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Allergic rhinitis in children with asthma: a questionnaire-based study

S. Hamouda, C. Karila, T. Connault, P. Scheinmann and J. de Blic

Université Paris Descartes; Assistance Publique des hôpitaux de Paris, Hôpital Necker Enfants Malades, Service de Pneumologie et d'Allergologie Pédiatriques, Paris, France

Clinical and Experimental Allergy

Summary

Background Allergic rhinitis (AR) and asthma frequently coexist but has rarely been evaluated in children.

Objective This prospective study aimed to estimate the prevalence of AR in asthmatic children, and ascertain whether AR is a risk factor for the severity of asthma.

Methods The questionnaire, modified from the adult form of the score for allergic rhinitis (SFAR), was completed by 404 asthmatic children aged 3–18 years seen in the outpatient clinic between June 2005 and July 2007. Each item was assigned a number of points with a final score ranging from 0 to 17. AR and asthma were classified according to ARIA and GINA 2004 recommendations, respectively.

Results AR was diagnosed in 237 patients (58.7%). It was intermittent in 57.8% of the patients and persistent in 42.2%. A total score ≥ 9 was discriminant for AR (sensitivity = 91.1%, specificity = 95.2%, positive predictive value = 96.4%, negative predictive value = 88.3%, Youden's Index = 0.86). The proportion of children having mild or moderate-to-severe asthma was independent of the presence of AR, 61.6% of moderate-to-severe asthmatic children and 55.4% of intermittent and mild asthmatic children having AR.

Conclusion AR and asthma are frequently associated (58.7%). The SFAR adapted for children seems to be a simple and a reliable tool to detect AR in asthmatic children.

Keywords allergic rhinitis, asthma, children

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Correspondence:

Prof. J. de Blic, Université Paris Descartes; Assistance Publique des hôpitaux de Paris, Hôpital Necker Enfants Malades, 149 rue de Sèvres, 75015 Paris, France.
E-mail: j.deblic@nck.aphp.fr

Introduction

The prevalence of allergic disorders, allergic rhinitis (AR) and asthma, has increased over the last decades [1–3]. These two conditions share physiopathologic links that need to be clarified further. The AR prevalence varies from one epidemiological study to another mainly because there is no standardized assessment of AR. Furthermore, the actual distribution of AR in patients with asthma is not well defined. There are few published reports about AR, as for asthmatic children. Indeed, information concerning AR has been limited to the reported nasal symptoms in asthma surveys in children.

Questionnaires are probably the best way to assess the prevalence of respiratory symptoms in epidemiological studies. The score for allergic rhinitis (SFAR) [4] is a valid questionnaire developed recently in adults as a diagnostic test of AR in the general population, in the absence of a doctor's diagnosis. The prevalence of AR among asthmatic

children has not been determined previously by use of a specific questionnaire. Our study aims to estimate the prevalence of AR in asthmatic children, to describe the main characteristics of the population of children with both asthma and AR and ascertain if AR is a risk factor for the severity of asthma.

Methods

Study population and questionnaire

Between June 2005 and July 2006, 404 asthmatic children – aged 3–18 years (mean age 9.04 ± 3.7 years) – and their parents filled in a questionnaire at the pulmonology and allergy clinics at Necker Enfants Malades Centre in Paris. All children had undergone previous allergy tests [skin prick test (SPT) and/or specific IgE]. Sensitization was defined by a mean weal diameter at least 3 mm greater than that of the negative control (Stallergenes,

Antony, France) or a specific IgE concentration > 0.2 KU/L (Pharmacia, Uppsala, Sweden). The questionnaire was modified from the adult form of the SFAR. An item about itching nose was added. Each item was assigned a number of points. The final score ranged from 0 to 17 (Table 1). The patient was considered to be either free of or affected by AR according to medical diagnosis (*gold standard*). AR and asthma were classified according to ARIA [5] and GINA 2004 [6] recommendations, respectively. Furthermore, the onset ages of AR and asthma, the treatment of

AR and the impact of AR treatment on daily life were also recorded. Association with another allergic condition (atopic dermatitis, conjunctivitis and/or food allergy) was also recorded.

Statistical analysis

Diagnosis based on the score of our paediatric questionnaire was validated against medical diagnosis by comparison of calculations for sensitivity, specificity and positive and negative predictive values for each score (Table 2). We used the receiver operating characteristics (ROC) curve and the Youden Index (i.e. sensitivity + specificity – 1) to express a specific threshold value describing children with AR with the best sensitivity and specificity. The χ^2 test was used for statistical analysis; a *P*-value < 0.05 was considered to be statistically significant.

Multiple correspondence analysis (MCA) and graphical analysis of the questionnaire's line items was used to examine construct validity. The Cronbach α coefficient was used to assess the homogeneity of our questionnaire.

Results

We found that a total questionnaire score ≥ 9 was a diagnostic threshold for AR. The corresponding sensitivity was 91.1% (range, 0.87–0.94), specificity was 95.2% (0.92, 0.97), the positive predictive value was 96.4% (0.94, 0.98) and the negative predictive value was 88.3% (0.84, 0.92). Questionnaire efficiency, assessed by determining the area under the ROC curve, was 0.96 (Fig. 1). Youden's Index reached the best value (0.86) at a score of 9.

The MCA showed that the first axis (29.5% of the inertia) allowed discrimination between the presence and

Table 1. Attributed score and distribution according to the questionnaire items

Items	Attributed points
Question 1: Nasal symptoms (blocked nose, runny nose, itching, sneezing)	0–4 (0–1 for each symptom)
Question 2: Itchy, watery eyes	0–2 (2 if yes)
Question 3: Months of the year	0–2 1 if more than 6 months 1 if pollen season (April–July)
Question 4: Trigger factors	0–2 2 if house dust mites and/or pollens 1 if animal and/or indoor moulds (maximum 2 points)
Question 5: Parents' perception of the allergy	0–2 (2 if yes)
Question 6: Previous positive allergy tests	0–2 (2 if yes)
Question 7: Previous medical diagnosis of the allergy	0–1 (1 if yes)
Question 8: Familial history of allergy	0–2 (2 if yes)
Total points	17

Table 2. Clinical characteristics of children with asthma and children with allergic rhinitis according to the age

	All age	3–5 years	6–11 years	12–18 years
All children (<i>n</i>)	404	101	208	95
Children with AR <i>n</i> (%)	237 (58.6)	40 (39.6)	130 (62.5)	67 (70.3)
Gender (M/F)	150/87	25/15	86/44	39/28
Mean age (years $\pm$ SD)	9.6 $\pm$ 3.5	4.6 $\pm$ 0.9	8.9 $\pm$ 1.45	14.1 $\pm$ 1.56
Positive SPT <i>n</i> (%)	194 (82)	23 (57.5)	111 (85)	60 (89.5)
Classification of AR <i>n</i> (%)				
Mild intermittent	112 (47)	21 (53)	62 (48)	29 (43)
Moderate to severe intermittent	25 (11)	1 (2)	13 (10)	11 (16)
Mild persistent	62 (26)	10 (25)	36 (27)	16 (24)
Moderate to severe persistent	38 (16)	8 (20)	19 (15)	11 (17)
Classification of asthma <i>n</i> (%)				
Intermittent	70 (30)	7 (17.5)	40 (30.7)	23 (34.3)
Mild persistent	37 (16)	12 (30)	19 (14.6)	6 (9)
Moderate persistent	103 (43)	15 (37.5)	61 (47)	27 (40.3)
Severe persistent	27 (11)	6 (15)	10 (7.7)	11 (16.4)
Associated allergic manifestation <i>n</i> (%)	133 (56)	27 (67)	71 (54)	35 (52)

AR, allergic rhinitis; SPT, skin prick test.

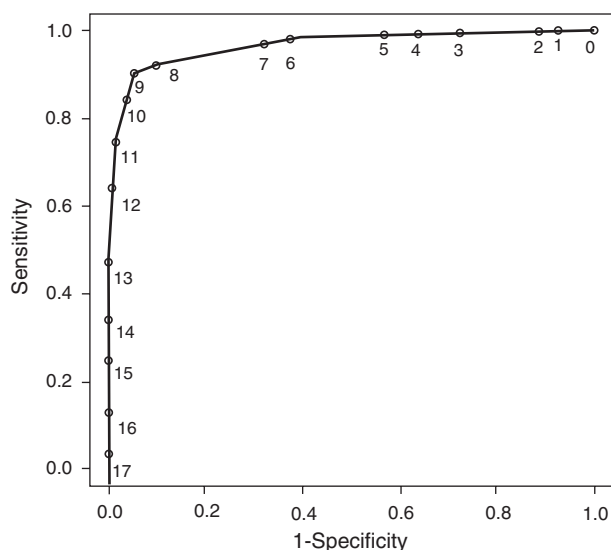


Fig. 1. ROC curve for allergic rhinitis diagnosis. Score ≥ 9 had a corresponding sensitivity of 91.1% and a specificity of 95.2%. ROC, receiver operating characteristics.

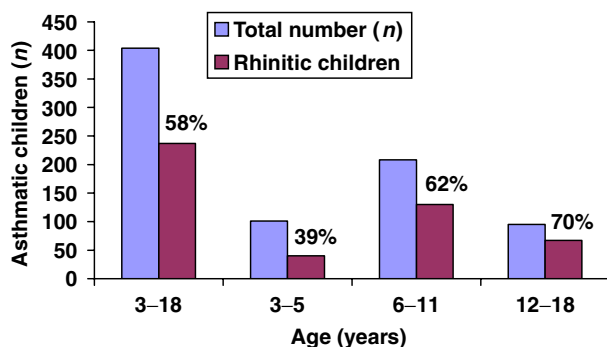


Fig. 2. Prevalence of allergic rhinitis in asthmatic children according to age.

the absence of AR. The second axis (9.7% of the inertia) discriminated between pollen-related and pollen-unrelated AR. The third axis (6.7% of the inertia) discriminated between AR associated with house dust mites (HDMs) and AR not associated with HDMs; however, patients (or their parents) may not be able to diagnose this condition on their own, unlike pollen-related AR. Analysis of the line items did not yield a single model grouping all items. The Cronbach α coefficient was 0.813, suggesting that all the items were appropriate for assessment of AR.

The overall prevalence of AR was 58.7% (237 of 404 children). The characteristics of age group are shown Table 1. The prevalence of AR increased with age (Fig. 2). The mean age of children affected by both asthma and AR was 9.6 ± 3.5 . Males were more commonly affected (sex ratio of 1.72). Children under 6 years of age were significantly less sensitized (57%) than children aged between 6 and 11 years (85%, $P < 0.0001$) and children aged between 12 and 18 years (89.5%, $P < 0.0001$). Eighty-two

Table 3. Clinical characteristics of 237 asthmatic children with allergic rhinitis according to skin prick tests results

	Positive skin prick tests (<i>n</i> = 194)	Negative skin prick tests (<i>n</i> = 43)
Mean age (years $\pm$ SD)	10 ± 3.4	7.7 ± 3.5
Classification of AR <i>n</i> (%)		
Mild intermittent	95 (49)	17 (14)
Moderate to severe intermittent	21 (11)	4 (10)
Mild persistent	46 (24)	16 (36)
Moderate to severe persistent	32 (16)	6 (14)
Classification of asthma <i>n</i> (%)		
Intermittent	59 (30)	11 (25)
Mild persistent	31 (16)	6 (14)
Moderate persistent	86 (44)	17 (40)
Severe persistent	18 (10)	9 (21)
Associated allergic manifestation <i>n</i> (%)		
Atopic dermatitis <i>n</i> (%)	65 (33)	12 (27)

AR, allergic rhinitis.

percent of children (*n* = 194) with AR had positive allergy tests. Most of these tested positive for allergy against HDMs (77.8%) and against pollens (45.8%) and half of them had multi-sensitization. AR diagnosis was not ruled out in children with negative allergy tests (18%) due to strong clinical signs of AR. There were no significant differences between children with positive and negative allergic tests in term of age, repartition of AR or asthma severity (Table 3).

The main manifestations of AR were blocked nose (81.9%) and sneezing (77.2%). Itchy, watery eyes were present in 51% of the cases. AR was mostly stimulated by HDMs (43%).

AR was classified as mild intermittent (47.3%), moderate to severe intermittent (10.5%), mild persistent (26.2%) or moderate to severe persistent (16%) according to ARIA. This was not affected by age or sensitization. AR rarely preceded the onset of asthma (17.3%). Half of the rhinitic children (47.3%) did not receive specific treatment. In treated children, Oral H1-antihistamines were prescribed in 41%, topical corticosteroids in 12% and immunotherapy in 14.3%.

Two-thirds of rhinitic patients felt seriously bothered by their AR, on a moderate (51%) to severe (15.2%) scale.

Fifty-six percent of children having both asthma and AR had a third disease, most frequently atopic dermatitis (32.5%). AR was not an independent risk factor for the severity of asthma regardless of its grade and SPTs results. Neither multi-sensitization nor allergic comorbidity worsened asthma in asthma and AR patients.

Discussion

These findings clearly contribute to further understanding of the association between AR and asthma in childhood.

This study assessed the prevalence of AR in asthmatic children through a specific questionnaire for the first time. A paediatric score cut-off value ≥ 9 allowed optimum discrimination between children with AR and those without. We found that 58.7% of asthmatic children had AR. This AR was more likely to be intermittent (57.8%).

Although the SFAR questionnaire was initially developed for the adult population, this work validates its use for children. The ISAAC questionnaire [7] that has been validated for children is less specific than the SFAR. The SFAR questionnaire yields a quantitative score that is more informative than a unidimensional instrument [8]. Our paediatric score (and sensitivity, specificity, positive predictive value and negative predictive value) was higher than that of the SFAR [4], probably because it was applied to a target population (asthmatic children) in which atopy was more frequent than in the general population.

Various epidemiological studies show a high frequency of AR in the Western asthmatic population. A cross-sectional study of the French population found that 82% of asthmatic adults suffered from AR [9]. Even though the ISAAC cohort has determined the prevalence of AR and its trends in childhood, these are not wellknown in asthmatic children [10]. As asthmatic patients do not overtly complain about nasal symptoms and/or these symptoms are not routinely sought by doctors, the AR frequency is underestimated in this group [11]. We found the AR prevalence to be 58.7%. Questionnaire based studies found a prevalence that ranged from 49% to 69% [12–16] (Table 4). According to the ISAAC questionnaire, Janahi *et al.* [14] reported the prevalence of asthma in Qatari schoolchildren to be 19.8%, and among them, 59.9% had AR. Another questionnaire-based study involving 333 asthmatic children with a median age of 7 suggested that 49.5% had AR [15]. A recent questionnaire-based survey undertaken in asthmatic children aged 3–16 years stresses the association between asthma and AR [16]. Of 369 patients studied, the findings for 68.8% were consistent with AR. Nevertheless, retrospectively, only 5.4% of patients regarded themselves as rhinitic and 23.8% had been diagnosed with AR according to file

records. A retrospective study in Italy found that children complaining of persistent wheezing were 10 times more likely to have a personal history of AR than the control group [17]. A USA registry of asthmatic patients aged 5–77 years showed that 73% of the 372 registered 5–11-year-olds had symptoms of AR [18]. Finally, in the Manchester Asthma and Allergic Study (MAAS) about 25% of the current wheezing children had concurrent rhinoconjunctivitis at 5 years of age [19].

Our study provides additional information regarding the clinical signs and the burden of AR in the asthmatic child. In contrast to Lack [20], who suggested that the child with AR rarely complains of nasal stuffiness, we found that the main manifestations of AR were blocked nose (81.9%) and sneezing (77.25%), consistent with the findings of Masuda *et al.* [15]. Forty-two percent of 747 healthy children followed since birth in a cohort study in TUCSON [21] had AR by the age of 6. The main symptom was rhinorrhoea (91%), followed by sneezing (76%). AR may cause more general symptoms (headache, anosmia, sleep disturbance) in adults [22]. Few studies have evaluated the impact of AR in children [23, 24]. Roberts *et al.* [23], using a specific questionnaire, recently showed that AR considerably impaired the quality of life in 36 children who were 8–16 years old and suffering from AR and/or asthma and/or atopic dermatitis. They mainly complained of a hearing deficit, the inability to concentrate and daytime somnolence. They complained much less about asthma than about AR. Similarly, we found that AR was troublesome in 67% of patients, despite it being most commonly intermittent. As in the survey of Kocabas *et al.*, a significant burden caused by rhinitis symptoms was reported by 41.2% of asthmatic children [16].

Linna *et al.* [25] found that all children with periodic AR tested positive for pollen allergy by SPTs. All children with perennial AR tested positive for HDM or animal allergy by skin tests, but only 14% tested positive for pollen allergy. After 10 years of follow-up, 23% of the patients initially with periodic AR had perennial AR; the opposite shift occurred in 16% of patients. Eighteen percent of our rhinitic patients were not sensitized to any inhalant allergen and AR was most commonly intermittent (57.8%). Eighty-six percent of children above 6 years of age were sensitized and only 57% of children between 3 and 6. Our results are in agreement with those of *et al.* [19] in the MAAS survey; almost half of the children reporting rhinoconjunctivitis were sensitized at 5. These results may be explained because not all children had both SPTs and specific IgE. It has also been speculated that some children may initially have only local IgE production [19]. In our series, children with positive and children with negative SPTs were comparable.

Various studies investigated associated allergic manifestations in children [20, 26, 27]. Sole *et al.* [27] reported that 10% of adolescents (13–14 years old) and 12.8% of

Table 4. Main studies on the prevalence of rhinitis in asthmatic children

Author	Year	Location	Number of children	Age group	Prevalence of rhinitis
Our study	2005	France	404	3–18	58.6
Huse [18]	1998	USA	372	5–11	73
Shamssain [13]	2001	England	3000		53% in boy 61% in girls
Sichletidis [12]	2004	Greece	2005	9–12	69%
Kocabas [16]	2005	Turkey	369	3–16	68.8
Janahi [14]	2006	Qatar	3283	6–14	59.9
Masuda [15]	2006	Japan	333	7	49.5
Marinho [19]	2007	England	815	5	25

children (6–7 years old) with both asthma and AR had associated eczema. Eczema was the most common association (32.5%) in our study. A recent study, involving 6600 children who were 9–11 years old, found a significant association between food allergy and asthma/AR, even in the absence of respiratory symptoms related to food allergy [28].

AR commonly precedes asthma. Our study and that of Huse et al. [18] did not demonstrate this chronological sequence. However, AR seems to be a risk factor for asthma [2, 29]. The more severe the AR, the more likely asthma is to occur [30]. Leynaert and colleagues [31, 32] have reported previously that AR – especially the perennial type – is an independent risk factor for asthma.

In the adult population, rhinitis is associated with a severe, corticosteroid-dependent asthma or with mild asthma with equal prevalence. However, rhinitis is more severe if associated with severe, corticosteroid-dependent asthma [33]. In contrast, our study did not find an association between AR and severity of asthma. The relatively high percentage of moderate to severe asthma in the investigated population is probably due to a referral bias of outpatients attending specialized allergy clinic. Our results are in agreement with those of Marinho in the MAAS study [19]. Various studies suggest that optimal management of AR would improve asthma [34–36]. Half of our patients were not treated for AR, probably because of its underdiagnosis. Even so, there was no difference in asthma severity between treated and non-treated groups. A recent study was developed among six European centres, targeting 183 children with a mean age of 10 years and AR triggered by pollens [37, 38]. For those without an initially associated asthma, pollen immunotherapy led to significantly fewer developing asthma during the 10-year follow-up period, leading to the question of whether specific immunotherapy should be considered to reduce the risk of progression towards asthma in children with isolated AR [39].

In summary, AR and asthma are frequently associated (58.7%). We found that although AR is possibly more intermittent, it often entails serious burden. The SFAR adapted to children seems to be a simple and reliable tool to detect AR in asthmatic children.

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