

Allergic sensitization is age-dependently associated with rhinitis, but less so with asthma

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Background: Epidemiologic data describing the association between allergic sensitization and asthma and allergic rhinitis in adults are scarce.

Objective: To determine the prevalence and impact of specific sensitization to airborne allergens on asthma and allergic rhinitis among adults in relation to age.

Methods: A random population sample (age 21-86 years) was examined with structured interview and analysis of specific IgE to 9 common airborne allergens. Of those invited, 692 (68%) subjects participated in blood sampling. IgE level of 0.35 U/mL or more to the specific allergen was defined as a positive test result.

Results: Allergic sensitization decreased with increasing age, both in the population sample and among subjects with asthma and allergic rhinitis. In a multivariate model, sensitization to animal was significantly positively associated with asthma (odds ratio [OR], 4.80; 95% CI, 2.68-8.60), whereas sensitization to both animal (OR, 3.90; 95% CI, 2.31-6.58) and pollen (OR, 4.25; 95% CI, 2.55-7.06) was significantly associated with allergic rhinitis. The association between allergic sensitization and rhinitis was consistently strongest among the youngest age group, whereas this pattern was not found for asthma. The prevalence of allergic sensitization among patients with asthma

decreased by increasing age of asthma onset, 86% with asthma onset at age 6 y or less, 56% at age 7 to 19 years, and 26% with asthma onset at age 20 years or more.

Conclusions: Sensitization to animal was associated with asthma across all age groups; allergic rhinitis was associated with sensitization to both pollen and animal and consistently stronger among younger than among older adults. Early onset of asthma was associated with allergic sensitization among adults with asthma. (*J Allergy Clin Immunol* 2015;■■■■:■■■■-■■■■.)

Key words: Adults, allergic rhinitis, allergic sensitization, asthma, epidemiology, specific IgE

The strong association between allergic sensitization and asthma and rhinitis has been well described in children, adolescents, and young adults.¹⁻³ However, data about the association of allergic sensitization with asthma, respiratory symptoms, and rhinitis in older adults are very limited.^{4,5} Because of the increasing proportion of elderly people in the general population worldwide, a better understanding of the impact of allergic sensitization on airway diseases in older ages is important.

Studies of allergic sensitization in relation to age have consistently reported an increase in prevalence from childhood to young adulthood, whereas thereafter it decreases with age.⁶⁻⁸ Normal aging partly explains the decrease in the prevalence of allergic sensitization with increasing age among adults,⁸ and a cohort effect may contribute as well.⁹ Similarly, the prevalence of allergic rhinitis is known to increase from childhood and adolescence to young adulthood, and thereafter it decreases by increasing age.^{10,11}

Both asthma and rhinitis are heterogeneous conditions and include both sensitized and nonsensitized phenotypes.¹²⁻¹⁴ Allergic sensitization is important to consider because it affects both the persistence and the severity of allergic respiratory diseases.^{15,16} A stronger impact of allergic sensitization on rhinitis than on asthma has been hypothesized.¹⁷ Furthermore, these diseases may be associated with different specific allergens. Moreover, the major airborne allergens differ by geographical area.^{18,19}

The aims of this study were to determine the prevalence and impact of allergic sensitization patterns to different airborne allergens on asthma and allergic rhinitis among adults, and to investigate the relationships by age. We therefore focused this work on the association of sensitization with asthma and rhinitis by age, including the age of onset of asthma.

METHODS

Study area

The study was performed within the Obstructive Lung Diseases in Northern Sweden Studies in Norrbotten, the northernmost county of Sweden. The county is sparsely inhabited, with approximately 250,000 inhabitants in an

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Abbreviations used

OR: Odds ratio

PAF: Population-attributable fraction

RR: Relative risk

area of 105,000 km². The climate is subarctic, with cold and long winters and mild summers. The study was approved by the Regional Ethical Review Board at Umeå University, Sweden.

Study population

The study population is presented in Fig E1 in this article's Online Repository at www.jacionline.org. In 2006, a random sample of the population of Norrbotten (n = 7997; age, 20-69 years) was invited to participate in a postal questionnaire study.²⁰ In addition, another randomly selected population sample aged 30 to 84 years, which had participated in a similar questionnaire study in 1996,²⁰ was invited to a follow-up (n = 7,004). Overall, 12,055 subjects (80% of invited) participated.

In 2008-2009, a randomly selected sample of questionnaire responders, stratified by the sex and age distribution of the population of Norrbotten, was invited to clinical examinations. Of the 1,016 invited subjects, 737 (73%) participated. At the time of examination, their mean age was 53 years (range, 21-86 years) and 50% were women. The examinations included a structured interview and blood sampling for specific and total IgE levels. The participants at the clinical examinations were representative for the entire study sample.²¹

Questionnaire

The Obstructive Lung Diseases in Northern Sweden questionnaire has been used in several national and international epidemiologic studies.^{11,22} Both the postal questionnaire and the structured interview focused on respiratory symptoms, asthma, rhinitis, chronic bronchitis, chronic obstructive pulmonary disease, comorbid conditions of airways diseases, and potential risk factors. The questionnaire has recently been validated against the Global Allergy and Asthma European Network questionnaire.²³

Allergic sensitization

Allergic sensitization was assessed by analyses of specific IgE antibodies in serum: birch, timothy, mugwort, cat, dog, horse, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, and *Alternaria*. The serum samples were analyzed with the Immuno CAP system (ThermoFisher, Uppsala, Sweden). Of all participants, 692 subjects (94% of the participants) participated in blood sampling, of whom 51% were women. A positive result was defined as an IgE level of 0.35 IU/mL or more to the specific allergen.

Definitions

The prevalence of asthma, wheeze, and allergic rhinitis was assessed by a positive answer to the following questions at the interview:

Physician-diagnosed asthma: "Have you been diagnosed as having asthma by a physician?"

Current asthma: "Yes" to *Physician-diagnosed asthma* or "Have you ever had asthma?" and 1 of the following questions: "Have you had wheezing or whistling in your chest at any time in the last 12 months?" or "Have you had attacks of shortness of breath at any time in the last 12 months?" or "Have you used asthma medication regularly or as needed in the last 12 months?"

Current wheeze: "Have you had wheezing or whistling in your chest at any time in the last 12 months?"

Asthmatic wheeze: "Yes" to *Current wheeze* and "Have you been at all breathless when the wheezing noise was present?" and "Have you had this wheezing or whistling when you did not have a cold?"

Ever allergic rhinitis: "Have you or have you had allergic rhinitis or hay fever?"

Current allergic rhinitis: "Yes" to *Ever allergic rhinitis* and 1 of the following questions: "Have you had sneezing, runny nose, or nasal congestion without having a cold in the last 12 months?" or "Have you used medication for rhinitis in the last 12 months?"

Family history of asthma (allergic rhinitis): Mother, father, or sibling reporting ever having had asthma (allergic rhinitis). The information was derived from 2 separate questions.

Any allergen: IgE level of 0.35 IU/mL or more to any of the specific allergens.

Any animal: IgE level of 0.35 IU/mL or more to cat, dog, or horse.

Any pollen: IgE level of 0.35 IU/mL or more to birch, timothy, or mugwort.

Statistical analyses

Statistical analyses were performed by using the Statistical Package for the Social Sciences for Windows, Version 20.0. For comparisons of proportions, the χ^2 test and Fisher exact test were used when appropriate. Mantel-Haenszel's test for trend was applied for the assessment of the relationship between the prevalence of allergic sensitization and variables with more than 2 categories. Because total IgE data were not normally distributed, the Mann-Whitney *U* test was used for comparisons of distribution between groups. A *P* value of less than .05 was considered statistically significant.

The study population was divided into 3 age groups of similar width and of approximately similar size: 21 to 40 years, 41 to 60 years, and 61 to 86 years at the time of examination. Multiple logistic regression analyses were used to calculate the association between allergic sensitization and current asthma and current allergic rhinitis, and the associations were expressed as odds ratios (ORs) with 95% CI. These analyses were adjusted for age group, sex, smoking habits, and family history of asthma (allergic rhinitis). The analyses were also performed separately in the 3 age groups. Two models were applied when analyzing the association of asthma and allergic rhinitis with sensitization to specific allergens: the allergens were included one by one, and by including all allergens in the same model. Similar models were applied by using the variables sensitization to "any pollen," "any animal," and "any allergen."

The percentage of asthma and rhinitis cases in the population attributable to sensitization to *any allergen* was calculated by using the formula $PAF = P(RR - 1)/RR$, where PAF is the population-attributable fraction, RR is the relative risk, and *P* is the percentage of cases with allergic sensitization. RR was estimated by the adjusted OR.

RESULTS**Prevalence of allergic sensitization**

The prevalence of sensitization to *any allergen* decreased with increasing age: 45% in the age group 21 to 40 years, 30% in the age group 41 to 60 years, and 15% in the age group 61 to 86 years ($P < .001$) (Table I). A similar trend of a decreasing prevalence by age was observed for the most common sensitizers: dog, cat, timothy, birch, and horse. Sensitization to mite was less common, and only 0.7% were sensitized to mold. No significant differences by sex were observed.

Prevalence of asthma and allergic rhinitis

The prevalence of allergic rhinitis, both current and ever reported, decreased significantly with increasing age, with the highest prevalence in the youngest age group (Table II). The prevalence of asthma, both when defined as physician-diagnosed and current asthma, and current and asthmatic wheeze did not differ significantly by age. No significant differences by sex for any of the disease entities were found.

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