PULMONOLOGY

RELATION OF THE PNEUMOCOCCAL POLYSACCHARIDE VACCINE (PPSV23) IN THE PROGNOSTIC OUTCOME OF PATIENTS WITH NON-CYSTIC FIBROSIS BRONCHIECTASIS

Dara Roberta Biatobock [1,2,3]; Milene da Silva Machado Paz[3]; Daniel Wenceslau Votto Olmedo[2,3]; Alessandra Galski Rosiak[2]; Carolina de Oliveira Nazareth[3]; Marcelle Oliveira Garcia[3]; Kamila Furtado da Cunha[3]; Débora Carvalho Rodrigues[3]; Edison Luiz Devos Barlem[1]; Pedro Eduardo Almeida da Silva [2]; Daniela Fernandes Ramos[2,3].

[1] Escola de Enfermagem, Universidade Federal do Rio Grande – FURG. Rio Grande, RS, Brazil.

[2] Núcleo de Desenvolvimento de Novos Fármacos - NUDEFA, Faculdade de Medicina, Universidade Federal do Rio Grande — FURG. Rio Grande, RS, Brazil.

[3] Núcleo de Pesquisa em Microbiologia Médica – NUPEMM, Faculdade de Medicina, Universidade Federal do Rio Grande – FURG, Rio Grande, RS, Brazil.

ABSTRACT

Considered a complex and heterogeneous disease that was previously underdiagnosed due to its distinct etiology, non-cystic bronchiectasis has a significant socioeconomic impact worldwide. The objective of this study was to evaluate the effect of the pneumococcal polysaccharide vaccine (PPSV23) on the prognosis of patients with bronchiectasis, using epidemiological and sociodemographic data and respiratory specimens evaluated by Gram staining and identification of *Pseudomonas aeruginosa*. The severity of bronchiectasis was classified using the FACED prognostic *score*. Of the 70 selected patients, 64.3% were women, with a mean age of 59 years and a history of smoking (80%). Among them, 65.7% reported not having received the pneumococcal polysaccharide vaccine, and 68.57% were not registered in the immunization database ($P < 0.000$). Substance use was higher in the unvaccinated group ($p = 0.0174$), as was the frequency of hospitalization among unvaccinated individuals (9/48) compared with vaccinated individuals (4/22). Furthermore, 55.7% were colonized by Gram-positive cocci, with a higher frequency of Gram-positive bacteria (35.71%) among unvaccinated individuals. Of the samples identified as Gram-negative, 90.9% (10/11) were confirmed as *P. aeruginosa*, and, 41.4% of patients with bronchiectasis were classified as having “mild” disease; the vaccinated group (22/70) was predominantly classified as having “mild” to “moderate” disease (63.6%; 14/22). Unvaccinated patients used antimicrobials more frequently (42.85%), and only those who reported using antimicrobials were classified as having “severe” disease. Given the significance of the association between self-reported use and respiratory infections, as well as between antibiotic use and the need for hospitalization, we emphasize the recommendation for Pneumococcal Polysaccharide Vaccine (PPSV23) immunization in patients with bronchiectasis as a highly important complementary alternative

in the treatment of the disease, which may help control exacerbations and lead to a favorable prognosis.

Keywords: Respiratory infection; Immunization; FACED Prognostic *Score*; Colonization.

INTRODUCTION

Since the emergence of the National Immunization Program (PNI) in 1973, Brazil has been outlining vaccination strategies in order to prevent the development of infectious diseases. Considering the impact that pneumococcal infections have on global morbidity and mortality, especially in extreme age groups and in immunodeficient individuals and/or those with chronic diseases, alternatives have been established to prevent infection and colonization by different serotypes of *Streptococcus pneumoniae*, mainly those associated with antibiotic resistance[1].

Recommended by the Brazilian Society of Immunizations (SBIm) and, therefore, included in the National Vaccination Calendar[2], the pneumococcal vaccine is available in two variations that differ due to their composition: polysaccharide (23-valent) or conjugated to carrier proteins (10- and 13-valent). The 10-valent (PCV10) and 13-valent (PCV13) pneumococcal conjugate vaccines are composed of 10 (1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, and 23F) and 13 serotypes of *S. pneumoniae* (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) conjugated to *Haemophilus influenzae* type b protein D, tetanus toxoid, diphtheria toxoid, and the diphtheria CRM197 protein, indicated for children from 0 to 10 years in two doses when PCV10 is used, and three doses when PCV13 is used[3].

Developed in 1983, the Pneumococcal Polysaccharide Vaccine (PPSV23) consists of the polysaccharide capsule antigens of 23 serotypes of pneumococcus (1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F), is indicated as a routine vaccination for people over 60 years of age and children over 2 years of age, adolescents, and adults at increased risk for developing pneumococcal diseases due to

conditions such as chronic kidney disease, immunosuppression, severe chronic heart disease, nephrotic syndrome, insulin-dependent diabetes mellitus, liver cirrhosis, and chronic respiratory diseases[4], such as bronchiectasis.

Characterized by irreversible airway dilation, commonly associated with lower respiratory tract colonization and excessive mucus production, non-cystic bronchiectasis is primarily characterized by a productive cough and dyspnea on minimal exertion[5]. Of distinct etiology, it is hypothesized that bronchiectasis is the final stage of lung damage caused by recurrent respiratory infections or due to autoimmune diseases, genetic abnormalities, and other acquired diseases[6].

A common feature of patients with bronchiectasis is chronic airway infection by potentially pathogenic microorganisms, which is closely linked to the progression of the inflammatory process and the deterioration of lung function. This condition contributes to recurrent exacerbations, increased hospitalization rates, and a significant decline in quality of life[7]. In this context, it is necessary to adopt therapeutic and clinical management strategies aimed at controlling infections, preventing structural damage, and improving long-term clinical outcomes. Therefore, this study sought to evaluate the role of Pneumococcal Polysaccharide Vaccine in the prognostic outcome of patients with bronchiectasis, aiming to identify possible associations that justify its recommendation and the role of immunization in the vicious cycle of the disease, seeking to identify factors that indicate improved quality of life, a decrease in secondary infections, and reduced mortality.

MATERIALS AND METHODS

Study population

This is a descriptive cross-sectional study with a quantitative approach, conducted from August 2018 to July 2019, with a study population consisting of adults with non-cystic

bronchiectasis (N-CB) diagnosed via chest computed tomography, treated at a specialized outpatient clinic at the Dr. Miguel Riet Corrêa Junior University Hospital of the Federal University of Rio Grande (HU-FURG), located in southern Rio Grande do Sul (RS).

Data collection

Epidemiological and sociodemographic data were collected using a structured questionnaire with the participants' consent, following approval by the FURG Ethics Committee in accordance with Opinion No. 14/2019 and Case No. 23116.006049/2018-10. At the end of each interview, respiratory samples were collected via oropharyngeal swab. Access to clinical data was obtained by reviewing patients' medical records. Vaccination information was collected through access to the immunization database, pursuant to Opinion 003/2019 issued by the collegiate body of the Municipal Center for Public Health Education (NUMESC) of the Epidemiological Surveillance Department of the city of Rio Grande.

Microbiological analysis

Microbiological analyses of oropharyngeal respiratory samples were performed using phenotypic methods, involving inoculation onto selective mannitol salt and MacConkey media followed by morphological and staining characterization via Gram staining, and molecular methods to identify *Pseudomonas aeruginosa* among non-fermenting Gram-negative bacilli. Polymerase chain reaction (PCR) to amplify the species-specific 16S rDNA gene of *P. aeruginosa* was performed as proposed by SPILKER et al. (2004), using the primers PA-SS-F (5' -GGGGGATCTTCGGACCTCA 3') and PA-SS-R (5' - TCTTAGAGTGCCCACCCG 3'), and the following amplification conditions: 95°C for 2 min; 35 cycles of 95°C for 30 seconds, 57°C for 45 seconds, 72°C for 1 minute, and 72°C for 5 minutes. Confirmation of the presence of a 956-bp amplicon was performed by 1.5% agarose gel electrophoresis using Blue Green Loading Dye I (Nova Biotecnologia)[8].

FACED Classification

The collected variables were tabulated, and patients were classified using the FACED prognostic *score*. Finally, following the recommendations of the original authors[9], bronchiectasis was stratified into three levels: mild (0–2 points), moderate (3–4 points), and severe (5–7 points), based on the previously established *scores* for the five variables comprising the *score*: forced expiratory volume in the first second (FEV_1), age, colonization by *Pseudomonas aeruginosa*, radiological extent of lung damage, and degree of dyspnea according to the modified Medical Research Council (mMRC) *score* (Table 1).

Inclusion and exclusion criteria

The study included adult patients with bronchiectasis diagnosed by chest computed tomography who were in the stable phase of the disease, were seen at the pulmonology outpatient clinic at HU-FURG during the period when samples were collected, and who voluntarily agreed to participate in the study. Patients without bronchiectasis, those with exacerbated bronchiectasis, and those under 18 years of age were excluded.

Statistical analysis

Statistical analysis was performed using SPSS software, which was used to estimate the frequency of sociodemographic variables in the study population. Pearson's chi-square test was used to assess the bivariate association between categorical and discrete variables, with a p-value of <0.05 considered statistically significant.

RESULTS

Of the 70 eligible patients with bronchiectasis, 64.3% (45/70) were female with a mean age of 59 years (ranging from 28 to 90 years), 81.4% (57/70) self-identified as white, 91.4% (64/70) were employed, and 61.4% (43/70) reported a monthly income between one and three

minimum wages, based on the minimum wage in effect in Brazil in 2019 of U$ 234.33 (Table 2).

Smokers accounted for approximately 80% of the study population, comprising current smokers (17.1%) and former smokers (62.9%). When comparing this variable with PPSV23 vaccination *status* (Table 3), 55.7% were current or former smokers who self-reported as unvaccinated, a group that accounted for more than half of the total population (39/70).

Still on the topic of substances, it was observed that 40% (28/70) had not been vaccinated and reported using alcohol and/or other substances (p = 0.0174) while 28.57% (20/70) were not vaccinated and did not use any substances, indicating that the consumption of these substances (alcohol and other drugs) is higher in the unvaccinated group.

Regarding the characteristic symptoms of bronchiectasis, 98.5% (69/70) of patients presented at least one symptom of the disease, and 54.3% (38/70) reported three or more symptoms, with recurrent cough and dyspnea being common in the sample (p = 0.791). Regarding chronic diseases, 77.1% (54/70) reported a diagnosis of another respiratory disease associated with bronchiectasis, with asthma, bronchitis, rhinitis, and emphysema being the most frequently cited (p = 0.665).

With regard to hospitalization, the past 12 months were used as the reference period for correlation analysis. It was observed that, among patients who reported at least one hospitalization episode during that period, the unvaccinated group had a higher frequency of hospitalization (9/48) compared to the vaccinated group (4/22) (Table 3).

Based on the microbiological analysis of oropharyngeal respiratory samples, predominant colonization by Gram-positive cocci was identified in 55.7% (39/70) of cases, followed by Gram-negative bacilli in 15.7% (11/70) and mixed (Gram-positive and Gram-negative) colonization in 25.7% (18/70) in the study population. To confirm colonization by *P.*

aeruginosa, PCR was performed on the Gram-negative bacilli, confirming that of the 11 clinical samples that that did not ferment lactose in the MacConkey medium, 10 (90.9%) isolates were confirmed as *P. aeruginosa*.

Regarding the FACED prognostic *score*, it was observed that 41.4% (29/70) of patients with bronchiectasis were classified as having mild disease; of these, the majority of vaccinated patients (22/70)—63.6% (14/22)—were classified as having mild to moderate disease (Table 3). Furthermore, vaccination appears to influence microbial diversity, as this study found a higher frequency of Gram-positive bacteria (35.71%) among unvaccinated individuals (25/70).

Considering the impact of the variables studied, we also analyzed the frequency of antibiotic use in the past 12 months and its distribution according to the FACED *score* classification between the vaccinated and unvaccinated groups. In this regard, it was found that unvaccinated individuals used antibiotics more frequently during the evaluation period (42.85%), and although there was no significant association (p = 0.3392), interestingly, only individuals who used antimicrobials were classified as having severe disease, while those who did not use antibiotics were classified as having milder forms, such as mild and moderate.

DISCUSSION

The prevalence of bronchiectasis in the general population has often been associated with high morbidity and certain factors related to a poor quality of life, such as pulmonary comorbidities, frequent exacerbations, associated psychological conditions—such as anxiety and depression—and limitations in physical capacity[10,11,12]. Based on the analysis conducted in this study, a socioepidemiological profile of the sample was constructed: predominantly female, over 60 years of age, with a history of smoking and substance use. A study conducted in the United Kingdom reported an increase in bronchiectasis across all age groups, though significantly more so in older age groups, with a higher incidence among women as well[13].

Goeminne et al.[14] identified advancing age as one of the additional risk factors for higher mortality rates from the disease, along with gender, smoking, and associated conditions, among others[14].

Although its etiology is multifaceted, bronchiectasis is considered the end stage of lung damage caused by recurrent respiratory infections, genetic abnormalities, and autoimmune and/or acquired diseases[6]. Furthermore, recurrent infections may be triggered by chronic colonization of pathogens, promoting exacerbations and contributing to the maintenance of Cole's cycle. This vicious cycle characterizes non-cystic bronchiectasis through infection, airway obstruction, and peribronchial fibrosis[15].

Considering the importance of alternatives aimed at reducing episodes of exacerbations and, thereby, positively impacting the disease prognosis, the performance of the Pneumococcal Polysaccharide Vaccine (PPSV23) was evaluated in the patients included in the study. The participants fall within the recommended age group for immunization and are also eligible due to their chronic lung disease — bronchiectasis — which allows us to infer a possible correlation between vaccination and the modulation of the clinical presentations observed.

Although the percentage of vaccinated individuals was low, there is significant agreement between self-reported data and actual immunization rates. It is suggested that immunization contributed to a decrease in infectious episodes, as reported by participants, and is also thought to be associated with a reduction in the number of tuberculosis cases specifically. Even in light of these data, anti-vaccine movements fueled by misinformation and political and cultural influences have been on the rise. Vaccine hesitancy poses a major public health problem, as it reduces vaccination coverage and may increase the risk of outbreaks of previously controlled diseases and hinder the achievement of herd immunity, thereby increasing morbidity and mortality. In this regard, our study observed more frequent antibiotic

use among unvaccinated individuals classified as having severe disease (*score* 3), thereby reinforcing the potential of immunization.

A recent study reveals that the average length of hospitalization for bronchiectasis in Brazil was estimated at 8.1 days and highlights the disease's impact on hospitalization rates, with 84% of patients seeking emergency care at healthcare facilities, indicating that the need for hospital care is strongly associated with symptom exacerbation[16].

According to the Brazilian consensus[15], the identification of potentially pathogenic microorganisms in the airways of patients with bronchiectasis is a finding associated with increased bronchial inflammation and progressive clinical deterioration. According to Martins et al.[17], the virulence and resistance of the microorganism infecting or colonizing the lower airways directly impact prognosis and highlight *Staphylococcus aureus* as a concerning agent of chronic infection, given its high infectious potential. In the present study, unvaccinated patients exhibited colonization by Gram-positive microorganisms more frequently (35.71%) compared to vaccinated patients (20%), suggesting that vaccination may act as an important protective and preventive factor against chronic colonization by potentially pathogenic microorganisms.

Pseudomonas aeruginosa stands out as one of the most common potentially pathogenic Gram-negative bacteria in bronchiectasis, both in the early stages of the disease and during exacerbations[18,19]. This microorganism is prominent in this disease due to its high adaptability and persistence, as it possesses virulence factors that increase inflammation and tissue damage, particularly during exacerbations, in addition to a high frequency of antimicrobial resistance and prognostic impact[18,19,20].

However, in our study, we observed a predominance of Gram-positive bacteria in clinical samples, differing from these findings. Furthermore, discrepancies are noted in the

findings of Dhar et al. [21], who reported a higher prevalence among younger and male individuals. In contrast, a comprehensive study involving a Spanish cohort of 2,047 patients revealed results consistent with ours, as the prevalence was higher among women (54.9%) and older patients, with a mean age of 64.9 years[22].

Although Gram-positive bacteria were predominant in this study, the detection of *P. aeruginosa* in individuals with bronchiectasis is emphasized in recent severity *scores*, such as the FACED[23]. The FACED and E-FACED *scores* take into account the presence of chronic colonization by *P. aeruginosa* as a factor in disease severity and progression[24].

Finally, we highlight variables that, although not considered significant in the chi-square test, suggest an influence on adherence to VPP23 immunization: households with 3 or more people per residence in 67.1% (47/70) of the sample appear to be related to non-vaccination ($p = 0.061$), a factor associated with income and basic education level ($p = 0.093$). Furthermore, self-reported employed workers showed adherence to vaccination ($p = 0.052$), presumably due to employer requirements or daily exposure.

CONCLUSION

In this study, we analyzed the clinical and microbiological profile of patients with bronchiectasis followed at a university hospital in Rio Grande do Sul, noting that the majority of patients were women (64.3%), employed, and had an income of up to three minimum wages. Smoking emerged as a significant factor, present in approximately 80% of the study population, particularly among individuals not vaccinated against *Streptococcus pneumoniae*. The absence of vaccination was associated with higher consumption of alcohol and other substances, as well as a higher frequency of hospitalizations and reports of recurrent respiratory infections.

From a microbiological perspective, Gram-positive cocci predominated (55.7%) in respiratory samples, although *P. aeruginosa* was confirmed in 90.9% (10/11) of the samples

of non-fermenting Gram-negative bacilli, highlighting its role as a significant pathogen in the colonization of patients with bronchiectasis. Analysis of the FACED *score* showed that most vaccinated patients had a mild to moderate classification, while the unvaccinated group exhibited greater antibiotic use and greater bacterial diversity, including a higher frequency of Gram-positive bacteria. These findings, analyzed in the context of intensifying anti-vaccine movements, reinforce the recommendation for immunization with the 23-valent pneumococcal polysaccharide vaccine for patients with bronchiectasis as a preventive measure, in addition to serving as a significantly important complementary alternative in the treatment of the disease, reducing exacerbations and leading to a favorable prognostic outcome.

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Tables

Table 1. *Scores* for the markers used in the FACED score.

Variable	Points
FEV_1	
≥ 50% than expected	0
< 50% than expected	2
Age	
< 70 years	0
≥ 70 years	2
Pseudomonas aeruginosa	
No	0
Yes	1
Number of lobes involved	
1-2	0
>2	1
mMRC dyspnea scale	
0-2	0
3-4	1

Source: Author.

Table 2. Main sociodemographic characteristics of the study population.

Feature	**N (%)**
Categorical variables	N=70
Sex	
Masculine	25 (35.7%)
Feminine	45 (64.3%)
Age	
≤ 29 years	1 (1.4%)
30 a 60 years	24 (34.3%)
>60 years	45 (64.3%)
Skin Color	
White	57 (81.4%)
Black	5 (7.1%)
Other	8 (11.4%)
Active Worker	
Yes	64 (91.4%)
No	6 (8.6%)
Income	
< 1 minimum wage	21 (30.0%)

1-3 minimum wages	43 (61.4%)
>3 minimum wages	6 (8.6%)
Location: House	
Rio Grande	67 (95.7%)
Nearby Cities	3 (4.3%)
Number of Residents	
< 3 people	23 (32.8%)
≥ 3 people	47 (67.2%)
Education	
Up to and including elementary school	53 (75.7%)
Up to and including high school	11 (15.7%)
Up to and including college	6 (8.6%)

Source: Author.

Table 3. Habits and prevalence of clinical characteristics among patients with bronchiectasis regarding adherence to the Pneumococcal Polysaccharide Vaccine (n=70).

Categorical variables	**Vaccinated N (%)**	**Unvaccinated N (%)**	***p* value**
Self-reported PPSV23			$p < 0.000$
Yes	18 (25.71%)	6 (8.57%)	
No	4 (5.71%)	42 (60%)	
Smoking			$p = 0.478$
Never	5 (7.14%)	9 (12.85%)	
Current	2 (2.85%)	10 (14.28%)	
Former smoker	15 (21.42%)	29 (41.42%)	
Substance Use			$p = 0.0174$
None	15 (21.42%)	20 (28.57%)	
Alcohol and/or other drugs	7 (10%)	28 (40%)	
Bronchiectasis Symptoms			$p = 0.791$
No symptoms	0 (0%)	1 (1.42%)	
1 or 2 symptoms	10 (14.28%)	21 (30%)	
3 or more symptoms	12 (17.14%)	26 (37.14%)	
Other Chronic Conditions			$p = 0.665$

None	4 (5.71%)	5 (7.14%)	
Respiratory	16 (22.85%)	38 (54.28%)	
Respiratory and Other*	2 (2.85%)	5 (7.14%)	
Hospitalization			$p = 0.311$
None	18 (25.71%)	39 (55.71%)	
Once	2 (2.85%)	8 (11.42%)	
Two or more times	2 (2.85%)	1 (1.42%)	
Respiratory Infections			$p = 0.447$
None	15 (21.42%)	26 (37.14%)	
Tuberculosis	6 (8.57%)	18 (25.71%)	
Pneumonia	1 (1.42%)	1 (1.42%)	
Both	0 (0%)	3 (4.28%)	
Colonization			$p = 0.531$
No Growth	0 (0%)	2 (2.85%)	
Gram-positive cocci	14 (20%)	25 (35.71%)	
Gram-negative bacilli	2 (2.85%)	9 (12.85%)	
Mixed	6 (8.57%)	12 (17.14%)	
FACED			$p = 0.516$
Unclassified	5 (7.14%)	11 (15.71%)	

Mild	9 (12.85%)	20 (28.57%)	
Moderate	5 (7.14%)	15 (21.42%)	
Severe	3 (4.28%)	2 (2.85%)	
Antibiotic Use			$p = 0.222$
Yes	17 (24.28%)	30 (42.85%)	
No	5 (7.14%)	18 (25.71%)	

*Recurrent non-respiratory infections. Source: Author.