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ORIGINAL ARTICLE

Temporal relationship of allergic rhinitis with asthma and other co-morbidities in a Mediterranean country: A retrospective study in a tertiary reference allergy clinic

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Abstract
Background: Allergic rhinitis is a global health problem which causes major illness and represents a risk factor for asthma. The primary aim of the study was to record the clinical pattern of allergic rhinitis and its temporal relation with asthma in a Greek population.
Methods: Three-hundred and sixteen subjects with documented diagnosis of allergic rhinitis in a two-year period were included in this study. All participants completed a standardised questionnaire with full retrospective epidemiological data for rhinitis; in addition, serum IgE measurement and skin prick tests with 22 common inhalant allergens were carried out, while spirometry was performed in subjects with self-reported or doctor-diagnosed asthma. All subjects with at least one positive skin test were included in study analysis.
Results: One-hundred and sixty five out of 316 patients (49.1%) stated self reported-asthma while in 63/316 (19.9%) asthma was documented with spirometry. One hundred out of 165 (60.6%) had rhinitis as first clinical manifestation while in 24/165 (14.5%) asthma symptoms appeared first; the remaining 31/165 (24.9%) reported simultaneous onset of upper and lower airways' symptoms. About 68.5% were sensitised to seasonal allergens exclusively, while 50% were sensitised to ≥ 1 of *Parietaria*, grasses sp., *Olea eur.* The duration of rhinitis in the subpopulation of patients with self-reported asthma ($n=165$) was significantly higher compared with non-asthmatics (mean=3.22 years, $p<0.001$). Survival analysis for the estimation of asthma onset showed that the mean time interval with rhinitis only is 16.6 years (median 12 years, incidence 0.0596).
Conclusions: The unique environmental conditions and the aerobiology of each area clearly affect the clinical features of respiratory allergy.

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Introduction

Allergic rhinitis is a global health problem which causes major illness and disability worldwide and according to rather conservative estimates, it occurs in over 500 million people around the world[1]. Large epidemiological studies have demonstrated a large variation in the prevalence of rhinitis symptoms throughout the world[2]. The International Study on Asthma and Allergy in Childhood Phase (ISAAC) I reported that the prevalence of rhinitis with itchy-watery eyes (rhinoconjunctivitis) over the past year varied between centres from 0.8% to 14.9% in 6–7-year olds and from 1.4% to 39.7% in 13–14-year olds. In ISAAC III[3], it was found that in the 6–7-year age group, there is a global increase in rhinitis prevalence across most countries. In the 13- to 14-year age group, there is also a global increase in allergic rhinitis in countries where low, medium and high prevalence rates were found during ISAAC Phase I. On the other hand, rates are levelling off or decreasing in countries with high prevalence. It is likely that environmental factors were responsible for the major differences between countries.

The clinical definition of rhinitis is difficult to use in epidemiological studies as it is rather impossible to obtain laboratory evidence of the underlying immune mechanism; so the use of questionnaires as the only diagnostic tool leads to an overestimation of allergic rhinitis. The attributable fraction of documented IgE sensitisation in patients with diagnosis of allergic rhinitis by questionnaires is almost 50%[4].

According to numerous epidemiological and clinical studies, rhinitis and asthma often co-exist and share common risk factors, including atopy as the most important, and might even be manifestations of the same disease[5]. The few longitudinal studies that have addressed the temporal relation between rhinitis and asthma in respiratory allergy report that rhinitis precedes the development of asthma in most cases, suggesting that it represents a risk factor for asthma[6,7]. However, comparison of the results of these studies is difficult mainly due to methodological reasons as they did not use standardised methods for the diagnosis of asthma and rhinitis.

Due to the clear differences in the features of allergic rhinitis between different populations and considering the lack of relevant data referring to the geographical area of Greece, we have conducted this study with the primary aim to record the clinical pattern of allergic rhinitis and its temporal relation with asthma in a Greek population. Secondly, the record of co-morbidities and the investigation of possible risk factors such as sex, age, pattern of sensitisation, smoking habit, allergic conjunctivitis, exercise-induced asthma and sinusitis, for asthma in subjects with allergic rhinitis in our area were additional goals of our study.

Patients and methods

Patients' characteristics—study design

All patients referred to the Outpatient Clinic of the Allergy Unit of 'Attikon' University Hospital with documented diagnosis of allergic rhinitis, from April 2006 until April 2008 were included in this study. Inclusion criteria of the study were: (a) documented diagnosis of allergic rhinitis; (b) age $\geq$12 years; and (c) non-visible nasal polyps in anterior rhinoscopy. The diagnosis of allergic rhinitis was based on the typical clinical symptoms and the documentation of sensitisation with skin prick tests (SPTs), to at least one inhalant allergen according to the recently published ARIA document[1].

The records of the present and past medical history of certain parameters (the reply options are presented in brackets) were obtained from each subject referred for rhinitis: (a) age (in years); (b) sex (male, female); (c) smoking habit (smoker, non-smoker, ex-smoker); (d) duration of rhinitis symptoms (years); (e) type of rhinitis (seasonal, perennial, perennial with seasonal exacerbation); (f) self-reported symptoms of asthma (yes, no); (g) past or present documented diagnosis of asthma—symptoms suggestive of asthma as in self-reported asthma combined with obstructive spirometric values—(yes, no) according to GINA guidelines[8]; (h) symptoms of exercise induced asthma (yes, no); (i) duration of symptoms of asthma (years); (j) allergic conjunctivitis (yes, no); (k) history of chronic sinusitis (yes, no); (l) familiar history of atopic diseases; rhinitis, asthma, atopic dermatitis and/or food allergy in either of the parents (yes, no); (m) history of gastrooesophageal reflux (yes, no); (n) total serum IgE (IU/ml); (o) pattern of sensitisation (monosensitisation, polysensitisation when more than one allergen); (p) type of allergens (seasonal, perennial or both); (q) specific allergens; and (r) past or present history of concomitant atopic disorders (none, atopic dermatitis, food allergy, both, oral allergy syndrome).

The diagnostic criteria for allergic rhinitis were two or more of the following symptoms for $>$1 h on most days (a. watery rhinorrhea, b. sneezing, c. nasal obstruction, d. nasal pruritus) with documented IgE-sensitisation to at least one inhalant allergen. The patient-reported asthma was assessed with positive reply to at least one of five questions (a. did you have an attack or recurrent attacks of wheezing?, b. do you have a troublesome cough at night?, c. do you experience wheezing, chest tightness, or cough after exposure to airborne allergens or pollutants?, d. do your colds "go to the chest" or take more than 10 days to clear up?, e. Are symptoms improved by appropriate asthma treatment?)[8].

Subjects attended the Allergy Clinic on two occasions, 1–2 months apart. During the first visit, all subjects completed the standardised questionnaire, a blood sample was taken for determination of serum IgE concentration in IU/ml, (UniCAP system, Phadia, Uppsala, Sweden) and then an allergist obtained a full medical history and performed physical examination. Arterior rhinoscopy was performed in all subjects. In addition, the consulting allergist provided explanations to any possible query about the questionnaire. At the second visit, SPTs were carried out in all subjects and spirometry was performed in subjects with self-reported or doctor-diagnosed asthma.

All subjects with at least one positive skin test were included in study analysis.

Skin prick tests

Atopy was assessed in all participants by SPTs, using a battery of 22 common inhalant allergens: *Dermatophagoides pteronyssinus, Dermatophagoides farinae, Phleum pr,*