

INTRODUCTION

The increased prevalence of respiratory allergy is associated with the influence of genetic and environmental conditions [1]. In developing countries, this increase has recently been associated with industrialization and lifestyle changes last decades [2]. In Asia and Africa, this change has occurred alongside marked expansion of urban areas and rural exodus [3].

Rhinitis, whether associated with asthma or not, is one of the most common allergic diseases in our setting. Its prevalence worldwide is estimated to be between 10% and 30% and in Spain, around 22%. The prevalence of asthma is 4%-10% worldwide and approximately 7% in Spain [4]. According to published data, 20%-50% of patients with rhinitis in Spain also have asthma, and 30%-90% of patients with asthma have rhinitis. [5].

The statistics show that foreign-born inhabitants accounts for 5% of the world's population [6]. Both adults and children, are exposed to allergens and lifestyles that differ from those of their countries of origin, thus highlighting the implication of the environment on the development of allergic diseases [7]. Children born shortly after settling in their new country have a similar allergic profile to that of the autochthonous population [8]. Few published studies analyze the profile of sensitization to relevant respiratory allergens in specific populations, and data are contradictory. A study in Italy revealed that immigrants become sensitized to multiple allergens more frequently than the autochthonous population and are especially sensitized to local allergens [8], while a study in Spain shows that the pattern of sensitization differs between the native and the migrant populations [9].

We explored potential differences between allergic sensitization profiles in the foreign-born population living in an area of Madrid, Spain, as well as the clinical characteristics of allergic respiratory disease (rhinitis, conjunctivitis and/or asthma) according to the patient's area of origin.

METHODS

We performed a prospective, observational, descriptive study to explore allergic sensitization patterns and the clinical characteristics of allergic respiratory diseases in foreign-born patients aged >12 years who attended the outpatient Allergy clinic. They

were consecutively included between January 2017 and December 2018. Patients were classified by ethnic group (Caucasian, Arab, Black, Asian and Latino) and their area of origin (Europe, Asia, Africa, and South America). The study was approved by the local Clinical Research Ethics Committee (HULP PI-2528). All patients signed an informed consent document.

Respiratory allergy was diagnosed using a standard work-up for allergic diseases (rhinitis with or without asthma), according to the updated ARIA guidelines for rhinitis [10] and the GINA guidelines for asthma [11]. We included demographic factors, comorbidities, allergic background and clinical reports. A detailed physical examination was also performed. The quality of life of patients with rhinoconjunctivitis was assessed based on ESRINT-15 [scores from between 0 (no limitation) to 6 (maximum limitation)] [12]. Control of asthma was assessed using the self-reported Asthma Control Test (ACT) score ranging from 5 (poor control of asthma) to 25 (complete control of asthma) [13].

Skin prick tests were performed with a panel of common aeroallergens. Histamine (10 mg/mL) was used as a positive control, and 0.9% saline solution was used as a negative control. A positive result was defined as a wheal >3mm larger than that of the negative control. Serum specific IgE was also assessed (ImmunoCAP, ThermoFisher Scientific, Sweden), with a value > 0.35 kU/L being considered a positive result. Lung function (including spirometry and the bronchodilator test), fractional exhaled nitric oxide, and eosinophil count in peripheral blood were assessed according to usual clinical practice.

The statistical analysis was performed using SPSS Statistics 26.0 for Windows. Continuous variables were described as mean, median, interquartile range, standard deviation, and range. Discrete variables were presented as a frequency distribution, and percentages, and 95% confidence intervals were calculated where necessary. Comparisons were made using 2-tailed tests, and statistical significance was set at $p < 0.05$. Discrete variables were assessed using Pearson's chi-square test or Fisher's exact test; continuous variables were assessed using the *t* test for independent samples.

RESULTS.

Data were collected from 150 foreign-born patients (73.3% female and 26.7% male) who consulted at the Allergy Department of Hospital Universitario La Paz, Madrid, Spain, with a diagnosis of respiratory allergy, between January 2017 and December 2018. Demographic variables are shown in table 1. Mean age was 38.38 years. The mean time

to onset allergic rhinitis/asthma symptoms after immigration was 8.47 ± 7.7 years. Significant differences ($p=0.007$) were observed between ethnic groups, with values ranging from 6.25 years in Caucasian to 13.42 years in Asian. No significant differences were recorded when the time to onset of respiratory symptoms was assessed according to area of origin. The mean time to development of rhinitis and conjunctivitis was 9 ± 6.8 years. The mean time to development of asthma was 7.73 ± 9 years.

Clinical characteristics are presented in table 2. Surprisingly we found that 17.3% of patients had only allergic asthma without rhinitis, in contrast with the 3.2% reported in another Spanish series [5], while 48.7% had only rhinitis and conjunctivitis. Statistically significant differences in forced vital capacity were found according to the area of origin ($p=0.008$), with results ranging from 67% in patients from Africa to 100% in patients from Europe.

Sensitization against allergens is reported in table 3. Statistical differences were found for grass pollen ($p=0.005$), *Cupressus arizonica* ($p=0.032$), and *Olea europaea* ($p=0.049$). Sensitization to grass pollen was more common among patients from South America, and sensitization to *C. arizonica* and *O. europaea* were more common among patients from Asia. According to the area of origin, statistically significant differences were found regarding levels of specific IgE to *C. arizonica* ($p=0.026$) with the highest levels in patients from Asia (mean 24.261 U/I). Specific IgE levels differed between ethnic groups for *Platanus acerifolia* ($p=0.023$), with lower levels in Caucasian patients (mean 1.88 kU/L). No significant differences between ethnic groups or area of origin were detected in other variables, such as comorbidities, allergic background, ESRINT and ACT scores, and eosinophil count in peripheral blood.

DISCUSSION

As of January 2018, foreign-born residents accounted for 13.4% of the population [893,276 people; (52.16% women and 47.84% men)] of the Community of Madrid. Mean age was 34.5 years. By continent, 41.65% were from Europe (more than a half, from Eastern Europe), 12.63% were from Africa (mainly Morocco), 34.36%, were from America (mainly South America), and 11.25% were from Asia (60% from China) [14]. Many publications report a probable relationship between time to onset of allergic symptoms and demographic variables such as length of residence in a new place and age on arrival [15, 16]. These results are similar to ours in adults, who become sensitized to

the same allergens as the local population after a mean of 8.47 years, although this figure is lower in other reports (4.5 years according to Álava et al in the same region of Spain [17]). In our population, the time to onset of allergic respiratory symptoms was lower in the Caucasian group and higher in the Asian group; Domínguez-Ortega et al [9] reported this time to be lower for Latinos (possibly because of the seasonal bias).

Even though we found a statistically significant predominance of sensitization to grass pollen in patients from South America and to *C. arizonica* and *O. europaea* pollen in patients from Asia, our data show that, the allergy sensitization profile in the foreign-born population we studied was similar to that of the local population after some time living in Madrid. Previous reports on immigrant sensitization profiles show contradictory results. Domínguez-Ortega et al [9] found significant differences in the sensitization pattern of respiratory allergy in immigrants living in Madrid. Studies in Italy also report differences in the sensitization profile, with a higher risk of sensitization to grass in patients from Sub-Saharan Africa and South America and a higher risk of sensitization to house dust mites in immigrants from South Asia [8]. A relevant difference between native residents and immigrants, as well as relevant differences between immigrant themselves, was reported by Ciprandi et al [18] in Italy, with more frequent sensitization to mites in people from South America, more frequent sensitization to *Parietaria* and birch in people from North Africa and South America, and more frequent sensitization to grass in people from South America. In our study sensitization to grass pollen was the most frequent type. According to Belver et al [19], the second most common type of sensitization was to *O. europaea* pollen. These data coincide partially with ours, although sensitization to *C. arizonica* seems to be as common as sensitization to *O. europaea*. *P. acerifolia* and mites was also considerable in the present study population. Our study may be subject to bias resulting from demographic and clinical factors. Most patients were from Tetuán neighborhood of Madrid, which is near our hospital and home to, large percentage of people from South America, thus explaining differences with other series reported in the Community of Madrid. The results could be affected by other sources of bias, such as the type of patient who consults most frequently, or how people view the severity of their symptoms. However, since study data were collected prospectively over 13 months, they cover all pollination periods. Results from cross-sectional studies [9] could be affected by seasonality.

To our knowledge, ours is the first study to report specific IgE levels, which were higher for *P. acerifolia* in Latinos (10.65 kU/L vs a mean of 7.29 kU/L), lower for *P. acerifolia* in Caucasians (mean 7.29 kU/L), and higher for *C. arizonica* in patients from Asia (24.26 kU/L vs mean of 11.13). A possible explanation for this difference could be previous exposure of Asians to other Cupressaceae such as *Juniperus chinensis* in their countries of origin. The statistically significant differences in forced vital capacity according to the area of origin (100% in patients from Europe, 78% in patients from Asia, 67% in those from Africa, and 93% in those from South America), could be due in part to the reference values used [20]. Most equations used in spirometry can be applied equally to different ethnic groups, although additional data are needed from other areas (eg Indian subcontinent, Africa, and Arab, Polynesian, and Latin American countries), to improve these equations in the future [21].

There were no statistically significant differences in the prevalence of allergic asthma or rhinitis, and/or conjunctivitis between ethnic groups or according to area of origin. Surprisingly we found that 17.3% of patients had only allergic asthma without rhinitis, in contrast to other Spanish series, in which only 5.2% had allergic asthma without rhinitis [5]. Rhinitis and conjunctivitis without asthma was recorded in 48.7%. No significant differences were found in comorbidities, allergic background, ESPRINT and ACT scores and blood eosinophil count. However, our results may have been affected by the small size of some of the groups (only 11 Asian and 13 African patients). Moreover, not taking into account other factors such as socioeconomic status and occupation, might also influence the results.

To conclude, sensitization and development of symptom of allergic disease in foreign-born patients seem to be influenced by environmental factors such as length of residence in the new country and prevalence of local allergen. Foreign-born residents have the same sensitization profile as the native population. Nevertheless, we did identify differences in the sensitization profile according to ethnic group and area of origin, thus highlighting the complexity of sensitization, in which both genetics and environmental factors interact. Prospective studies with a larger sample are needed to determine whether significantly different patterns can be identified in foreign-born patients.

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