



Sensitization to aeroallergens in an atopic population of Algiers (Algeria)

S. Lahiani · K. Djenouhat · F. Benaissa · I. Bitam · H. Sadi-Guettaf

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Abstract Aeroallergen sensitization is increasing worldwide. The optimal management of allergic disease requires the identification of the allergic sensitivities of the patient. The aim of the present study was to evaluate the profile of specific IgE reactivity of patients with clinically suspected allergic diseases seeking medical care in Algiers. The prevalence of 29 aeroallergens' sensitization was investigated by using in vitro test *Allergy screen*, for 1461 patients diagnostics allergic at *Mustapha Pasha* Hospital in Algiers (Algeria), from the period between January 2016 and June 2019. Patients were categorized according to the demographic and clinical aspects. Statistical tests were applied to differentiate between age, gender, season of maximum attack and the polysensitization. The prevalence of sIgE was 55% (807/1461). The age groups of 16–40 years and ≤ 16 were more sensitized than that of ≥ 40 years. House dust mites, namely *Dermatophagoides pteronyssinus*

and *Dermatophagoides farinae*, elicited most prevalent sIgE results (29.22% (427) and 25.05% (366), respectively), followed by *Alternaria alternata* and *Cladosporium herbarum* (17.72% (259) and 12.93% (189), respectively). Allergic rhinitis, urticaria, conjunctivitis and asthma were recorded as the common symptoms. Moreover, a significant correlation has been found in patients with polysensitization, especially between dust mites and molds. Following the increasing trend, house dust mite sensitization still held the dominance like in any other Mediterranean population reported earlier. Determining the allergic profile in this region will facilitate early diagnosis, management and prevention of allergic diseases.

Keywords Aeroallergens · Sensitization · Diagnosis · Allergy · Algiers

S. Lahiani (✉) · F. Benaissa · H. Sadi-Guettaf
Department of Biology, Faculty of Science, University of M'hamed Bougara Boumerdes, Boumerdes, Algeria
e-mail: sadjialahiani@yahoo.fr; s.lahiani@univ-boumerdes.dz

K. Djenouhat
Faculty of Medicine, University of Algiers, Algiers, Algeria

I. Bitam
Superior Graduate School of Food Science and Agri-Food Industries, Algiers, Algeria

1 Introduction

Allergic diseases are very common and alter the quality of life of patients, and the prevalence of asthma, allergic rhinitis, conjunctivitis and atopic eczema symptoms is notable between different centers throughout the world (Beasley 1998).

Asthma and upper respiratory tract disorders pose a significant socioeconomic burden as a result of a reduced quality of life. The most recent and revised

estimate on the global epidemiology of atopic asthma under the Global Burden of Disease project suggested that around 334 million people worldwide are asthma sufferers (Asher and Pearce 2014). In addition, according to earlier reports, 1–10% of adults are estimated to have asthma and 10–32% are estimated to have allergic rhinitis (Pawankar et al. 2008).

Among the symptoms related to allergic manifestations, asthma is the most severe symptom. In fact, approximately 50% of the asthma sufferers are from developing countries (Compalati et al. 2007).

In Algeria, few studies of the prevalence of allergic diseases in the general population have been published; in fact, some regional data indicate that major causative agents implicated are pollen grains, fungal spores and house dust mites (Meharzi et al. 2017).

Indeed, many studies have shown that the distribution of aeroallergens and pattern of exposure significantly differs in different countries and even different regions within a country (Oncham et al. 2018). However, the spectrum of aeroallergen sensitization is diverse and affected by several factors, and climate change is one of the most important factors (D'Amato et al. 2010).

And because weather in the north of Algeria is hot and humid, it results in a high prevalence of allergic asthma (Lahiani and Galleni 2017). Despite having such a serious health risk, the clinical as well as basic research on “Molecular Allergology” in Algeria has never been given the deserved interest. This has rendered the accurate diagnosis and therapeutic intervention of allergy quite difficult in this country. While in Western countries the recombinant allergen-based advanced diagnostic tools such as Immuno-CAP (Westwood et al. 2016) and allergen microarray (Lupinek et al. 2016) have revolutionized molecular diagnosis, Algeria is still behind, relying on the century-old skin prick test using crude allergen extracts in most parts of Algeria. Moreover, it is clear that the allergen extracts prepared from crude natural extracts of allergenic source are not standardized. Apart from diagnosis, Western countries have witnessed a quantum leap in the therapeutic measures of allergy within the last few decades. These therapeutic measures refer to immunotherapy with hypoallergenic variants, allergen-derived peptides/fragments and genetically engineered allergen derivatives (Lupinek et al. 2016). On the other hand, such advanced immunotherapeutic tools are absent in Algeria, and

the first step for this approach is the precise determination of the allergenic profile. More interestingly, the test result can be used as index for diagnosis and to draft a therapeutic strategy (Linhart et al. 2019; Herzum et al. 2005). So, it is essential to identify the suspected aeroallergen for an atopic individual by using serum-specific immunoglobulin E (sIgE) assay. Thus, the objective of this study was to study the prevalence and trends of allergic sensitivity to common allergens among atopic patients in Algiers (Algeria), from January 2016 to June 2019, and to establish clinical and epidemiological characteristics for this population.

2 Methods

2.1 Patients

A hospital-based retrospective study was carried out in the Department of Immunology and Allergology at University Hospital of *Mustapha Pasha* in Algiers (Algeria). A total of 1461 patients (839 female and 622 males), 1 month to 92 years of age (median age 28.0 years) with doctor-diagnosed atopic symptoms (namely allergic rhinitis, bronchial asthma and atopic dermatitis), were included in this study. Patients were categorized into three age groups: ≤ 16 years (median age 11.0 years), 16–40 years (median age 26.5 years) and ≥ 40 years (median age 47.0 years). And for clinical and epidemiological characteristics, patients are accompanied by a questionnaire completed by their allergist doctor; the questionnaire includes the record of the personal history, namely age, sex, time and season of maximum attack.

2.2 Specific IgE level to aeroallergen

Our hospital is the main health center for the north of Algeria, covering the needs of over 3 million people. In this study, patients underwent specific IgE level by using serum allergen-specific immunoglobulin E (sIgE) assay and by the allergy testing panel according to the manufacturer's manual of this panel with extracts of mite, animal dander, molds and pollens.

Patients were subjected to sIgE assay for a panel covering 29 aeroallergen extracts including 17 types of pollens, namely: cypress (T23), olive tree (T9), mimosa (T19), eucalyptus (T18), date tree (T214), ash

(T15), oak (T7), plane tree (T11), grasses (GX7), cereal grasses (gcerTUN), pellitory (W21), wormwood (W6), ambrosia (W1), *Franseria acanthicarpa* (W3), plantain (W9), lamb's-quarters (W10) and daisy (W7), five types of molds, namely *Aspergillus fumigatus* (M3), *Alternaria alternata* (M6), *Cladosporium herbarum* (M2), *Candida albicans* (M5), *Penicillium chrysogenum* (M1), and two types of house dust mites, namely *Dermatophagoides pteronyssinus* (D1) and *Dermatophagoides farina* (D2).

2.3 Statistical analysis

The population characteristics were described by counts and percentages which are categorical variables, and presented by means and standard deviation for age which is a continuous variable.

One-way ANOVA has been used to compare the numbers of patients of different age groups and has been followed by the post hoc Tukey's test to find out which specific groups' means are different. Responses to different antigenic extracts in both male and female patients are tested by a paired *t* test. Pearson's test has been applied to show correlations between different studied allergens.

All statistical tests were performed using R statistical software version 3.3 (R Core Team 2016). All *p* values were two-tailed. *p* < 0.05 was considered statistically significant.

3 Results

3.1 Demographic and clinical features revealed through specific IgE test

The patients' details are given in Table 1. The majority of the patients (900; 61.60%) were adults. The number of patients diagnosed with rhinitis was 564 (34%), urticaria was 272 (17%), conjunctivitis was 258 (16%) and asthma was 199 (12%), and other symptoms were also found with a lower percentage. The prevalence in our patients, determined by specific IgE assay, was 55.23% (807 patients), and 74% represented a respiratory allergy.

Table 1 Clinical and epidemiological characteristics of the study population

Characteristics	Sensitive patients, <i>n</i> (%)
Sex	
Male	622 (42.57%)
Female	839 (57.42%)
Age	
≤ 16 years	561 (38.4%)
≥ 16 years	900 (61.6%)
Symptoms	
Rhinitis	564 (38.6%)
Urticaria	272 (18.61%)
Conjunctivitis	258 (16%)
Asthma	199 (12%)
Bronchitis	146 (9%)
Atopic dermatitis	110 (7%)
Digestive symptoms	54 (3%)

3.2 Sensitization profile of the aeroallergens detected by sIgE essay

In the present study, we investigated the sensitizing potential of some common airborne pollens, animal dander, molds and house dust mites (HDM) among the local population. In general, test results indicate that women and young people are the most affected, HDM is the main cause of allergic disease in our population, the two most sensitized age groups are ≤ 16 years and 16–40 years, followed by fungi, and the season of maximum attack is the spring for all allergens tested and winter for animal dander (Table 2).

Despite that allergy to pollen is important, the sensitivity analysis for each allergen revealed that among pollen, cypress, olive tree and marguerite were comparatively less frequent elicitors of sIgE tests (7–3% reactivity). Other tested pollen extracts indicated low to negligible results in less than 1% of the population (Fig. 1).

Among the molds, *Alternaria alternata* (17.72%) was the most sensitive, followed by *Cladosporium herbarum* (12.93%), *Aspergillus fumigatus* (7.8%) and *Candida albicans* (2.25%). And for animal dander tested extract, we found similar percentage for the cat and the dog (3.69% and 3.9%), respectively, and a relatively low sensitivity for the horse (1.3%).

Table 2 The aeroallergen distribution according to age, sex and seasons; we grouped allergenic sources into four categories: the house dust mite (HDM) represented by two species D1 and D2; pollen regroups species T23, T9, T19, T18, T214, T15, T7, T11, GX7, gcerTUN, W21, W6, W1, W3, W9, W10 and W7; animal dander comprised cat, dog and horse; and finally fungi formed by the five species of molds: M3, M6, M2, M5 and M1

	HDM	Pollen	Animaldander	Fungi
Age				
< 16 years	374	223	79	217
16–40 years	328	201	45	301
> 40 years	91	84	7	110
Sex				
Female	459	284	74	387
Male	334	224	57	241
Season				
Spring	315	191	29	354
Summer	70	39	24	63
Winter	143	46	45	71
Autumn	265	232	33	140

Lastly, house dust mite extract was found to be the most prevalent aeroallergen for the population studied. *Dermatophagoides pteronyssinus* and *D. farinae* showed 29.22% and 25.05% sIgE-positive results, respectively (Fig. 1).

In addition, a high serum level of specific IgE against HDM was observed, in comparison with other allergens tested (unpublished data), and it might also be related to the high exposure to indoor allergens in the Algiers population.

3.3 Categorization of the sensitive patients according to age

In the next step, the distribution of the number of patients among different age groups (≤ 16 years, 16–40 years and ≥ 40 years) was tested by one-way ANOVA. Significant differences were observed among age groups (Fig. 2).

Sensitization to all allergens was significantly different (p value = 0.02) between the age groups of ≤ 16 and ≥ 40 years and also between the age groups of ≥ 40 and 16–40 years, while there is no significant difference (p value = 0.9) between the age groups of ≤ 16 and 16–40 years.

3.4 Mono- and polysensitization

Based on the previous results, we observe that some allergens are remarkably more allergenic than others. And out of 1461 patients, 807 (55.23%) were found to be sensitized to at least one of the 29 aeroallergen extracts tested.

For this, we will search for the number of positivities for 18 allergens most incriminate in monosensitivity and polysensitivity. The results obtained are represented in Table 3.

Very high and significant correlations were found between D1 and D2, M2, M3 and M6. Also high and significant correlations were found between M6 and D2, W1, W9, W10 and W7. Very low correlations were obtained between E1 and other allergens with mainly E7 ($r = 0$).

4 Discussion

The most common cause for the development of allergic sensitization in humans depends on the degree of the patients' exposure to allergens. Detection of the sensitizing aeroallergens is of great importance in diagnosis and management of the disorder.

In this study, we found that 55% of our patients are sensitive to at least one allergen; this prevalence is relatively high compared with that of other studies (Chang et al. 2013; Sun et al. 2019). But, for negative patients, the result can be explained by three hypotheses: (1) the diagnostic method is usually based on the clinical signs; clinical symptoms of allergic diseases are complex; some symptoms are obvious; and allergen test is very important to avoid misdiagnosis. (2) The allergic hypersensitivity may be classified as IgE-mediated or not (Johansson et al. 2001). And (3) the specific IgE level may be different before and after allergic reactions and the results of allergy testing panel also have differences in different stages of the disease. Generally, in serious allergic reaction, the sIgE is all consumed and false-negative result may be obtained (Eigenmann 2005). Therefore, the serum-specific IgE test is a very important test for identifying the allergen involved, and a complete analysis of the patient's clinical symptoms and history of the disease should also be performed to clarify the diagnostic.

Furthermore, the high rate of negative IgE tests may also be due to the fact that our population is sensitive

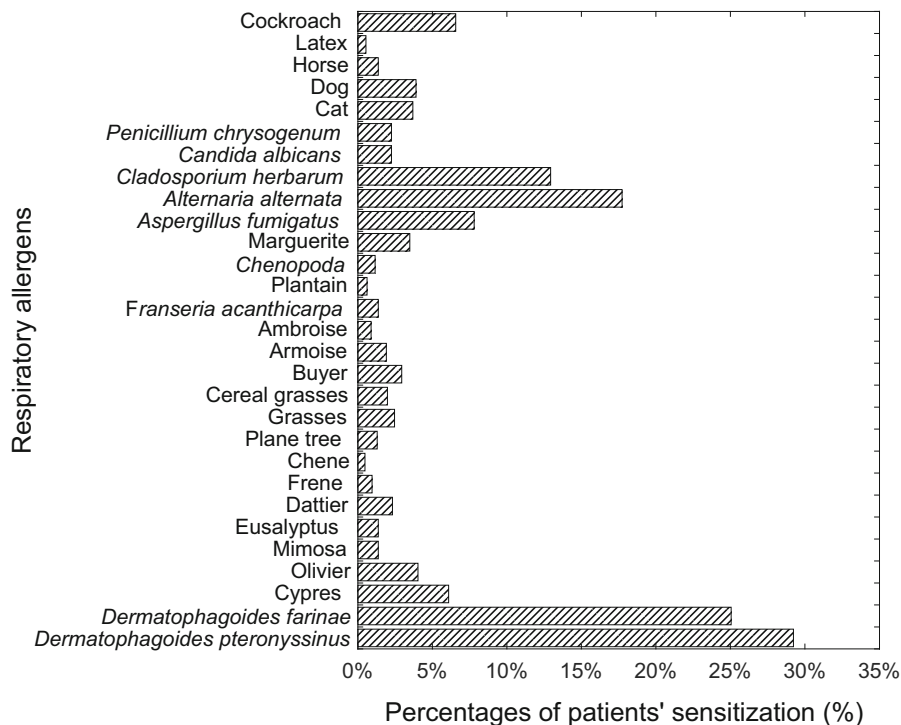


Fig. 1 Percentage of patients' sensitization to different respiratory allergens tested (*Dermatophagoides pteronyssinus* (D1), *Dermatophagoides farinae* (D2), cypress (T23), olive tree (T9), mimosa (T19), eucalyptus (T18), date tree (T214), ash tree (T15), oak tree (T7), plane tree (T11), Grasses (GX7), Cereal grasses (gcerTUN), pellitory (W21), wormwood (W6),

ambrosia (W1), *Franseria acanthicarpa* (W3), plantain (W9), lamb's-quarters (W10), daisy (W7), *Aspergillus fumigatus* (M3), *Alternaria alternata* (M6), *Cladosporium herbarum* (M2), *Candida albicans* (M5), *Penicillium chrysogenum* (M1), cat (E1), dog (E5), horse (E3), latex (K82) and cockroach (I6))

to other allergenic sources that are not included in our diagnostic panel.

This study shows a similar prevalence of persistent rhinitis and conjunctivitis in our series than in the population of the Mediterranean countries (Ait-Khaled et al. 2007) and, rather surprisingly, that 74% of atopics patients have a respiratory allergy against 26% with food allergy (unpublished data), and it is probable that this difference is due to the fact that the specific IgE assay was carried out in different stages of the disease as indicated above.

In this study, we described the prevalence of respiratory allergies in Algiers, and our results show that house dust mite species and fungi are the major allergenic sources; these data have been confirmed by epidemiological studies of exposure to these species and the development of allergic asthma (Calderón et al. 2015; Twaroch et al. 2015). It has recently been reported that increasing urbanization can have a direct negative effect on the prevalence of allergic disease by

promoting the growth of these microorganisms (Allen and Koplin 2019; Botha et al. 2019). In addition, these authors have suggested that exposure to these microbes activates immunoregulatory mechanisms that reduce the risk of inappropriate immune disorders.

In addition, high exposure to perennial allergens as a consequence of the meteorological conditions in the subtropical region, especially in the north of Africa, has been reported (Acevedo et al. 2019; Reinmuth-Selzle et al. 2017). These conditions promote the development of mites, thus explaining the high frequency of positive results with HDM allergy tests observed in our study. Similarly, the high serum levels of specific IgE against HDM in comparison with other allergens tested might also be related to the high exposure to indoor allergens of the north African countries, as previously suggested (El Fekih et al. 2014).

The three arthropods tested: *Dermatophagoides pteronyssinus* (D1), *Dermatophagoides farinae* (D2)

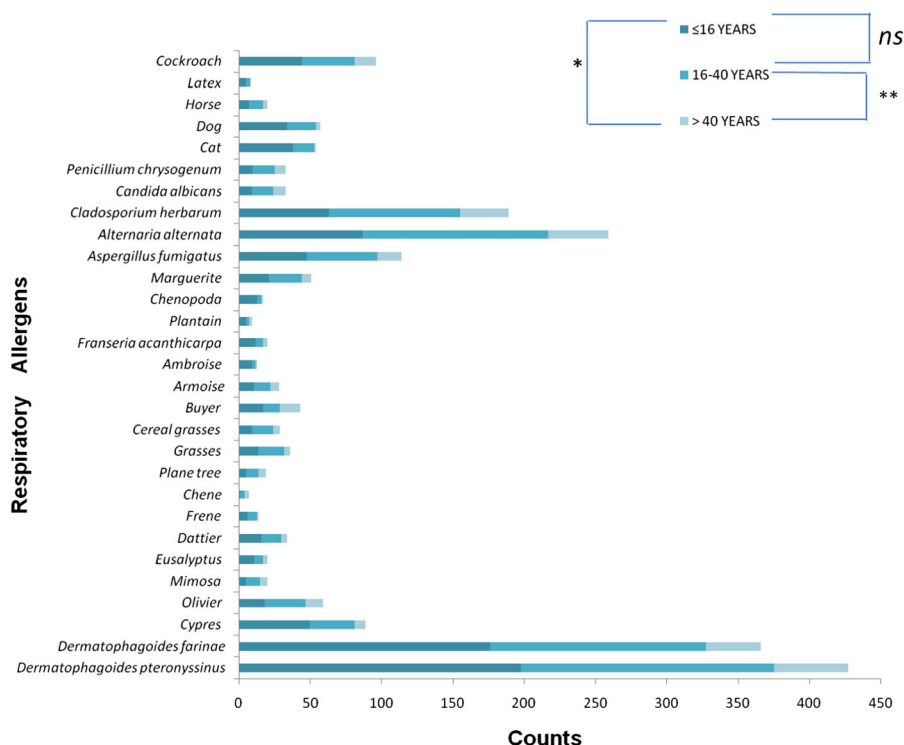


Fig. 2 The distribution of respiratory allergens by age group. We analyzed the allergenic profile of our patients according to three age groups; the allergenic sources show significant variations depending on the age of patients (*Dermatophagoides pteronyssinus* (D1), *Dermatophagoides farinae* (D2), cypress (T23), olive tree (T9), mimosa (T19), eucalyptus (T18), date tree (T214), ash (T15), oak (T7), plane tree (T11), grasses (GX7),

cereal grasses (gcerTUN), pellitory (W21), wormwood (W6), ambrosia (W1), *Franseria acanthicarpa* (W3), plantain (W9), lamb's-quarters (W10), daisy (W7), *Aspergillus fumigatus* (M3), *Alternaria alternata* (M6), *Cladosporium herbarum* (M2), *Candida albicans* (M5), *Penicillium chrysogenum* (M1), cat (E1), dog (E5), horse (E3), latex (K82) and cockroach (I6))

and *Blattella germanica* (I6), were the most common aeroallergens, followed by various types of fungal spores, when pollens and animal hair are the least incriminated, whereas pollens were proven as the highest sensitizing aeroallergens among Europeans (Heinzerling et al. 2013), and mold sensitization is mostly found in the tropical countries of Asia like Singapore and Malaysia (Tham et al. 2016).

It has been reported that climate change is influencing plant physiology and can influence intensity of pollination, the fruiting patterns and sporulation of fungi, as well as the allergen content and allergenicity of pollen grains, fungal spores and other aeroallergen particles (Behrendt and Becker 2001).

In our study, we found that our population is sensitive to several tree pollen allergens. So, the most incriminated species are cypress and olive tree (6.09 and 4.04, respectively). The study conducted by Gassner et al. (2019) attests that the sensitization to

pollen tree varies according to the pollen count and may be masked by pollen from other trees that flower at the same time of year. In the Mediterranean countries, cypress is the most important pollinating taxa, and it represents the half of the total pollen production (Charpin et al. 2019).

And even, the olive tree is one of the oldest cultivated plants in the Mediterranean region. Pollen from cultivated olive trees plays an important role in terms of allergy in Algeria.

However, in recent studies, the prevalence of cypress (T23) and olive tree (T9) was 18.7% and 32.5%, respectively, in Mediterranean countries (Benyounes et al. 2019).

Moreover, the sensitization to ash pollen (*Fraxinus americana* T15) (16.3%) reported by Benyounes was more frequent than to birch pollen (*Betula verrucosa* T3) (15.3%). These rates are remarkably higher than those mentioned in our study.

Table 3 Correlation between respiratory allergen: we have used Pearson's test to evaluate the correlations between different studied allergens

Allergen source	<i>r</i>	<i>p</i> value
<i>Dermatophagoides pteronyssinus</i> D1		
<i>Dermatophagoides farinae</i> D2	0.9443	<i>p</i> = .000 (***)
<i>Penicillium chrysogenum</i> M1	− 0.766	<i>p</i> = .027 (*)
<i>Cladosporium herbarum</i> M2	0.9593	<i>p</i> = .000 (***)
<i>Aspergillus fumigatus</i> M3	0.8359	<i>p</i> = .010 (**)
<i>Alternaria alternata</i> M6	0.8426	<i>p</i> = .009 (***)
<i>Dermatophagoides farinae</i> D2		
<i>Dermatophagoides pteronyssinus</i> D1	0.9443	<i>p</i> = .000 (***)
Pellitory W21	− 0.7664	<i>p</i> = .027 (*)
<i>Cladosporium herbarum</i> M2	0.9895	0 (***)
<i>Aspergillus fumigatus</i> M3	0.9187	<i>p</i> = .001 (***)
Ambrosia W1		
Plantain W9	0.8974	<i>p</i> = .002 (**)
Lamb's-quarters W10	0.8967	<i>p</i> = .003 (**)
<i>Penicillium chrysogenum</i> M1	0.7936	<i>p</i> = .019 (*)
<i>Alternaria alternata</i> M6	− 0.8773	<i>p</i> = .004 (**)
<i>Franseria acanthicarpa</i> W3		
<i>Candida albicans</i> M5	− 0.7071	<i>p</i> = .05 0(*)
Plantain W9		
Ambrosia W1	0.8974	<i>p</i> = .002 (**)
Lamb's-quarters W10	0.9271	<i>p</i> = .001 (***)
Lamb's-quarters W10		
Wormwood M6	− 0.8405	0(***)
Daisy W7		
<i>Alternaria alternata</i> M6	− 0.8122	<i>p</i> = .014 (*)
Dog E5		
Horse E3	0.8556	<i>p</i> = .007(**)
<i>Aspergillus fumigatus</i> M3		
<i>Cladosporium herbarum</i> M2	0.9047	<i>p</i> = .002(**)

Statistical tests were performed using R statistical software (R Core Team 2016). *p* values *p* < 0.05 was considered statistically significant

It is important to note that in urban areas, nonindigenous varieties and species of trees that also release pollen with a high risk of causing allergies are most commonly planted. Indeed, for our population allergenic sources such as ash, oak, plane tree, grasses, grain Gramineaceous, parietal, sagebrush, Artemisia, ambrosia, *Franseria acanthicarpa*, plantain and lamb's-quarters reveal low to negligible results in less than 1% of the population, and it must be due to the fact that these plants are not grown in large cities like Algiers and therefore the population studied is not exposing to these allergenic sources.

In our study, we found that *A. alternata* is the top sensitizer. Furthermore, allergenic potentials of common molds have been studied from Algeria, and

Meharzi et al. reported that principal molds sensitive allergens from Algeria are: *Cladosporium*, *Penicillium*, *Alternaria*, *Aspergillus*, *Aureobasidium*, *Mucor*, *Scytalidium*, *Paecilomyces* and *Fusarium* (Meharzi et al. 2017). Hence, it is important to include those species in the diagnostic panel.

Prominent airborne fungi, such as *Cladosporium herbarum*, *Alternaria alternata* and *Aspergillus fumigatus*, have been found to release higher amounts of allergens after germination under humid conditions (Green et al. 2003), and certain allergens are expressed only following germination (Sporik et al. 1993).

A recent study carried out in the Maghreb region shows that sensitivity to *Alternaria* was 24.3% and

that this awareness increases with age ($p < 0.01$) (Amon-Tanoh-Dick et al. 2018).

In our study, the prevalence was 17.72%. In the literature, the prevalence of *Alternaria* sensitization ranges from 7.5 to 17% in the general population in some parts of Australia or the USA, while it rarely exceeds 5–7% in Europe (Simon-Nobbe et al. 2008). This allergen produces frequent sensitization, according to the regions of the world and the populations studied, and prevalence rates vary from 3 to 12% in the general population and from 13 to 39.4% in atopic subjects (Simon-Nobbe et al. 2008).

It has been reported that atopic patients tend to become sensitized to local allergens prominent in their living environments, but the allergenicity of aeroallergens in different age groups varies in different parts of the world. Overall, we also found young adults (≤ 16 years and 16–40 years of age) were more sensitized than the age group ≥ 40 years. This is probably atopic March being the main reason for discrepancy between children's allergic sensitization prevalence and that of the adults (Arshad et al. 2001).

In this study, we found that the seasonal pattern of attacks showed that most patients suffered in spring and autumn. In most cases, inhalation of house dust mite allergens and molds were the perennial allergic causes, while seasonal allergies were mainly caused by pollen. Hence, many studies found that summer and winter are the seasons of maximum attack caused by the same allergens (Ghosh et al. 2017).

Almost all of our patients have sensitivity to more than two allergens, and we found a very significant correlation between some allergens, which can be explained in part by the co-existence of several species and the presence of cross-reactivity between these allergens (Yamamoto et al. 2019; Sidenius et al. 2001).

Allergy is significantly affected by climate change, and most studies on allergens and climate change focus on HDM, pollens and molds. Our study showed that HDM sensitization was common in Algiers and highlighted the increased sensitization from younger patients. Secondly, the diagnostic panel is inadequate to the Algerian population. Better than this diagnostic method, allergists continue to rely on obsolete, less characterized and less standardized allergen extracts. The use of the recombinant allergen preparation is relatively expensive. Hence, the current objective in Algeria should be to ensure the availability of sources

of high quality of allergens and allergen extracts for locally prevalent aeroallergens which is required for the diagnosis and therapy of allergic patients.

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Authors contributions L.S., D.K. and B.I. designed the study. L.S., B.I. and D.K. contributed to the data collection. L.S. and G.H. analyzed and interpreted the data. L.S. and B.F. performed the statistical analyses and interpretation of the results. All authors read and approved the submitted manuscript.

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Compliance with ethical standards

Conflict of interest The authors have no conflict of interest to declare.

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