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## Artículo original

### A cross sectional study: Fungal sensitization in Polypoid Chronic Rhinosinusitis

### Estudo transversal: sensibilização fúngica em rinossinusite polipóide crônica

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## Abstract

**Introduction:** Few data is published concerning the prevalence of fungal sensitization in patients with Polypoid Chronic Rhinosinusitis.

**Objective:** Our aim was to determine the prevalence of fungal sensitization in a sample of adult patients with Polypoid Chronic Rhinosinusitis followed at an ENT clinical setting.

**Methods:** All adult patients with Polypoid Chronic Rhinosinusitis, submitted to sinus surgery between September 2012 and December 2013, were invited to participate. Prick tests were done with *Alternaria alternata*, *Cladosporium herbarum*, *Aspergillus fumigatus*, *Curvularia lunata*, *Fusarium monilifo*, *Dermatophagoydes pteronyssinus* and grass pollen extract (extracts Merck®). T student and Chi-square tests were determined using SPSS v22, and applied when appropriate. A *p* value <0.05 was considered significant.

**Results:** 63 patients were included (60% men), mean age (SD) 45 (15.4) years old. 14.3% had at least one positive skin prick test for molds (9.5%

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for *Alternaria alternata*, 4.8% for *Cladosporium herbarum*, 6.3% for *Aspergillus fumigatus*, 4.8% for *Curvularia lunata* and 4.8% for *Fusarium monilifo*, 40% were allergic to dust mite and 27% to pollen. We failed to detect an association between fungal sensitization and age ( $p=0.838$ ), gender ( $p=0.674$ ) and *Dermatophagoydes pteronyssinus* sensitization ( $p=0.074$ ), but we found a positive association between fungal and grass-pollen sensitization (41.2% vs 4.3%,  $p<0.001$ ).

Conclusion: Almost a sixth of our patients were mold sensitized. The routine determination of fungal allergic profile may improve the assessment of patients with Polypoid Chronic Rhinosinusitis, increasing the awareness to Allergic Fungal Rhinosinusitis diagnosis.

**Keywords:** Fungi, Hypersensitivity, Nasal Polyps, Sinusitis

### **Resumo**

Introdução: São escassos os dados publicados relativamente à prevalência da sensibilização fúngica em doentes com Rinossinusite Crónica Com Polipose Nasal (RSCcPN).

Objetivo: O objetivo do nosso trabalho foi determinar a prevalência da sensibilização a fungos e a aeroalergéneos comuns numa amostra de doentes adultos com RSCcPN seguidos numa consulta de Otorrinolaringologia.

Métodos: Todos os doentes com RSCcPN, submetidos a cirurgia endonasal entre setembro de 2012 e dezembro de 2013, foram convidados a participar no estudo. Realizaram-se testes cutâneos prick com *Alternaria alternata* (Aa), *Cladosporium herbarum* (Ch), *Aspergillus fumigatus* (Af), *Curvularia lunata* (Cl), *Fusarium monilifo* (Fm), *Dermatophagoydes pteronyssinus* (Dp) e mistura de gramíneas (Merck®). Foram

aplicados os testes T student e Qui-quadrado conforme apropriado; um valor de  $p<0.05$  foi considerado para atribuição de significância estatística (SPSS v22).

Resultados: Foram incluídos 63 doentes (60% homens), com idade média (DP) de 45 (15.4) anos. 14.3% dos doentes tiveram pelo menos um teste prick positivo para fungos (9.5% para Aa, 4.8% para Ch, 6.3% para Af, 4.8% para Cl e 4.8% para Fm), 40% estavam sensibilizados a ácaros e 27% a pólenes. Não foi encontrada associação entre sensibilização a fungos e idade ( $p=0.838$ ), sexo ( $p=0.674$ ) e sensibilização a Dp ( $p=0.074$ ), mas observou-se associação positiva entre sensibilização a fungos e pólenes (41.2% vs 4.3%,  $p<0.001$ ).

Conclusão: Cerca 1/6 dos nossos doentes evidenciaram sensibilização a fungos. A determinação por rotina do perfil alérgico, nomeadamente fúngico, nos doentes com RSCcPN, poderá melhorar a sua abordagem clínica, aumentando a acuidade diagnóstica para Rinossinusite Alérgica Fúngica.

**Palabras chave:** sensibilização fúngica, rinossinusite crónica com polipose nasal, rinossinusite alérgica fúngica

### **Introduction**

Chronic Rhinosinusitis (CRS) reaches about 10.9% of European population<sup>1</sup> and has a significant geographic variation (7-27%)<sup>1</sup>. Prevalence of CRS in Portugal is estimated to be 13%<sup>2</sup>. 10 to 20% of all cases or CRS are due to fungus<sup>3</sup>. Allergic Fungal Rhinosinusitis (AFRS), the most common form of Fungal Rhinosinusitis<sup>4,5</sup>, was described in 1983 by Katzenstein and is responsible for 5 to 10% of all cases of CRS. Causative fungi are variable with *Aspergillus* (13%)<sup>5</sup>, *Bipolaris*, *Curvularia*, *Alternaria*, *Cladosporium*, *Fusarium*, *Helminthosporium* being

the more common. The diagnostic criteria for AFRS were suggested by Bent and Kuhn<sup>6</sup>, and include: type I fungal hypersensitivity confirmed by history, skin tests, or serology; nasal polyposis; typical characteristic on CT scan; eosinophilic mucus without fungal invasion into sinus tissue; and positive fungal stain of sinus contents removed intraoperatively or during office endoscopy. AFRS is a well-recognized entity, but few data is published concerning the prevalence. The real prevalence of AFRS in general population is unknown<sup>5,7</sup>, and the incidence is variable too<sup>8</sup>, although it has been suggested that exceeds in hot and humid climates<sup>5</sup>. The prevalence of AFRS in patients with CRS was studied by Shrestha and is about 22%<sup>9</sup>, however the prevalence in patients with Polypoid Chronic Rhinosinusitis (PCRS) is about 12.1% in another study<sup>10</sup>.

There was no data published concerning the prevalence of mold sensitization in patients with CRS or PCRS. In Portugal, there is no data about the prevalence of AFRS and mold sensitization, neither in general population nor in patients with CRS or PCRS.

We thought that patients with PCRS would benefit of assessment fungal sensitization profile. Our aim was to determine the prevalence of fungal and common aeroallergens sensitization in a sample of adult patients with PCRS followed at an ENT clinical setting. As a secondary objective, we proposed to calculate the prevalence of sensitization to other inhalant allergens and the prevalence of self-reported asthma and to identify associations between fungal sensitivity and asthma, aspirin allergy, dust mite an grass-plots sensitivity, diabetes and smoking.

## **Methods**

We conduct a Cross Sectional Study, and the inclusion of the patients was sequentially throughout the study. All adult patients with PCRS, submitted to functional endoscopic sinus surgery between September 2012 and December 2013, were invited to participate. They filled out a survey and were referred to skin prick fungal tests. Prick tests were done with *Alternaria alternata* (*Aa*), *Cladosporium herbarum* (*Ch*), *Aspergillus fumigatus* (*Af*), *Curvularia lunata* (*Cl*), *Fusarium monilifo* (*Fm*), *Dermatophagoydes pteronyssinus* (*Dp*) and grass pollen extract (extracts Merck®). In the case of positivity in Prick tests, patients were sent to immunology consultation for evaluation and orientation. Our study was approved by ethics committee (IRB approval n° 077/CE/SR). T student and Chi-square tests were determined using SPSS v22, and applied when appropriate. A *p* value < 0.05 was considered significant.

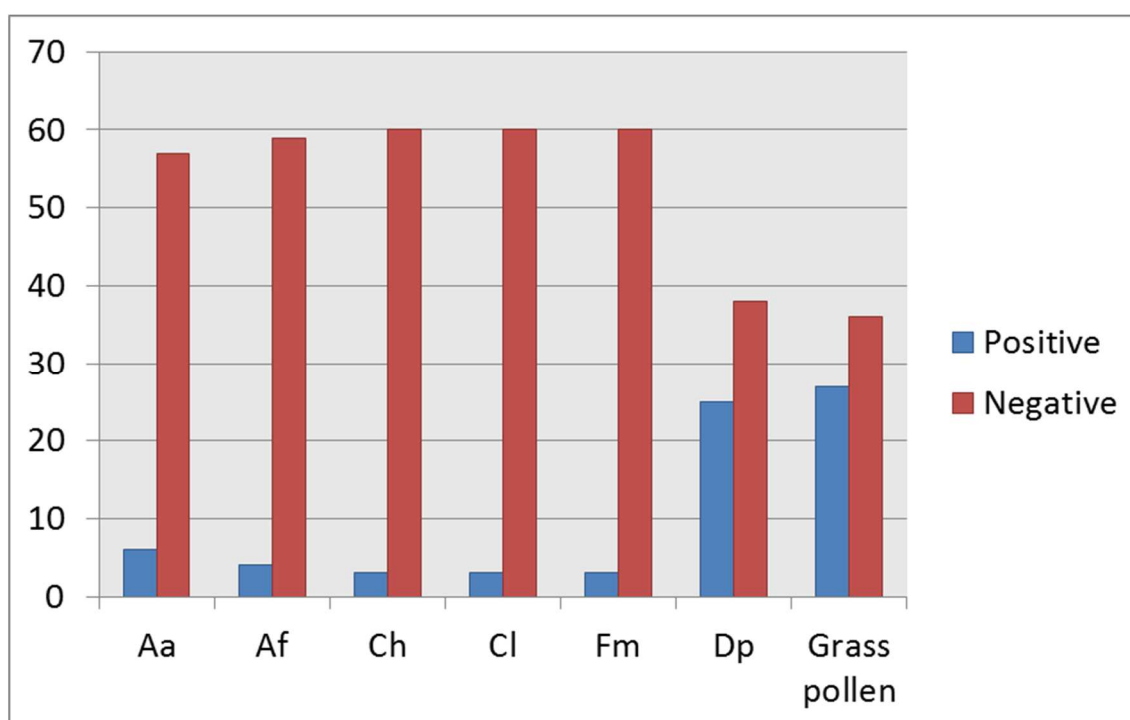
## **Results**

63 patients were included (60% men), and mean age (SD) were 45 (15.4) years old. 14.3% of our patients had at least one positive skin prick test for molds, 9.5% for *Aa*, 4.8% for *Ch*, 6.3% for *Af*, 4.8% for *Cl* and 4.8% for *Fm* (Table 1 and Graphic 1). 40% of the patients were allergic to dust mite and 27% to pollen. 33% of patients report asthma.

We failed to detect an association between fungal sensitization and age (*p*=0.838), gender (15.8% in men vs 12.0% in women, *p*= 0.674), asthma (*p*=0.342), aspirin allergy (*p*= 0.557), diabetes (*p*=0.293) and smoking (*p*=1). There was no association between fungal and *Dp* sensitization (*p*=0.074), but we found a positive association between fungal and grass-pollen sensitization (41.2% vs 4.3%, *p*<0.001).

Positive Fungal Sensitization (%/N)	
<i>Alternaria alternata</i>	9.5/6
<i>Aspergillus fumigatus</i>	6.3/4
<i>Cladosporium herbarum</i>	4.8/3
<i>Curvalaria lunata</i>	4.8/3
<i>Fusarium monofilo</i>	4.8/3

**Table 1:** Results of skin prick test for molds



**Graphic 1:** Results of skin prick test for molds, dust mite and pollen.

Aa - *Alternaria alternata*; Af - *Aspergillus fumigatus*; Ch - *Cladosporium herbarum*; Cl - *Curvalaria lunata*; Fm - *Fusarium monofilo*; Dp - *Dermatophagoydes pteronyssinus*.

## **Discussion**

In the last decade, the medical community has recognized AFRS as a unique clinical entity strongly associated with nasal polyps. Type I fungal hypersensitivity is one of the five criteria necessary to diagnose AFRS. As we know, there are not studies about mold sensitization in patients with PCRS.

About 1/2 of our patients are sensitized to at least one aeroallergen, and that is consistent with other studies. About 14% of our patients were mold sensitized, and we didn't find similar studies in literature to compare data. The most frequent mold was *Alternaria alternata*, followed by *Aspergillus fumigatus*. There are some limitations of our study that should be noted, as the small sample size, lim-

ited geographic location, and the fact that it is an observational study.

Further studies are needed to corroborate these results, particularly with increased sample size, and comparison with a control group.

### **Conclusion**

Half of our patients were sensitized to almost one aeroallergen. Almost a sixth of our patients were mold sensitized. Given the significant prevalence, it seems important to test fungal sensitivity in patients with PCRS. The routine determination of fungal allergic profile may improve the assessment of patients with PCRS, increasing the awareness to AFRS diagnosis.

**Conflicts of Interest:** No conflict of interest was declared by the authors.

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