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*Research article*

## **The relationship between mold sensitization and allergic diseases: a retrospective study (Jeddah, Saudi)**

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**Abstract:** *Background:* fungi are a common trigger of allergic diseases. In spite of that fungal clinical allergies are underdiagnosed. In Saudi, fungi are a common indoor trigger. *Objective:* to determine allergic diseases associated with mold sensitization (MS) in Jeddah-Saudi. *Methods:* a retrospective study between period of (March 2016 to March 2017). Sample size is 51 patients with positive MS. Data was extracted by medical students from Laluna private clinic in Jeddah, Saudi. Test panel used was 30 RAST sIgE in vitro inhalant allergens (MEDIWISS Analytic GmbH company). This panel contains the most common inhalant allergens in Saudi. Each allergen is separate with severity scores from zero to 6. Allergic diseases diagnosis (and any other clinical diagnosis) was extracted from the same files. Results were collected in excel sheet in several columns: demographic data, allergic diseases, common molds in Saudi and other positive inhalants sensitization. *Results:* sample is 51 patients with MS. Gender distribution: females 28 (55%), males 23 (45%). Most common MSs are: aspergillus fumigatus 35 (69%), alternaria 32 (63%), 29 (57%), candida 13 (25%) and penicillium 9 (18%). Allergic diseases associated with MS are: allergic rhinitis and allergic fungal sinusitis 23 (45%), asthma 14 (27%), urticaria and angioedema 11 (22%) and atopic dermatitis (AD) 10 (20%). Other disease associated with MS are: hypothyroidism, obesity and facial pigmentations. *Conclusion:* Unfortunately, mold allergic diseases are underdiagnosed in spite of its high prevalence. In Jeddah, Saudi, the commonest MSs are: aspergillus fumigatus, alternaria followed by cladosporium, candida. Most common diseases associated with MSs are: respiratory allergic diseases (allergic rhinitis, allergic fungal sinusitis, asthma) followed by skin allergic diseases (urticaria, angioedema and AD). MSs are of mild class severity, however clinical allergic diseases due to mold are severe. This means that sensitization class level doesn't reflect the clinical severity.

**Keywords:** inhalants; inhalant allergy; aspergillus; candida; alternaria; fusarium; cladosporium; allergic fungal sinusitis

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## 1. Introduction

Unfortunately, allergy prevalence is increasing worldwide due to multifactorial issues. Factors which can be related are: genetic and inheritance, air pollution, bad life styles and exposure to different allergens. Inhalant allergens can be divided into indoors and outdoors. Indoor allergens are: house dust mites, animals (mainly cat in Saudi), molds and cockroach. Outdoor allergens are mainly pollens. Allergy treatment has to cover three lines: allergen avoidance, pharmaceutical treatment and immunotherapy [1].

In western region of Saudi, indoor inhalant allergens are the most common. This area include several cities like: Makkah, Jeddah and Taif. Respectively, the main aeroallergens in Makkah city are: american cockroach, mites, cat and dessert palm pollens. This distribution is sense except for desert palm pollens because Makkah is a valley area. However, in Taif city the commonest inhalants are: mites, american cockroach and pollens. Pollens in Taif are logic because it's a high altitude and an agricultural area [2].

Molds are diverse and are a common sensitizers of clinical allergies like: alternaria, cladosporium, penicillium, and aspergillus. Fungal allergens commonly trigger allergic diseases in respiratory tract (RT) like: allergic rhinitis, allergic fungal sinusitis and asthma, however they can trigger AD also. Spores of some of these molds are inhaled from the environment and induce IgE allergic cascade. Molds are common both inside and outside homes and patients have to search for their source and avoid future exposure [3].

Fungi are two types: those which can't live in RT and those which can. molds which can't accommodate in RT can trigger mold allergies by inhalation of spores like alternaria and cladosporium and are called (mold aeroallergens). Their allergic severity and impact depend on their air exposure levels. In contrast, molds which can live in RT may trigger allergy even with low air concentration! They are candida, aspergillus, penicillium. They may cause serious lung diseases like: fixed airflow obstruction, bronchiectasis and lung fibrosis. That's why these molds are considered more serious than mold aeroallergens, fortunately they are rare [4].

## 2. Methodology

A retrospective study conducted in Jeddah city (Saudi Arabia). Sample size is 51 patients with positive sensitization to molds: 28 females, 23 males. MS mean's positive sIgE RAST inhalants in vitro blood test to common molds in Saudi. Any patient with negative MS were excluded. This study was started at March 2016 and finished at March 2017. Data was collected by medical students from Laluna private medical center (Jeddah, Saudi). sIgE RAST inhalant in vitro blood test results were collected in excel sheet and result tables was extracted.

Panel of this test is from (MEDIWISS Analytic GmbH company), composed of 30 inhalant allergens. These inhalants were considered as a common allergens in Saudi and the gulf region. Each inhalant allergen is separate with its results and severity class. This is in compare to other companies

which give results as a mix of inhalant allergens like Phadia company. Separate allergens are better because of avoidance and immunotherapy.

Severity classes are from zero to 6. Zero class mean's negative sensitization. One to six classes are positive sensitizations and divided as follow: mild for 1 and 2, moderate for 3 and 4, sever for 5 and 6. This division can give an idea about the sensitization severity level. However, RAST results have to be related to clinical history. Positive sensitization without clinical symptoms is atopy and don't need an avoidance advice. Clinical allergy mean's that both are positive and need to be treated as a clinical allergic disease.

Excel sheet were divided into several columns. First: demographic data like age, sex and file numbers. Second: allergic diseases like allergic rhinitis, sinusitis, asthma, atopic dermatitis, food allergy, urticaria and angioedema. Third: common molds in Saudi like aspergillus (fumigatus, niger and fulvus), cladosporium (herbarum), alternaria, fusarium and candida. Fourth: other inhalant allergens like: house dust mites, insects, animals, birds and pollens (trees, weed and grass).

### 3. Result

Total patients sample with positive MS is 51. Gender distribution is a little bit in favor of females 28 (55%), males 23 (45%) (Table 1).

**Table 1.** Sex distribution of positive MSs.

	Male	Female	Total sample
Patients with positive MS	23	28	51
%	45%	55%	100%

Frequency of positive MSs in descending order are: aspergillus fumigatus 35 (69%), alternaria 32 (63%), cladosporium 29 (57%), candida 13 (25%) and penicillium 9 (18%). Aspergillus niger, aspergillus fulvus and fusarium are rare MSs (Table 2).

**Table 2.** Frequency of positive MSs/total sample.

	Frequency of positive MSs	Percentage per (51 sample)
Aspergillus Fumigatus	35	69 %
Alternaria	32	63 %
Cladosporium	29	57 %
Candida	13	25 %
Penicillium	9	18 %

MSs severity is generally mild. Class 2 sensitizations: Alternaria, cladosporium and fusarium. Classes between 1 and 2: candida 1.8, aspergillus fumigatus 1.7, penicillium 1.4. class 1 sensitizations: aspergillus niger and fulvus (Table 3).

**Table 3.** Average MS class severity levels.

	Class
Alternaria	2
Cladosporium	2
Fusarium	2
Candida	1.8
Aspergillus fumigatus	1.7
Penicillium	1.4
Aspergillus niger	1
Aspergillus fulvus	1

Allergic diseases are the most common association with MSs. Allergic respiratory airway diseases are the most common association with MS: allergic rhinitis, allergic fungal sinusitis 23 (45%), asthma 14 (27%). Allergic skin diseases comes in the next order: urticaria, angioedema 11 (22%), AD 10 (20%). Other allergic diseases are rarely associated with MS: food allergy 5 (10%), drug allergy 4 (6%), allergic conjunctivitis (4%) (Table 4).

**Table 4.** Frequency of association of allergic diseases with MS.

	Frequency of association of allergic diseases with MS	Percentage per (51 sample)
AR, sinusitis, AFS	23	45
Asthma	14	27
Urticaria	11	22
AD	10	20
Food allergy	5	10
Drug allergies	4	8
Allergic conjunctivitis	2	4

#### 4. Discussion

Mold allergy prevalence is high amongst inhalant allergies. Inhalants in vitro sIgE survey to allergic patients is one way to discover this fact. In USA, this survey have shown that 44% of allergic patients were allergic to molds. These molds are: alternaria, helminthosporium, aspergillus, candida and curvularia. This mean that allergists have to educate health professionals more about mold allergies. unfortunately, allergy specialty is rare and most of mold allergies diagnosis is missed [5].

Early life exposure to mold is a risk factor to allergic diseases. It was shown in (Hahm MI et al., 2016) study that early exposure to mold allergens is a major risk factor to allergic rhinitis in Asian kids. This condition necessitate that health professionals have to ask all allergic child mothers about any source of mold exposure. Indoor common mold sources are: ignored air conditioning without wash for longtime, leaky roofs, store rooms and any mold inside homes which can be seen by human eyes. Other risk factors to allergic rhinitis are: allergic history during pregnancy, high level total IgE [6].

In Europe, *Alternaria alternata* is considered as the most common fungus which can trigger allergic diseases. However, this study show that alternaria is the second common fungus after *aspergillus fumigatus* in Jeddah, Saudi. This mean that alternaria is still a main trigger of allergies worldwide. Alt a 1 protein part of alternaria is the major triggering epitope. Additionally, alternaria complex structure may cause multiple sensitizations. That's why, it was noted that allergic diseases caused by this fungus are more severe than other's [7].

Mold allergy is different from other inhalant allergies. First: mold allergy patients are more prone to asthma specially if the triggering mold is *alternaria alternata*. Second: asthma due to mold allergy is more sever, more exacerbations, more inhaled steroid use, more hospitalizations and less controlled asthma. That's why all inhalant allergy test panels have to include the common fungi in the local are as they are a common triggers of allergy [8].

Allergic rhinitis morbidity due to mold allergy is more severe than other aeroallergens. First: nasal symptoms are more sever (nasal congestion and blockage). Second: mold allergic rhinitis patients are more prone to asthma. Third: mold allergy patients have higher level of nasal fractional exhaled nitric oxide (FeNO). Fourth: these patients are more prone to allergic fungal sinusitis than others. So, any allergic (rhinitis, sinusitis) which is chronic, sever and weakly responsive to treatment we should consider mold allergy [9].

Mold allergy can be diagnosed by either: in vivo SPT test or in vitro blood test. It was shown that in vivo SPT is more sensitive than in vitro blood test in mold allergy diagnosis and SPT is considered as the golden standard diagnosis. Unfortunately, SPT solutions for common molds aren't always available in compare to in vitro blood test which have wide variety of mold allergen types. Which allergy test to use? It depends on each case but for summary: in vivo SPT is more sensitive while in vitro blood test is more practical [10].

Role of allergy immunotherapy (AIT) in mold allergy is still under research, however the current evidence is that AIT can improve allergic RT diseases like asthma and allergic rhinitis. AIT to mold aeroallergens is the immunotherapy which is available currently. This type of fungi can't live in respiratory tract (*alternaria*, *cladosporium*). Unfortunately, we don't have AIT to molds which can live in respiratory tract (*candida*, *aspergillus* and *penicillium*). However, the main AIT practical point for mold aeroallergens is that each mold have to be alone in each AIT because mold proteases can't be mixed together [11].

## 5. Conclusion

Unfortunately, mold allergic diseases are underdiagnosed inspite of its high prevalence. In Jeddah, Saudi, the commonest MSs are: *aspergillus fumigatus*, *alternaria* followed by *cladosporium*, *candida*. Most common diseases associated with MSs are: respiratory allergic diseases (allergic rhinitis, allergic fungal sinusitis, asthma) followed by skin allergic diseases (urticaria, angioedema and AD). MSs are of mild class severity, however clinical allergic diseases due to mold are more sever. This mean that sensitization class level don't reflect the clinical severity.

## Conflict of interest

No conflict of interest needs to declare.

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