

ORIGINAL ARTICLE

Respiratory allergy to airborne fungi in São Luís – MA: clinical aspects and levels of IgE in a structured asthma program

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Abstract

Introduction: Respiratory allergies are becoming increasingly frequent, especially based on studies of asthma and rhinitis. It is estimated that 20–30% of the world's population is affected. Allergic reactions are caused by the production of IgE antibodies specific to inhaled allergens, such as fungi in the air. This study aimed to analyze the level of specific IgE against airborne fungi in patients with a clinical diagnosis of asthma and rhinitis/sinusitis. **Methods:** In total, 158 patients enrolled in the Program of Support for Asthmatic Patient, and 20 controls were studied. Clinical data from the period of 2007–2008 were surveyed using a protocol form. ELISAs were performed to quantify the levels of total and specific IgE. **Results:** Of the 158 patients diagnosed with asthma, 71 had rhinitis and 32 had sinusitis. There was a predominance of females and residents of urban areas. The main symptoms reported were dyspnea, cough, wheezing and nasal obstruction. There was a statistically significant relationship between dyspnea and seropositivity for *Fusarium* ($p=0.01$) and *Penicillium* ($p=0.005$) and between cough and seropositivity for *Aspergillus* ($p=0.007$). **Conclusions:** Anti-*Penicillium* (79.7%) and anti-*Fusarium* IgE (77.8%) were found to have the highest prevalence of seropositivity in individuals with asthma and rhinitis/sinusitis. Sensitivity to fungi was higher in symptomatic individuals. The identification of environmental fungi is essential for the diagnosis of respiratory allergy.

Keywords

Education, environmental development, epidemiology, rhinitis/sinusitis

History

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Introduction

Fungi are important pathogens associated to airway diseases. There is a great interest in understanding the dynamics of the involvement of airborne fungi in respiratory allergies. Interest in the role of fungi in this process is growing, particularly in tropical areas with high humidity [1,2]. As fungi and their spores are frequent particules in the environment, specific antibodies detection may be used to evaluate allergies mediated by IgE, in pneumonitis and allergic bronchopulmonary mycosis [3–5].

The airborne fungal flora vary between study areas and may or may not have features in common [6–8]. Spores account for many of the fungal elements that are found in the atmosphere. When inhaled, these airborne allergens are potentially responsible for allergic respiratory diseases, such as asthma and rhinitis/sinusitis [9,10].

Specific IgE detection is one of the most important *in vitro* methods for the diagnoses of immediate hypersensitivity [11]. High levels of specific IgE are strongly associated with allergies, which are increasingly prevalent [12,13]. However, levels can be high in several conditions, such as skin and intestinal parasitosis, myeloma, hyper-IgE syndrome, Wiskott–Aldrich syndrome, aspergillosis and pulmonary filariasis. In Brazil, increased levels are often observed in non-atopic patients [14].

The occurrence of large numbers of fungal spores in various regions emphasizes the importance of studying the airborne fungi in Brazil, and especially in Maranhão, where the humidity is high [5,8,9,15,16]. This research aimed to examine serum concentrations of IgE specific to airborne fungi in patients with a clinical diagnosis of asthma and rhinitis/sinusitis.

Patients and methods**Area of research**

Island of São Luís, capital of Maranhão State, Brazil, is placed in the center of Maranhão seashore, at 2°20'00"LS a

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2°45'00"LS, longitude 44°01'21" LnW a 44°24'54" LnW. It is located in the North of the state, limiting with the Atlantic Ocean; South to Estreito dos Mosquitos, which separates it from the continent; East to São José Bay and West to São Marcos Bay [17].

Sample calculation

To calculate the sample size, Epi Info 3.4.2 (2007, Atlanta, GA) statistical software was used. The calculation was based on the prevalence of asthma in the reference service at 5% significance.

Patients

The study sample consisted of 158 patients enrolled in the Program of Support for Asthmatic Patient (PAPA), University Hospital, Federal University of Maranhão (HUUFMA) and 20 controls. Through-chip protocol, clinical data were obtained from patients in the period from 2007 to 2008.

From these subjects, 10 ml of total blood was collected by intravenous puncture after signing the Instrument of Free Consent. The serum was separated and aliquoted for storage in a freezer at -20°C until the moment of performing the techniques.

Inclusion and exclusion criteria

The following was considered as a criterion for inclusion in the group of asthmatics: be patient with asthma and rhinitis/sinusitis, controlled and/or uncontrolled, being a nonsmoker or ex-smoker for more than 5 years and being accompanied at PAPA for at least one year. Patients who refused to signing the consent form and participate in the collection of peripheral blood (10 ml) were not included.

For the non-asthmatic control group, the inclusion criteria were asked if they would like to participate in the study and signed an informed consent form and answering the question, if they had a history of asthma or asthma in the family, if the answer was negative, they were included. Furthermore, they would not have allergic diseases.

Isolation and airborne fungi identification

Airborne fungi were monthly collected by Bezerra [18], in five areas (North, South, Center, East and West) in the city of São Luís, Maranhão, Brazil, from January to December 2007. Fungal spores were collected by passive gravitational settling on Petri dishes containing Sabouraud agar, 1.5 m height, for 15 minutes [3,16]. A total of 1510 colony forming units (CFUs) were recovered, corresponding to 20 fungi genera. The species will be identified later by microculture technique and electronic microscopy.

Only the genera *Aspergillus*, *Penicillium*, *Fusarium* and *Neurospora* showed detectable amounts of protein and were used as antigens to sensitize ELISA plates to investigate the concentration of specific IgE by ELISA index (EI) [19].

Antigenic extraction

The protocol for the extraction of antigens from filamentous fungi was performed as follows, based on the literature [20,21] with certain modifications: the fungi were cultivated in an

appropriate medium (Sabouraud ágar) for five days of culture before washing five times with phosphate-buffered saline (PBS) and transferring the culture to screw-cap tubes containing previously sterilized glass beads and PBS and fungus at a ratio of 3:1. The tubes were vortexed for 15 minutes and centrifuged for one hour at 14 500 rpm in a refrigerated centrifuge. The supernatant was collected, and the protein was quantitated. The stock was aliquoted and stored at -20°C until use. Stocks were diluted to 50 $\mu\text{l/ml}$ in PBS before use.

The sera from 158 patients with clinically characterized respiratory diseases and sera from 20 healthy controls were subjected to ELISA to detect the concentrations of total and specific IgE against fungi.

Polystyrene plates with 96 wells containing immobilized monoclonal antibodies of the anti-IgE type formed specific complexes with serum IgE through high-affinity bonds. The plates were then washed to remove proteins that had not interacted. A secondary antibody conjugated to peroxidase was added to form a ternary complex with the immobilized IgE, followed by washing. Next, 3-3',5-5'-tetramethylbenzidine and hydrogen peroxide were added to the solution, which under the action of the immobilized peroxidase, produced a blue color. A strong acid was added to the mixture to halt the reaction, producing a yellow color. A reading was performed at a wavelength of 450 nm. The absorbed intensity was proportional to the concentration of IgE in the sample.

Optical densities were determined spectrophotometrically at 450 nm. The rates of antibodies were expressed as the EI, according to Alves et al. [22]. The EI is calculated by the ratio between the mean optical density of the study group and the optical density of three samples of sera from subjects with no specific IgE (multiplied by 3 δ , where δ is the average standard deviation of optical densities of sera from the group of non-allergic individuals).

EI values equal to or higher than 0.102 ($\text{EI} \geq 0.102$) were considered to be positive for total IgE; 0.603 ($\text{EI} \geq 0.603$) for IgE anti-*Aspergillus* spp.; 0.466 ($\text{EI} \geq 0.466$) for IgE anti-*Penicillium* spp.; 0.298 ($\text{EI} \geq 0.298$) for IgE anti-*Neurospora* spp.; and 0.565 ($\text{EI} \geq 0.565$) for IgE anti-*Fusarium* spp.

Statistical analysis

Statistical analysis was performed using the software Stata/SE 9.0 for Windows (Stata Corporation, College Station, TX). For the comparison of numerical variables between two groups, the *t*-test was used. When comparing three or more groups or categories, ANOVA followed by Tukey's *post hoc* test was used at $p < 0.05$. For categorical variables, the chi-square test was used, followed by the chi-square partition at $p < 0.05$. If one of the frequencies expected in the 2×2 contingency tables was less than 5, we opted for Fisher's exact test. The Pearson correlation was used to study the relationship between total IgE levels and age (years). The correlation coefficient Phi (ϕ) was used to verify the correlation between positivity for two fungi concomitantly. We considered a p value < 0.05 as the significance criterion.

Ethical aspects

This research protocol was approved by the Ethics Committee in Research of HUUFMA under substantiated opinion

N° 406/06. The Term of Informed Consent was signed by the parents or guardians of the minors who participated in this research.

Results

From January to December 2007, a total of 1510 CFUs were recovered, corresponding to 20 fungi genera. The main gender found in all regions was *Aspergillus* (33.5%), *Penicillium* (18.8%), *Cladosporium* (14.2%), *Curvularia* (10.6%) and *Fusarium* (7.6%). In this study, we used the genders *Aspergillus*, *Penicillium*, *Fusarium* and *Neurospora* as antigens.

A total of 158 patients with a diagnosis of asthma were studied. In total, 71 (44.9%) of these patients had rhinitis and 32 (20.2%) had sinusitis. Table 1 shows the demographic and

Table 1. Demographic and clinical characteristics of the sample of cases and controls in the study^a.

Variables	Cases (n = 158)	Controls (n = 20)	Total (n = 178)
Age, years ^b	46.13 (±13.90)	26.55 (±5.8)	43.93 (±14.0)
Genre			
Female	120 (75.9)	9 (45.0)	129 (72.5)
Male	38 (24.1)	11 (55.0)	49 (27.5)
Residence site			
Urban area	112 (70.9)		
Rural area	46 (29.1)		
Region			
North	14 (8.9)	4 (20.0)	18 (10.1)
South	9 (5.7)	0 (0)	9 (5.1)
East	65 (41.1)	11 (55.0)	76 (42.7)
West	32 (20.2)	1 (5.0)	33 (18.5)
Central	38 (24.1)	4 (20.0)	42 (23.6)
Nutrition			
Malnourished	4 (2.5)		
Eutrophic	70 (44.3)		
Overweight	60 (38.0)		
Obese	24 (15.2)		
Sensitization to fungi			
<i>Neurospora</i>	123 (77.8)	6 (30.0)	129 (72.5)
<i>Fusarium</i>	123 (77.8)	3 (15.0)	126 (70.8)
<i>Aspergillus</i>	71 (44.9)	6 (30.0)	77 (43.2)
<i>Penicillium</i>	126 (79.7)	7 (35.0)	133 (74.7)
IgE total ^b	2.49 (±1.09)	0.10	2.22
Severity of asthma			
Intermittent	8 (5.1)		
Mild persistent	44 (27.8)		
Moderate persistent	93 (58.9)		
Severe persistent	13 (8.2)		
Asthma control			
Controlled	99 (62.7)		
Partially controlled	30 (19.0)		
Uncontrolled	29 (18.3)		
Rhinitis	71 (44.9)		
Sinusitis	32 (20.2)		
Treatment			
BD ^c	119 (75.3)		
CI ^d	59 (37.3)		
CO ^e	3 (1.9)		
LABA ^f + CI	90 (57.0)		
Xantin	9 (5.7)		
None	6 (3.8)		

^aData expressed in n (%), except where indicated.

^bData expressed as mean.

^cBD = short-action beta-agonist.

^dCI = inhaled corticosteroid.

^eCO = oral corticosteroid.

^fLABA = long-action beta-agonist.

clinical characteristics of 158 cases and 20 controls in the study ($n = 178$). Of the 158 patients studied, 120 (75.9%) were female and 38 (24.1%) were male. The mean age was 46.13 ± 13.90 years. In total, 112 patients (70.9%) were from an urban area and 46 (29.1%) were from the countryside. In all, 65 patients (41.1%) lived in the East Zone of São Luís; 38 (24.1%) lived in the downtown area; 32 (20.2%) lived in the West Zone; 14 (8.9%) lived in the North Zone; and 9 (5.7%) lived in the South Zone.

Of the 20 controls in the study, 11 (55.0%) were male and 9 (45.0%) were female. The mean age was 26.55 (maximum of 41 and minimum of 19 years). Eleven subjects (55.0%) lived in the East Zone of São Luís; 4 (20.0%) lived in the downtown area; 4 (20.0%) lived in the North Zone; 1 (5.0%) lived in the West Zone; and zero lived in the South Zone.

More than half of the patient population was overweight. Seventy subjects (44.3%) were normal, 60 (38.0%) were overweight, 24 (15.2%) were obese and 4 (2.5%) were malnourished.

The main triggers of symptoms, assessed by clinical data, included dust (33.5%, 53/158), smoke (21.5%, 34/158), climate change (8.2%, 13/158), pets (5.7%, 9/158) and fungi (5.1%, 8/158). Only 48.1% of the patients themselves recognized exposure to a triggering factor; 51.9% did not associate the appearance of symptoms to a trigger factor.

Regarding the treatment of asthma, it was found that 119 atopic individuals (75.3%) used short-action agonists; 90 (57.0%) used a combination of beta-agonists and long-action and inhaled corticosteroids; 59 (37.3%) used inhaled corticosteroids; 9 (5.7%) used xanthine; and 3 (1.9%) used oral corticosteroids. Six asthmatic patients (3.8%) were not using any medication.

The most frequently reported symptoms were dyspnea, cough, wheezing and nasal obstruction. There was a statistically significant relationship between dyspnea and seropositivity for *Fusarium* ($p = 0.01$) and *Penicillium* ($p = 0.005$) and between coughing and seropositivity for *Aspergillus* ($p = 0.007$).

The mean total IgE was $2.49 (\pm 1.09)$ among cases and 0.10 among controls. Total IgE levels had significantly higher values in males ($p = 0.01$). Using the Pearson correlation between age (years) and total IgE, there was no statistical significance.

The atopic individuals (genetically predisposed to be sensitized more easily to common environmental antigens, producing IgE antibodies quickly and in larger quantities) with professions at asthma risk (painters, bakers, bricklayers, carpenters, industrial and health professionals) did not differ from the other subjects in fungal sensitization.

Figure 1 shows the seropositivity to fungi in patients by age group high. A prevalence of seropositivity to fungi was noted in the age range of 40–59 years, particularly for the genera *Penicillium* and *Fusarium*.

Specific IgE antibodies against fungi (anti-*Neurospora*, anti-*Fusarium*, anti-*Aspergillus* and anti-*Penicillium* IgE) were screened in the aforementioned 178 blood samples. Among the 158 patients enrolled in the PAPA, 126 (79.7%) were sensitized to *Penicillium*; 123 (77.8%) were sensitized to *Neurospora*; 123 (77.8%) were sensitized to *Fusarium*; and 71 (44.9%) were sensitized to *Aspergillus*. Among the

Figure 1. Sensitization to fungi by age. Trendline is the average age interval. Bars represents percentage.

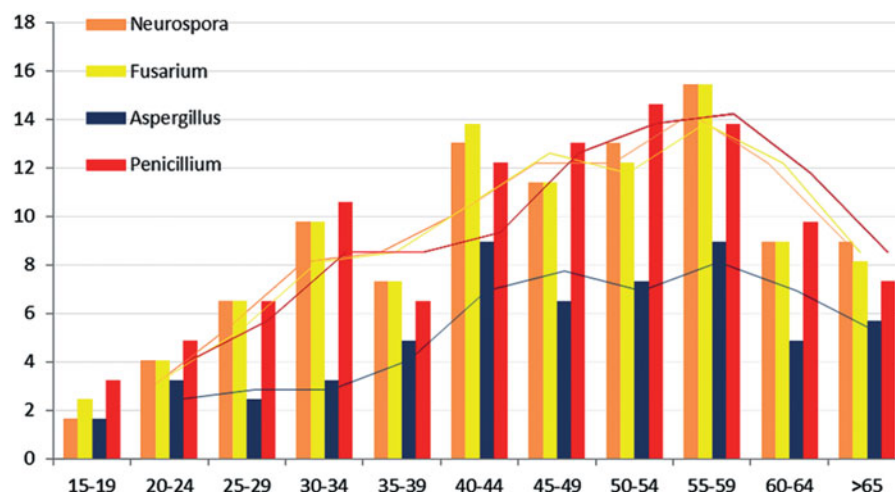
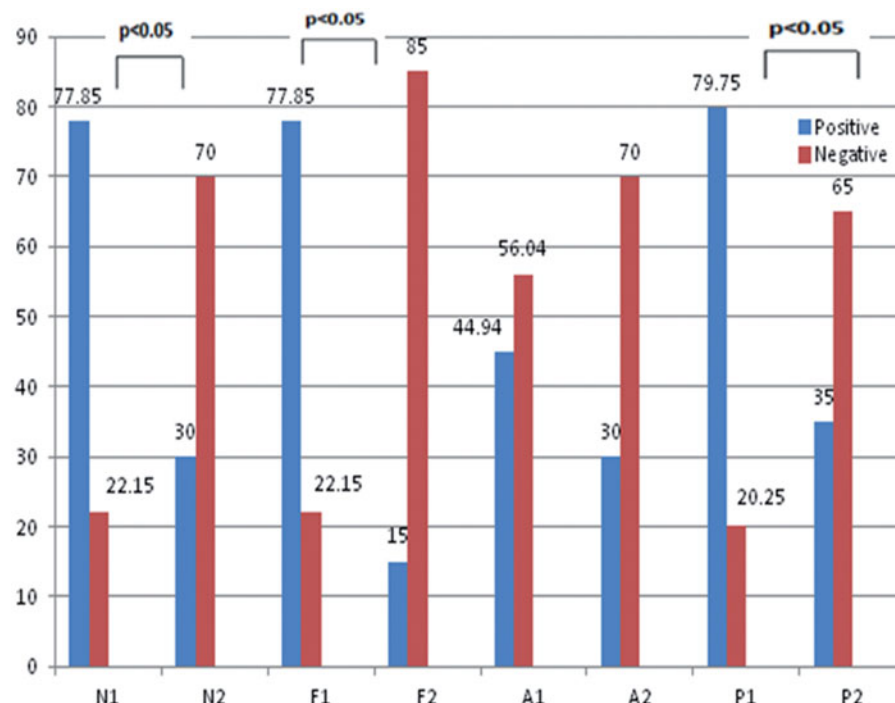


Figure 2. Comparison to IgE positivity per group (case x control). N1 (*Neurospora*-sensitized patients), N2 (controls sensitized to *Neurospora*), F1 (*Fusarium*-sensitized patients), F2 (controls sensitized to *Fusarium*), A1 (patients sensitized to *Aspergillus*), A2 (controls sensitized to *Aspergillus*), P1 (patients sensitized to *Penicillium*) and P2 (controls sensitized to *Penicillium*).



20 subjects in the control group, 7 (35.0%) were sensitized to *Penicillium*; 6 (30.0%) were sensitized to *Neurospora*; 6 (30.0%) were sensitized to *Aspergillus*; and 3 (15.0%) were sensitized to *Fusarium*.

There was a statistically significant difference in sensitization to fungi between the case group and the control group, with higher seropositivity in the former. This phenomenon is shown in Figure 2.

It was found that the asthmatics included a proportionally greater number of polysensitized individuals (sensitized to two or more fungi) than did the controls. Figure 3 shows sensitization to fungi in patients according to the severity of asthma. Using the correlation coefficient Phi (ϕ), the pair of fungi that showed the highest combined positivity was *Neurospora* and *Fusarium*.

Of the 158 patients, 93 (58.9%) had moderate to persistent asthma; 44 (27.8%) had mild persistent asthma; 13 (8.2%) had severe persistent asthma; and 8 (5.1%) had intermittent

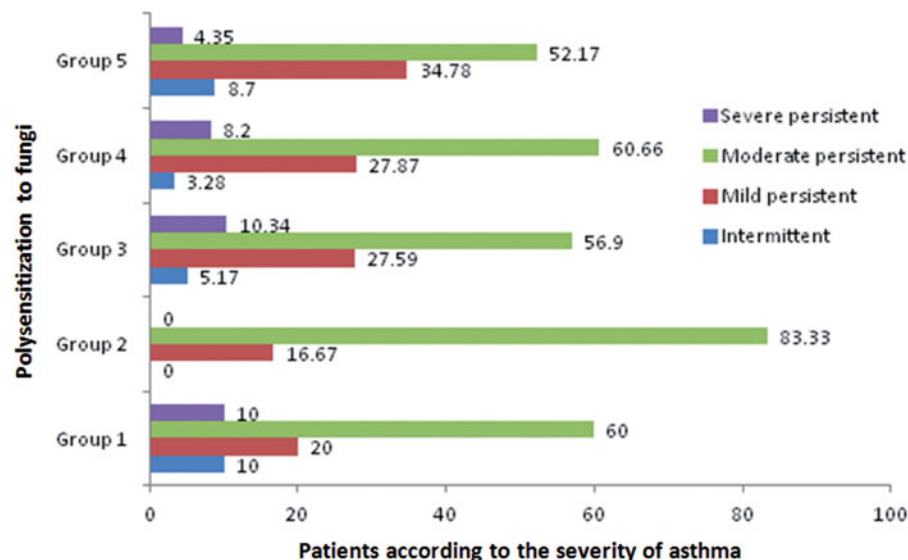
asthma. According to the level of asthma control, 99 cases (62.7%) were controlled; 30 (19.0%) were partially controlled; and 29 (18.3%) were uncontrolled. Regarding the analysis of sensitization to fungi, according to the classification of asthma by severity and the level of control, there was no statistical significance.

The presence of rhinitis was observed in 71 patients (44.9%), with statistical significance among patients with or without sensitization to *Fusarium* ($p = 0.02$) and *Penicillium* ($p = 0.01$). Sinusitis was present in 32 individuals (20.2%), with no significant relationship with sensitization to fungi.

Discussion

Regarding age, most individuals seropositive for specific IgE against airborne fungi were aged between 40 and 59 years. Females comprised the majority of those seropositive for specific IgE against allergens related to four genera of fungi

Figure 3. Distribution of patients according to Polysensitization related to the classification of asthma. Group 1 (sensitized to a single fungus; $n = 10$), Group 2 (sensitized to two fungi; $n = 6$), Group 3 (sensitized to three fungi; $n = 58$), Group 4 (sensitized for four types of fungi $n = 61$) and group 5 (not sensitized; $n = 23$) ($n = 158$). Chi-square test. Value of $p = 0.96$.



(anti-*Neurospora*, anti-*Fusarium*, anti-*Aspergillus* and anti-*Penicillium* IgE), and seropositivity for anti-*Penicillium* IgE in the studied individuals was the highest. The seropositivity of individuals for specific IgE against allergens related to the four genera of fungi was predominant in the East Zone of São Luís, MA, and there was a significantly higher number of sensitized individuals among the cases ($p < 0.001$). Most patients had moderate persistent asthma or uncontrolled asthma, and the high sensitization to the fungi studied reinforces the importance of knowing the main allergens in a specific location.

Fungi are important triggers of the symptoms of respiratory allergies, and four airborne fungi are noteworthy: *Aspergillus* sp., *Penicillium* sp., *Alternaria* sp. and *Cladosporium* sp [37]. These fungi can cause respiratory symptoms following inhalation of particles of their spores and can serve as food for certain mites. The national and international literature describes the importance of these organisms and their treatment, including immunotherapy for the allergies caused by them [23].

In a study by Gender et al. [23], the total IgE geometric mean was significantly higher in asthmatics than in non-asthmatics. Total IgE values were also higher in men than in women, in non-Hispanic black people and Mexican Americans than in non-Hispanic white people, in people below the 12th grade of education, in the poorest individuals, in those with the highest cotinine levels in the serum, in those who were overweight and in those with at least one positive specific IgE test. In this study, total IgE levels were also higher in males and asthmatics.

The increase in occupational respiratory diseases has attracted the attention of health professionals for the work environment. It is known that in most cases of asthma/rhinitis, occupational have immunological mechanisms. However, less than 5% of total IgE are mediated by limiting the use of the allergy tests in diagnosis [17,24]. This gives a better understanding to the study, whose patients with risk occupations for asthma did not differ from the others as sensitization to fungi.

In this study, only eight patients (5.1%) identified fungus as a trigger of their symptoms and 53 (33.5%) identified dust, involving concomitant exposure to dust mites, fungi and other agents [25]. In a study by Santos et al. [12], only one-third of patients recognized fungi as aggravating their symptoms.

In this study, 158 patients had asthma (58.9%, moderate persistent; 27.8%, mild persistent; 8.2%, severe persistent; and 5.1%, intermittent); 44.9% of these patients had rhinitis; and 20.2% had sinusitis. In the aforementioned study by Coimbra [25], most patients had rhinitis (90%) and asthma (80%), and most often, moderate persistent asthma (56%), as in this study. The severe persistent asthmatics had a low prevalence of sensitization in this study. These results may be related to the place of residence of these patients, which showed a less number of fungi isolated.

In Malaysia, Goh et al. [26] found that 72.73% of subjects had positive specific IgE against *Penicillium*. The result, which is similar to that of the patients in the PAPA (79.7%), can be explained by the use of ELISA in both studies and the high frequency of *Penicillium* in Brazil and Malaysia.

Osorio et al. [27] found hypersensitivity to fungi, mainly in the genera *Penicillium* and *Aspergillus*, in 12 of 13 asthmatic schoolchildren in their study in the state of Recife.

A Mexican study [28] involving pediatric patients with respiratory allergy correlated positive skin tests with fungi, total IgE, specific IgE and fungal cultures from the environment, showing that the most frequent allergens were *Rhizopus*, *Aspergillus*, *Cladosporium* and *Candida*. Total IgE was found to be high in 77.2% of patients, and specific IgE was found to be high in 31.4%.

As in this study, Santos et al. [12] found a large number of patients who were sensitized to more than one fungus. In this Portuguese study, the most sensitizing fungal species were *Aspergillus fumigatus* (46%), *Aspergillus niger* (36%), *Alternaria tenuis* (34%), *Cladosporium herbarum* (38%), *Penicillium roqueforti* (32%), *Fusarium moniliforme* (31%), *Curvularia spicifera* (29%), *Candida albicans* (28%) and *Rhizopus nigricans* (26%). The origin of polysensitization to

fungi is explained by co-sensitization or cross-reactivity phenomena. Polysensitization also includes mites, cockroaches, pollen and other allergens.

In a study in Florianópolis, Brazil [6], on 155 patients who underwent the measurement of specific IgE against various allergens at an ENT clinic, 2.6% were sensitive to *Penicillium notatum*, *C. herbarum* and/or *A. fumigatus*. It was also found that only sensitivity to fungi was among the main positive predictive factors for nasal surgery.

Chavasco et al. [29] verified the presence of IgE in the sera of all patients with a positive skin test specific for *Pisolithus tinctorius*. In a study on the fungal flora in air conditioners in intensive care units in Teresina, Mobin and Salmito [8], most frequently found genera were *Aspergillus* and *Trichoderma*. In this study, seropositivity for *Aspergillus* spp. was the lowest (44.9%) in asthmatics, despite its high incidence in the atmosphere of São Luis.

A Spanish study [1] performed in Barcelona showed the importance of fungi in rhinitis, regardless of whether it was associated with asthma. The major sensitizing fungus was of the genus *Alternaria*. An effective tool was used to separate patients into those who were only sensitized to fungi and those who were simultaneously sensitized to fungi and other allergens. Much of the first group showed no chronic productive cough. There was a prevalence of rhinitis and mild persistent or intermittent asthma, with few cases of sinusitis. In this study, there was a statistically significant relationship between cough and seropositivity for *Aspergillus* ($p=0.007$), and moderate persistent asthma and mild persistent asthma were prevalent.

The literature infrequently cites the genus *Neurospora* as an aeroallergen among fungi [21]. In this study, the genus *Neurospora* showed high seropositivity (77.8%) in patients.

Before requesting the measurement of specific IgE in patients with respiratory allergies, one should be aware of the major allergens in the region because this test is relatively more expensive than skin tests and total IgE measurement are. Thus, this protocol avoids the bad practice of requesting the analysis of specific IgE against agents with which the patient has no contact [27]. The panel of fungi included in this study was based on data previously collected in São Luís, MA [30], on airborne fungi [18,22,31,32] and sensitization to fungi in the Brazilian population [3,6,7,16].

The air contains a large number of fungi in both the interiors of houses and the external environment. Their proliferation is favored by humid environments in fabrics usually used for linings, drapes and carpets; in clothing and leather goods; in books and old papers; and in fillings for sofas, pillows and cushions. Such information is essential for the control of fungi, decreasing sensitization and, consequently, the prevalence of respiratory allergies [23].

In the Brazilian Northeast, especially in the coastal regions, fungi find a suitable environment in which to develop due to moisture and high temperatures. Mendes et al. [33] mainly identified *Aspergillus*, *Botryodiplodia* and *Curvularia* in Aracaju. Pereira et al. [30] identified a large number of potentially pathogenic airborne fungi on the beaches of São Luís, MA: 22.5% *Aspergillus* sp., 14.5% *A. niger*, 21.2% *Penicillium* sp., 5.6% *Rhizopus* sp., 2.9% *Curvularia curvata*, 4.2% *Nigrospora* sp., 2.9% *Microsporum*

nanum, 2.9% *Gliocladium* sp., 2.9% *Trichoderma* sp., 2.9% *Alternaria alternata*, 1.4% *Scopulariopsis brevicaulis*, 1.4% *Scolecobasidium* sp., 1.4% *Chaetomium globosum*, 1.4% *Fusarium solani*, 2.9% *Cladosporium* sp., 1.4% *Paecilomyces lilacinus*, 1.4% *Rhinochlaidiella* sp., 1.4% *Phialophora verrucosa* and 4.2% *Fonsecaea pedrosoi*.

Mezarri et al. [16] found a higher prevalence of the fungi *Cladosporium* (17.86%) and *Aspergillus/Penicillium* (15.03%) in the atmospheric air of Porto Alegre (RS).

In a study of the fungal flora in the pediatric and neonatal intensive care unit of a tertiary hospital, Melo et al. [34] found that the most frequent genera were *Penicillium* spp., *Cladosporium* spp. and *Chrysosporium* spp.

In studies on air quality in indoor hospital environments, Quadros et al. [35] and Lacaz et al. [36] found the following fungal genera to be the most common: *Aspergillus* and *Penicillium*, followed by *Cladosporium*, *Trichoderma*, *Acremonium* and *Fusarium*.

From an analysis of Table 1, among asthmatics in this study, the following results were obtained. The lowest positivity in the serological results was obtained (44.9%) for the genus *Aspergillus*. The highest percentage of positivity was observed (79.7%) for *Penicillium*. Concerning the genera *Neurospora* and *Fusarium*, a high degree of positivity was also found (77.8%). These findings suggest that exposure to a greater amount of airborne fungal allergens can increase the number of cases of respiratory allergy.

Therefore, the results of this study are in agreement with the literature, reinforcing that the selection of allergens for research must be based on patient assessment, the clinical framework and allergens of local importance. In addition, more studies should be performed to further elucidate the role of fungi in respiratory allergies.

This study with a large number of patients sensitized to *Penicillium*, *Fusarium* and *Neurospora* spp., or less frequently to *Aspergillus*, shows the importance of these sensitizations. Patients with asthma alone or associated with rhinitis/sinusitis were more sensitized than the control group.

However, this study has limitations in the statistical analysis. The control group differed significantly from the study group. Besides, the prick test was not conducted to confirm allergy to fungi of the study. In the analysis of protein production, no different nutritional medium were tested, which may have limited the detection of antigens in other fungal genera.

Conclusions

In short, based on the data obtained in this study, the following aspects of the causal relationship between exposure and the symptoms of respiratory allergy may be noted.

This study shows the importance of airborne fungi sensitizations in asthma alone or associated rhinitis/sinusitis. Combined diagnosis of total IgE test, specific IgE and clinical aspects is very useful for deciding specific therapies.

Declaration of interest

There was no conflict of interest (economic, personal, scientific, healthcare, educational, religious and social) interfering with the search results.

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