events associated with the presence of micronuclei in the cells of the oral mucosa, a method that was recently proposed as an important prognostic marker that could directly interfere in the maintenance of the quality of life of these individuals.[26]

In the present study, it was identified a mean age of 60 years, which is in agreement with the other data presented previously. However, these studies, as well as the present study, were carried out in a scenario prior to the pandemic, which may greatly influence the prevalence of the disease in the populations studied in the future. A recently published study evaluated factors associated with bronchiectasis during the SARS-CoV-2 pandemic and the median age of patients was 25 years, demonstrating that the pandemic may have caused a higher incidence of the disease in younger populations.[27] In this regard, studies with greater statistical power, such as population-based studies on this disease, should be further encouraged, mainly because the virus directly attacks the respiratory system.

Regarding the comorbidities reported in the study, tuberculosis was the only one that presented itself as a risk factor, with a statistical difference among patients diagnosed with the disease. Lung damage related to tuberculosis is considered one of the main contributors to the etiology of bronchiectasis. In addition, it is worth noting that although a significant reduction in the incidence of tuberculosis has been observed in recent years, there is still a considerable number of cases of tuberculosis each year. In addition, it is important to highlight that tuberculosis is the second infectious disease caused by a single infectious agent that kills the most people worldwide, behind only SARS CoV-2, the causative agent of COVID-19. An estimated 10.6 million individuals developed the disease and 1.3 million people died worldwide in 2022.[28] A study carried out with a Chinese population demonstrated that patients with post-tuberculosis bronchiectasis had a lower prevalence of bilateral bronchiectasis and higher rates of right upper lobe involvement. This association is an important factor to be studied in the Brazilian population, where tuberculosis rates are worrying.[28]

Chronic bacterial infections play an important role in the pathophysiological cycle of the disease. Although was not observe a statistical difference between the major groups of bacteria evaluated in the study, it was possible to verify that more than half of the bronchiectasis patients were colonized by gram-positive cocci, which have been considered the main etiological agents of community-acquired and nosocomial pneumonias, which can impact the decline in lung function, favoring exacerbation, in addition to contributing to increased morbidity and mortality in these patients.[29] Furthermore, recent studies have demonstrated an increase in the prevalence of Staphylococcus aureus isolated in patients with non-cystic fibrosis bronchiectasis, indirectly impacting the severity of this disease.[30,31] Therefore, this is a point that deserves attention so that future studies can evaluate the bacterial correlation with the progression of the disease in the population studied.

Currently, different studies have demonstrated that the pathophysiology of bronchiectasis is largely associated with the persistence of colonizing microorganisms and the identification of these microorganisms in the upper airways, a factor that ends up rigorously influencing the treatment and evolution of the disease,[32,33] so that, recently, the Brazilian Consensus on the disease itself defines that the presence of potentially pathogenic microorganisms in the airways of these patients should be categorized as a chronic infection, due to the influence of these "colonizers" on exacerbations, loss of lung function

and also on the worsening of quality of life.[33]

The most common symptom observed in patients with bronchiectasis is productive cough, which can directly affect the patient's quality of life. In the present study, it was observed that the presence of productive cough is a risk factor, which may be related to hypersensitivity and hyperresponsiveness of the airways in patients who present this symptom.[34] However, previous studies have largely associated productive cough with smoking, COPD, asthma, i.e., overlap syndromes with bronchiectasis, and have not described a risk relationship between productive cough and the disease alone.[35,36] The presence of this symptom may promote a risk related to the acceptance of treatments, such as inhaled antimicrobials and/or inhalation therapies.[34]

The involvement of more than 2 lobes has been shown to be a risk factor for the bronchiectasis patients evaluated. Thus, this factor is directly related to the development of the disease and lung involvement, as it is one of the points raised by the available diagnostic tools, such as the FACED prognostic score, recently proposed in the Brazilian Consensus on Bronchiectasis. In general, the lobes are detected through computed tomography and are described as direct and indirect signs in the small airways and are occasionally visualized in lobes without dilation of the central bronchi.[33]

This study is an initial approach carried out with the studied population and will serve as a basis for studies with greater evaluative capacity on the factors associated with and prevalence of bronchiectasis in southern Brazil. The study had several limitations, such as the small sample size, which influences the statistical power for performing robust analyses. The lack of information available in the data collection instrument (medical records) was also a limitation, as it prevents the determination of important variables in the clinical picture of bronchiectasis. Furthermore, despite being a pilot study, the present work was carried out in a short period of time, preventing a temporal evaluation of the profile of bronchiectasis patients in the studied population. However, this small-scale pilot study demonstrated promising results for possible factors associated with the prevalence of bronchiectasis in the population and may guide future studies.

CONCLUSION

Finally, given the current Brazilian scenario, where tuberculosis is becoming a serious problem that could have a drastic impact on the development and prevalence of the disease in Latin America, the authors recommend that there be monitoring, covering a larger number of samples, in which the different factors associated with bronchiectasis are evaluated together as a way of understanding the real needs of the population. From this perspective, these studies could impact the clinical application of the disease, demonstrating better predictions for prognostic, therapeutic and patient management outcomes. In short, it can be concluded that future studies should focus on the correlation between tuberculosis, bacterial colonization and bronchiectasis, seeking to focus on the factors associated with the disease itself.

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Author´s contribution

D. Olmedo, D. Biatobock and A. G. Rosiak: collaborated with the writing, review and approval of the final version.

E. Luza, M. C. Ribeiro, M.M. Paz and K. O. Sanchotene: collaborated with the analysis and interpretation of the data and approved the final version.

L. Zhang, M. O. Xavier and P. E. A. da Silva: collaborated with the design of the study, analysis and interpretation of the data and approved the final version.

D. F. Ramos: collaborated with the design of the study, analysis of the results, writing and critical review of the content and final approval of the article.

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