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Allergen sensitizations in southern Italy: a 5-year retrospective study in allergic respiratory patients

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Key words

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Summary

The assessment of the distribution of allergen skin test sensitizations is highly recommended for the optimal management of allergic respiratory conditions. We aimed at evaluating the distribution of allergen sensitizations in individuals with asthma and/or rhinitis in the Southern region of Italy, and at exploring whether changes in the frequency of allergen sensitizations occurred after a 5-year period. Demographic data and skin prick test sensitizations to allergens from asthmatics and/or rhinitis attending the Division of Respiratory Diseases, University of Palermo, Italy in 2005 (Phase 1) and in 2010 (Phase 2) were extrapolated and retained for analysis. A total of 2033 allergic respiratory patients were included (1002 in Phase 1 and 1031 in Phase 2). In both investigations, the most prevalent allergen sensitization was towards Parietaria; however, a significant reduction in the rate of prevalence after 5 years was recorded (from 60% to 48% of skin test positive patients, $p<0.0001$). Up to one out of two subjects showed sensitization to dust mites in both Phases. Interestingly, Cypress pollen sensitization almost doubled from Phase 1 (17%) to Phase 2 (29%; $p<0.0001$). Overall, the mean number of skin test sensitizations for each patient increased from 2.7±1.6 in Phase 1 to 3.1±1.8 in Phase 2 ($p<0.0001$). The present findings confirm the prevalent role of Parietaria sensitization in the allergic population of the Mediterranean area of Southern Italy, and document the increase of Cypress sensitization. These observations could contribute to a proper management of chronic allergic respiratory conditions in this region.

Introduction

Allergen sensitization is commonly recognized as an important risk factor for the development of asthma and rhinitis (1-9). In addition, the acute exposure to allergens towards which the subject is sensitized may be responsible for the exacerbation of upper and lower airway symptoms. Most importantly, allergen-specific immunotherapy is the only treatment that modifies the natural course of allergic respiratory diseases. Thus, the identification of the aeroallergen skin test sensitization becomes mandatory for the optimal management of allergic respiratory conditions (10). Skin prick testing with allergen extracts is recommended as first-line method to detect sensitivities to inhalant allergens. However, the nature and number of aeroallergens differ according to geographical variability, vegetation characteristics and seasonal changes, even within the same region, thus making the application of preventive and therapeutic strategies a rather difficult task (11). For these reasons, the knowledge of the pattern and distribution of aeroallergen sensitivities in a specific geographic area is a pre-requisite for the choice of the most

appropriate therapeutic approach to chronic allergic respiratory diseases.

Epidemiological studies on the distribution of pollen sensitizations throughout Italy are scarce. Because of the wide geographical variability of the Italian regions and the growing diffusion of new botanical species, the prevalence of allergic sensitizations in subjects suffering from upper and lower respiratory symptoms may largely vary. We aimed at investigating the distribution of allergen sensitizations in individuals with asthma and/or rhinitis living in the Southern region of Italy (Sicily), and at assessing whether changes in the prevalence of allergen sensitizations occurred after a 5-year period.

Materials and methods

This is a retrospective study that includes two periods of observation, with a five year interval, conducted at the Respiratory Allergy Outpatient Clinic of the Division of Respiratory Diseases, University of Palermo, Italy. Palermo is the largest city in Sicily, the Italian island located in the Mediterranean Sea with mite climate conditions. The Outpatient Clinic is accredited as reference regional centre for allergic respiratory diseases; as a consequence, the study population consisted of allergic individuals living in the wide western part of Sicily, comprising an area of 200 km^2 and a population of about 1.5 million people. The records from the allergic patients are stored in the electronic format, which allows for any information related to the clinical history to be easily accessible.

All consecutive patients with a diagnosis of current allergic asthma and/or rhinitis, and no history of specific immunotherapy were included in the study. The diagnoses of asthma and rhinitis were performed in accordance with the GINA (12) and ARIA (13) guidelines, respectively. Demographic data and skin prick test sensitizations to aeroallergens performed in subjects with documented allergic respiratory conditions in the years 2005 (Phase 1) and 2010 (Phase 2) were extrapolated from the clinical database.

The skin prick test methodology, as well as the type and quality of the allergen extracts, were identical in the two Phases. Skin prick tests were performed and interpreted according to European guidelines (14) using the 10 most common regional commercial allergen extracts (Lofarma Laboratories, Milan, Italy): *Alternaria tenuis*, *Parietaria*, *Olea europaea*, *Mix compositae*, *Mix graminacee*, *Cupressus sempervirens*, *Dermatophagoides pteronyssinus (DPT)* and *Dermatophagoides farina (DF)*, cat and dog denders. Histamine hydrochloride (10 mg/mL) and glycerol saline were used as positive and negative controls, respectively. The mean wheal size was recorded after 15 minutes and skin prick test was considered positive with a wheal size of 3-mm or greater (15). Antihistamines and corticosteroids were stopped as required before the skin test.

The local ethics committee approved the retrieval of the clinical information and their analysis. Data are reported as mean±SD. The statistical package we employed was StatView 5.0.1 (Abacus Concept, Berkeley, CA). Statistical significance was accepted at $p<0.05$.

Results

A total of 2033 allergic subjects with a diagnosis of asthma and/or rhinitis were included: 1002 individuals were evaluated from January to December 2005 (Phase 1), and 1031 subjects from January to December 2010 (Phase 2). The two populations did not differ in terms of age distribution and frequency of respiratory diseases. Subjects from Phase 1 ranged 8–77 years (mean age 34±14 yrs), and included 123 individuals with asthma (12.3%), 532 with rhinitis (53.1%), and 347 individuals with diagnosis of asthma and concomitant rhinitis (34.6%). Subjects from Phase 2 ranged 6–81 years (mean age 35±16 yrs), and included 232 individuals with asthma (22.5%), 327 individuals with rhinitis (31.7%), and 472 subjects with diagnosis of asthma and concomitant rhinitis (45.8%).

The distribution of the allergen skin test sensitizations in Phase 1 and 2 is depicted in Figures 1 and 2. In 2005, the most prevalent allergen sensitization in our allergic population was towards *Parietaria* (60% of the studied population). Up to one out of two subjects showed skin test sensitization to *D. Pteronyssimus* and *D. Farinae*. Interestingly, the prevalence of *Olea* sensitization was the third most frequent skin test positivity. After 5 years, the skin test positivity to *Parietaria* remained the most frequent allergen sensitization; however, a significant reduction in the rate of prevalence was recorded (48% in 2010, $p<0.0001$). In addition, a reduction in the prevalence of *Composita* between the two observations was observed (from 11% in 2005 to 7% in the 2010, $p=0.001$). The prevalence of *D. Farinae* slightly but significantly increased from 2005 to 2010 (50% vs. 54%, $p=0.04$), while no statistically significant change was recorded for the distribution of *D. Pteronyssimus*, *Graminacee*, *Olea* and *Alternaria* skin test positivities. The most interesting finding was the increase of Cypress pollen sensitization, which almost doubled between 2005 and 2010 (17% vs 29%, respectively;

Figure 1 - Distribution of the outdoor skin test sensitizations among the allergic population in the two observations.

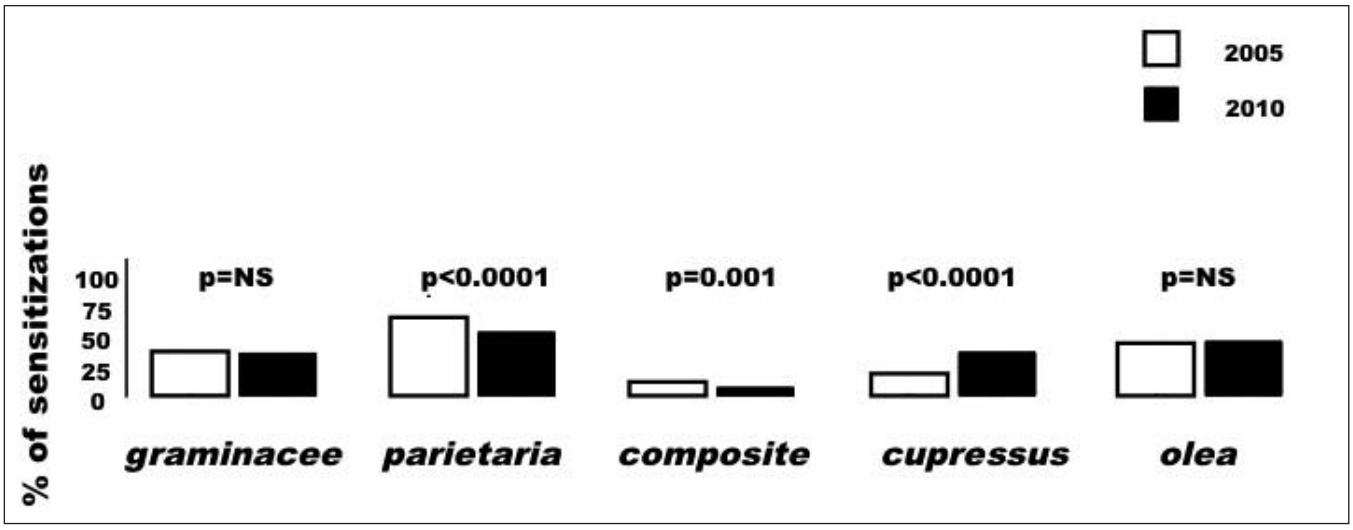
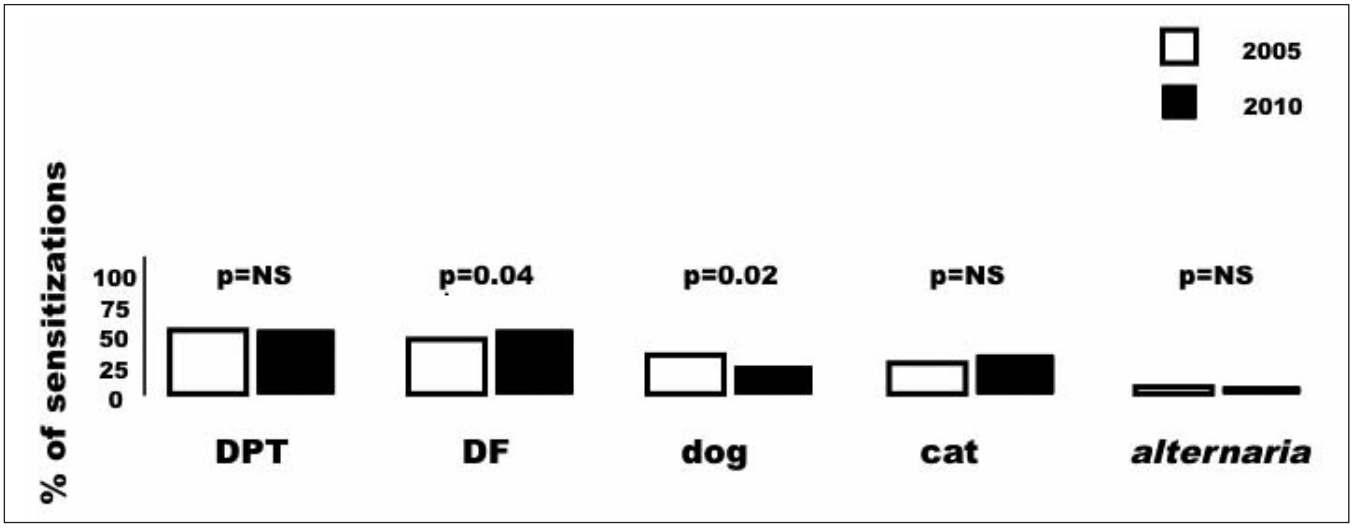


Figure 2 - Distribution of the indoor skin test sensitizations among the allergic population in the two observations.

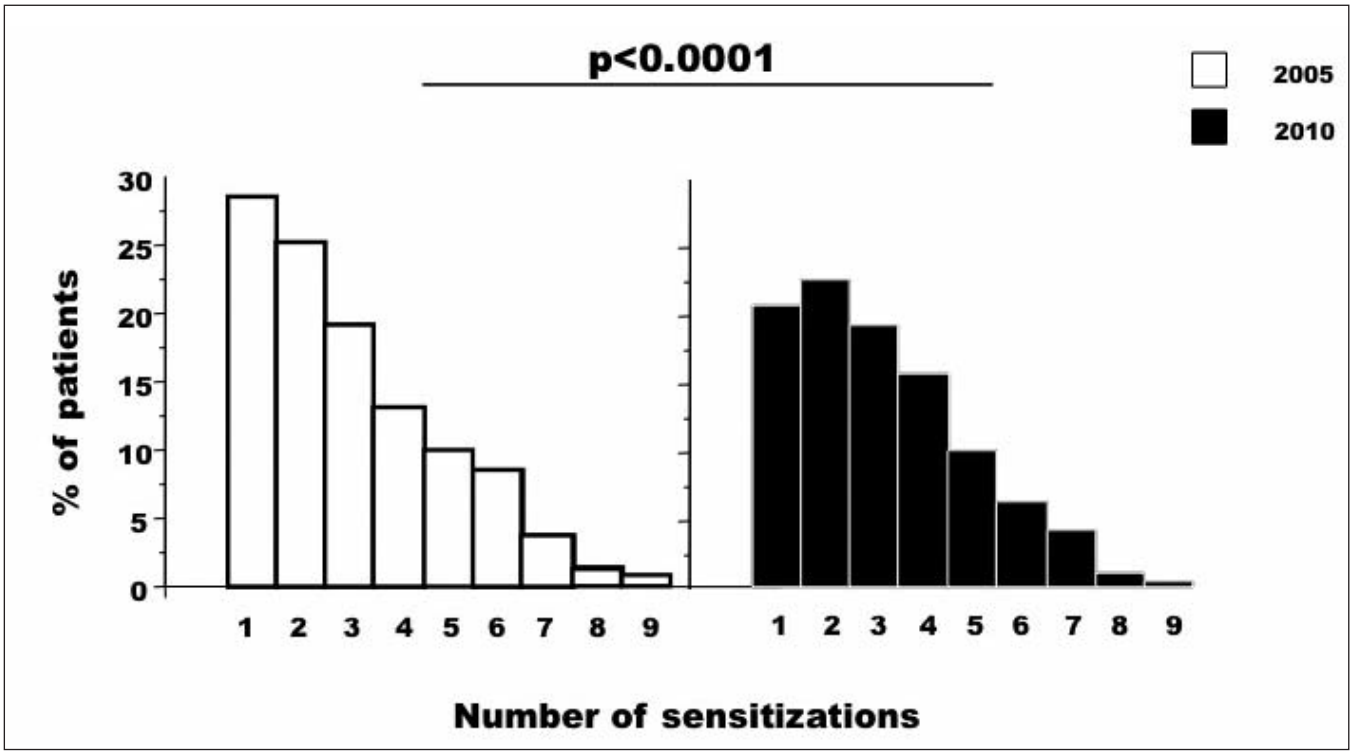


p<0.0001). Finally, the number of skin test sensitizations for each patient increased with time: the mean number of sensitizations was 2.7±1.6 in Phase 1 and 3.1±1.8 in Phase 2 (p<0.0001). Of note, the proportion of patients who were sensitized to only one allergen significantly decreased from 28.5% in Phase 1 to 20.9% in Phase 2 (p=0.003). The frequency distribution of the number of sensitizations is shown in Figure 3. In both phases, age *per se* did not affect the number of allergen sensitizations (data not shown).

Discussion

The findings from the retrospective study on allergen sensitizations in allergic asthmatics and/or rhinitics of the Southern region of Italy can be summarized as follows: 1) the most frequent allergen sensitization was towards *Parietaria*; 2) after 5 years, a significant decrease in the prevalence of *Parietaria* sensitization and a significant increase in the prevalence of Cypress sensitization were docu-

Figure 3 – Frequency distribution of the number of skin test sensitizations among the allergic population in the two observations.



mented. In addition, an increase in the number of sensitizations for each patient from the first to the second observation was recorded.

The distribution of sensitizations towards aeroallergens is believed to influence the occurrence of exacerbations of both asthma and rhinitis symptoms (16). A body of evidence demonstrates that these two diseases are strongly associated and share several risk factors (17): rhinitis frequently precedes asthma, and is associated with increased severity and health resource use in asthma. In this context, the exposure to allergens could favor the development and the exacerbation of asthma in individuals with rhinitis, and sensitization to allergen could be envisaged as the common link between the two clinical entities. On this basis, it is reasonable to assume that both the duration and the intensity of exposure to aeroallergens influence the occurrence and the severity of asthma and rhinitis (18). Therefore, the knowledge of the distribution of sensitizations to various allergens in each region is a key strategy to manage the allergic diseases of the upper and lower respiratory tract.

The duration and intensity of exposure to aeroallergens depend on geographic locations and climatic conditions. Regional variations in rates of sensitization to inhalant allergens have been shown in several large European studies such as the GA^{2}LEN network (19), the European Community Respiratory Health Survey I (ECRHS I) (20), and the International Study of Asthma and Allergies in Childhood (ISAAC) (21). However, very little is known with regard to the Southern region of Italy. The observed high proportion of *Parietaria* sensitized patients in our study is clearly related to the Sicilian climate conditions, which are characterized by hot summers and short, mild winters that favor the growth and flowering of *Parietaria* for almost the entire year. This is particularly true in the Western part of Sicily, where the medial annual temperature is relatively high (>18° C in the period 1971-2000, with average temperature of 11.5° C in the coldest month, February, and 26.6° C for the hottest month, August), as well as the average relative humidity (62.3%, with a minimum of 57% in July and maximum of 67% in December and January), while the average annual rainfall is low (855 mm). The allergic sensitization profile in our study is comparable with findings in other Mediterranean centers, as demonstrated in the GA^{2}LEN network (19) and in the

ECRHS I study (20), and in contrast with the pattern of distribution observed in Northern Europe, where the climatic and environmental conditions are considerably different (22). In particular, the observations of high rates of sensitization to *Parietaria* and Olive and the low rates of sensitization to Alternaria in the current study are comparable to those observed in the Mediterranean centers participating to the GA²LEN network. More recently, Ariano and colleagues (23) found high levels of sensitizations to *Parietaria Officinalis* in the Northern Mediterranean area of Italy among a large population of allergic respiratory patients.

Parietaria is a genus of the *Urticaceae* family, and *Parietaria officinalis* and *judaica* are the most common allergenic species of this genus. *Parietaria judaica* grows in coastal Mediterranean areas such as Spain, Southern France, Italy, Albania and Greece. This allergenic plant, which is responsible for many cases of severe pollinosis, has two very long flowering periods. Its pollen spreads at the beginning of spring and is constantly present during the spring and summer seasons, often reaching a peak level with daily mean values of more than five hundred pollen grains per cubic meter of air at the end of April and in May. A shorter pollination period is observed from the end of August to October. *Parietaria* pollen allergy is relevant also for the severity of the clinical manifestations: the pollen grain of the *Parietaria* is less than 12-15 micron in diameter and able to reach the peripheral airways, thus inducing more severe asthmatic symptoms.

As shown by Ariano et al. (23), a progressive increase in the duration of the pollen seasons for *Parietaria* (+85 days) in the observed period of 27 years in Western Liguria (Mediterranean coastal of Northern Italy) has been documented, with approximately 25% increase in the total pollen load. This was followed by a parallel increase in the proportion of patients allergic to *Parietaria*. Our results differ form those of Ariano and colleagues, although the *Parietaria* sensitization remained the most prevalent among our allergic subjects. Possible explanations for this discordance are the different time periods of observation (27 vs. 5 yrs), and the different geographical area (Northern vs. Southern Italian coastal regions).

One of the most intriguing findings of the present study is the increase of sensitization to *Cupressus sempervirens* between 2005 and 2010, which almost doubled in five years. Cypress pollination is characterized by a wide variability with very high concentrations in Mediterranean coastal areas. This pollen is the most common airborne allergen of the winter months in some Mediterranean areas. Two possible interpretations could explain the increased prevalence of Cypress sensitization. The first explanation is related to the increased use of *Cupressaceae* plants for gardening and reforestation, while the second one relies in the interaction of Cypress pollen with air pollution (24). Papa et al. (25) conducted a 4 year retrospective study, analyzing anamnestic data and skin prick tests in 1397 allergic subjects from Central Italy. The authors found a significant increase of the annual sensitization rate for skin test positivity to *Cupressus sempervirens,* from 7% in 1995 to 22 % in 1998. The Italian Association of Aerobiology supported a survey on the prevalence of aeroallergens in the Italian territory (26), showing that the prevalence of *Cupressus* sensitization in Southern regions of the country was 20%. The trend for increased prevalence of sensitization to *Cupressacea* was also described by Ariano et al. (27) in a study performed in the Ligurian coast of Italy with a 10 year-follow up. Our findings are in agreement with the above-described observations.

An additional finding is the increased number of sensitizations to allergens for each patient, with a proportional decrease of monosensitized individuals. This trend is confirmed in other longitudinal studies, but a clear interpretation has not been provided. Whether this has clinical implications requires further evaluation, although we can speculate that the efficacy of a therapeutic approach based on specific immunotherapy would be affected by the increased number of polisensitized subjects. Age per se did not seem to influence the number of allergen sensitizations. This information lends support to the concept that the allergic status should be evaluated in all individuals with respiratory symptoms in whom an allergic component is suspected, regardless of age.

The present study has the advantage of having a two-sample design, which reduces selection bias in the assessment of sensitization distribution. Moreover, the study has the merit of extending the observation to the geriatric age. We also acknowledge some limits. First, the study did not include healthy subjects: thus, the estimate of prevalence in the general population was not possible, nor a comparison between the distribution of allergen sensitizations in subject with or without respiratory diseases. Second, the seasonal pollen count was not directly available, thus not allowing to correlate the environmental levels of the tested allergen exposure in the enrolled subjects with changes on the prevalence of sensitizations. Despite these limitations, the observed changes in the distribution of al-

lergen sensitization in allergic respiratory patients are novel with regard to the Southern region of Italy.

In conclusion, the present findings confirm the prevalent role of *Parietaria* sensitization in the allergic population of the Mediterranean area of Southern Italy and document the impressive increase of Cypress sensitization. These observations may contribute to a proper management of chronic allergic respiratory conditions in this region.

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