Allergic rhinitis: similarities and differences between children and adults*

Adriana Izquierdo-Domínguez[1], Ignacio Jauregui[2], Alfonso del Cuvillo[3], Javier Montoro[4], Ignacio Dávila[5], Joaquín Sastre[6], Joan Bartra[7], Marta Ferrer[8], Isam Alobid[9], Joaquim Mullol[10#], Antonio Luis Valero[11#]

[1] Servicio de Alergología, Consorci Sanitari de Terrassa and Clinica Diagonal, Barcelona, Spain

[2] Servicio de Alergología, Hospital de Basurto, Bilbao, Spain

[3] Unidad de Rinitis y Asma, UGC ORL. Hospital de Jerez. Cádiz, Spain

[4] Unidad de Alergia, Hospital Universitario Arnau de Vilanova, Facultad de Medicina, Universidad Católica de Valencia "San Vicente Mártir", Valencia, Spain

[5] Servicio de Inmuno-Alergia, Hospital Clínico, Salamanca, Spain

[6] Servicio de Alergia, Fundación Jiménez Díaz, Madrid, Spain

[7] Servicio de Neumologia y Alergia, Hospital Clínic i Universitari, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain

[8] Departamento de Alergia, Clínica Universitaria Navarra, Pamplona, Spain

[9] Unitat de Rinologia i Clínica de l'Olfacte, Servei d'Otorinolaringologia, Hospital Clínic, IDIBAPS, Centro de Investigación Biomédica em Red en Enfermedades Respiratorias (CIBERES), Barcelona, Spain

[10] Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Unitat de Rinologia i Clínica de l'Olfacte, Servei d'Otorinolaringologia, Hospital Clínic, Universitat de Barcelona. Centro de Investigación Biomédica en Red en Enfermedades Respiratorias (CIBERES), Barcelona, Catalonia, Spain

[11] Servicio de Neumología y Alergia, Hospital Clínic i Universitari; Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS); and CIBER de Enfermedades Respiratorias (CIBERES). Barcelona, Catalonia, Spain

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* These authors shared senior responsibilities.

Abstract

Background: Allergic rhinitis (AR) is a highly prevalent disease worldwide. Although a number of studies have described AR, no studies compared children and adult AR populations. The objective was to compare the AR characteristics between two AR cohorts of children and adults.

Methods: Two AR cohorts (children and adults) from Spain were studied through observational cross-sectional multicentre studies. AR was classified based on classical (allergen exposure), original (o-ARIA), and modified (m-ARIA) ARIA criteria. AR was evaluated by Total 4-Symptoms Score (T4SS), and disease severity by Visual Analogue Scale (VAS, 0-100 mm). AR comorbidities were also evaluated.

Results: A total of 5,405 patients (1,275 children, 4,130 adults) were studied. According to symptom's duration, intermittent AR was more frequent in children than in adults. Using o-ARIA severity, more children than adults had moderate/severe AR while, using m-ARIA, more children than adults had severe AR. T4SS was higher in adults than in children. Moreover, VAS was also higher in adults than in children. In addition, asthma atopic dermatitis and conjunctivitis were more associated to children than adults with AR, the frequency of this comorbidities increasing according to higher severity.

Conclusions: AR in children was more intermittent, severe, with less symptoms but with more comorbidities than in adults. These results suggest AR has similarities but also significant differences between children and adults.

Key words: ARIA-classification, characteristics of allergic rhinitis, children and adults, comorbidities

Introduction

Allergic rhinitis (AR) is a worldwide health problem in adults, adolescents, and children generating a significant impact on quality of life (QoL) and on medical care burden [1]. Rhinorrea, nasal itching, sneezing, nasal congestion, and in one third of patient's loss of smell [2, 3], are characteristic nasal symptoms of AR, being also associated with ocular symptoms such as pruritus/itching, redness, and watery eyes in 60-70% of patients. Even though AR symptoms are not life threatening they can be very bothersome, negatively affecting patient's quality of life and work/school productivity, therefore causing a significant burden to the person and society [4]. The symptoms have the potential to impair physical and mental components of QoL, associated with sleep disorders and breathing issues in childhood and adolescence, associating performance difficulties in learning, behaviour, and attention [5]. As in adults, asthma is also frequently associated with AR in children [6, 7].

According to the aeroallergens sensitization, AR is usually classified in perennial, seasonal, and occupational. According to ARIA (Allergic Rhinitis and its Impact on Asthma), symptom's duration can be classified as intermittent (IAR) or persistent (PER) AR in both adults [9, 10] and children [11]. According to o-ARIA (original), AR severity can be classified also in both adults [9] and children [12] based on the impairment of four health-related quality of life (HRQL) items: sleep, daily activities/sports/free time, work productivity/school performance, and bothersome symptoms. Recently, a modified ARIA severity classification (m-ARIA) has been proposed for both adults [8, 9] and children [12].

Until recently, a number of AR studies in both children and adults have been published on epidemiology, clinical characteristics, quality of life, and disease management [13]. However, no study has directly compared the clinical characteristics between adults and children with AR. The objective of this study was to compare AR characteristics between two AR cohorts (children and adults) based on data from two major prospective, observational studies used for the validation of ARIA classification in Spain.

Materials and methods

Two observational, cross-sectional, multicentre studies were performed with data collection consecutively in two phases, one study in children and one in adults.

Study design and population

Children Cohort. A total of 334 investigators (from allergy, otorhinolaryngology, and paediatric centres) participated in the AR study on paediatric population. Patients were recruited if they fulfilled the following inclusion criteria: 1) 6 to 12 years old, 2) a previous diagnosis of AR made by an allergist, 3) a parental informed written consent, and 4) children should have not received any treatment (untreated) for their AR during the 2 weeks preceding inclusion at least.

Adult Cohort. In adults, the study was performed by 760 investigators (allergy, otorhinolaryngology, and general practice centres), patients aged 18 years or older with an established diagnosis of AR. Patients were considered suffering from AR if they had: 1) suggestive symptoms of rhinoconjunctivitis within the two previous years or more confirmed with skin prick test positivity, and 2) at least one positive skin prick test and/or serum-specific IgE to an aeroallergen clinically relevant. The populations were recruited from all regions of Spain to avoid any geographic or seasonal influence.

All patients signed a written informed consent to participate in the study. The protocol was approved by the Ethics Committee of Hospital Clínic de Barcelona.

Study outcomes

Demographic data (age, gender, height, and weight), place of residence, and household characteristics, were obtained. The investigator filled in the type of AR according to the classifications based on allergen exposure (seasonal, perennial, occupational) and duration of AR was classified according to original (o-ARIA) ARIA guidelines as persistent (PER, symptoms appearing >4 days a week and >4 weeks) or intermittent (IAR, symptoms for ≤4 days a week or ≤4 weeks) [8,11]. Severity of AR was classified as mild or moderate/severe according to the presence (moderate/severe) or not (mild) of any of the following items: a) sleep disturbance, b) impairment of daily activities, leisure, and/or sports, c) impairment of school (children's cohort) / work (adult's cohort) performance, and d) bothersome symptoms [8].

In addition, the modified (m-ARIA) ARIA classification was also included which categorizes AR severity into mild (no affected items), moderate (1-3 affected items) and severe (all 4 affected items) for either adults [9] or children [12]. We applied this modified criterion to untreated AR paediatric and adult patients.

AR symptoms in both populations were assessed using the Total four Symptom's Score (T4SS) by calculating the sum of scores for nasal congestion, rhinorrhea, nasal itching, and sneezing. Each nasal symptom was scored on a scale from 0 to 3 (0, no symptom; 1, mild; 2, moderate; 3, severe) resulting in a T4SS ranging from 0 to 12. In addition, children and adults were asked to evaluate the severity of their disease over the last week using a visual analogue scale (VAS), from 0 to 100 mm were 0 is none and 100 is maximum severity.

Finally, the incidence of comorbidities such asthma, conjunctivitis, and atopic dermatitis was analysed according to the severity of AR using m-ARIA criteria and compared between children and adults.

Statistical analysis

A descriptive analysis of the studied population, both in terms of demographic characteristics and the distribution of patients

Table 1. Frequency of allergic rhinitis (AR) according to different classifications, symptom's score, and severity in both children and adults from Spain.

AR outcomes		Adults (N=4,130)	Children (N=1,275)	p-value
Classical	Seasonal [1]	2,658 (64.9)	767 (60.7)	p<0.001
	Perennial [1]	1,444 (35.1)	497 (39.3)	p<0.001
ARIA	Intermittent [1]	2,120 (51.5)	756 (59.5)	p<0.001
	Persistent [1]	1,996 (48.5)	515 (40.5)	p<0.001
Symptoms	T4SS 2 (0-12)	6.5 ± 2.8	6.2 ± 2.9	p<0.01
Severity	VAS [2] (0-100mm)	39.8 ± 23.6	37.0 ± 25.5	p<0.0001

[1] N (%); [2] mean ± standard deviation; ARIA, Allergy Rhinitis and its Impact on Asthma; T4SS, Total four Symptom's Score; VAS, Visual Analogue Scale.

according to allergen exposure with the two ARIA classifications (o-ARIA and m-ARIA) was performed. We compared both cohorts and databases from studies in children and adults and created a database in common statistical analysis included a cross-comparison analysis of the differences between o-ARIA and m-ARIA classifications, concomitant pathologies and the scores of severity evaluations T4SS, and VAS in the two cohorts. All variables to be analysed were described for the total sample. Continuous variables were resumed by means of number of valid cases (N), mean, standard deviation, median, and extreme values; categorical variables were described by means of number of valid cases (N) and percentages (%) in each category, while variables with an asymmetric frequency distribution were described using the medians and their 25–75 percentiles. Comparisons were made using the appropriate tests (Chi-squared, Mann-Whitney, or Kruskal-Wallis) in each case. For all comparisons, a level of statistical significance of p value <0.05 was considered. Data were entered in a Microsoft Access Database and was analysed using SPSS 15.0 (SPSS Inc., Chicago, IL, USA).

Results

Demographic characteristics of the patients

A total of 5,405 patients [1,275 (23.6%) children and 4,130 (76.4%) adults] were included, the mean age of patients being 37.5 ± 13.4 years for adults and 9.1 ±1.9 years for children. Gender distribution was 41% of girls (children's cohort) and 52% of women (adult's cohort).

AR classification

AR symptoms were assessed using two symptom's scores (VAS and T4SS) in both populations. By both T4SS and VAS, nasal symptoms were significantly higher in adults than in children

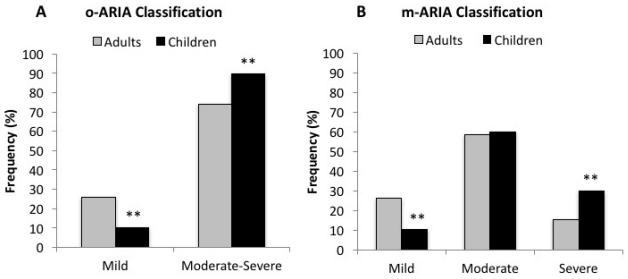

Figure 1. Frequency of allergic rhinitis (AR) patients according to A) original (o-ARIA), and B) modified (m-ARIA) severity criteria. **, p<0.001 compared to adults with AR.

(Table 1).

Using the classification by sensitizing allergen, seasonal AR was more frequent in adults and perennial in children while, according to ARIA classification, IAR was more frequent in children and PER in adults (Table 1). According to ARIA severity, the frequencies of moderate/severe (in o-ARIA) and moderate (in m-ARIA) were the predominant in both cohorts (Figure 1). Using m-ARIA, children had a lower frequency of mild and higher of severe than adults.

AR comorbidities

Most of children (76.5%) had at least a concomitant disease. The most frequent comorbidity in AR patients was conjunctivitis followed by asthma and atopic dermatitis, in both children and adult cohorts (Table 2). The frequencies of conjunctivitis, asthma, and atopic dermatitis were significantly higher in children than in adults (Figures 2, 3, and 4). Additionally, food allergy was more frequent in children and drug allergy in adults (Table 2). In addition, the frequencies of asthma (Figure 2) and atopic dermatitis (Figure 4), but mainly of conjunctivitis (Figure 3), increased accordingly to disease severity (m-ARIA), being significantly higher in children than in adults with AR and in all levels of severity.

Discussion

The main findings of this study were: 1st) The distribution of patients with moderate/severe in o-ARIA and moderate in m-ARIA predominated in both children and adults; 2nd) children had more intermittent AR than adults; 3rd) adults reported more severe nasal symptoms, by both T4SS and VAS, than children; and 4th) children with higher levels of severity reported more frequently than adults comorbidities such as conjunctivitis, asthma, and atopic dermatitis).

AR is the most common chronic disease in childhood and adults in many countries [10]. To our knowledge, this is the first study in recent years comparing the differences between two large cohorts of children and adults suffering from AR in Spain.

Table 2. Allergic rhinitis comorbidities in both children and adults cohorts.

Comorbidities	Adults (N=4,130)	Children (N=1,275)	p-value
Asthma, n (%)	849 (20.0)	631 (49.5)	p<0.0001
Conjunctivitis, n (%)	1,166 (28.0)	689 (54.4)	p<0.0001
Atopic dermatitis, n (%)	435 (10.5)	507 (40.0)	p<0.0001
Food allergy, n (%)	178 (4.3)	127 (10.0)	p<0.0001
Drug allergy, n (%)	249 (6.0)	35 (3.1)	p<0.001

n, number of patients

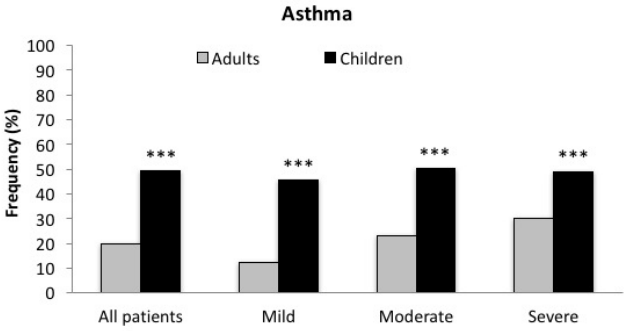

Figure 2. Frequency of asthma comorbidity in allergic rhinitis (AR) patients according to modified (m-ARIA) severity criteria. ***, p<0.0001 compared to adults with AR.

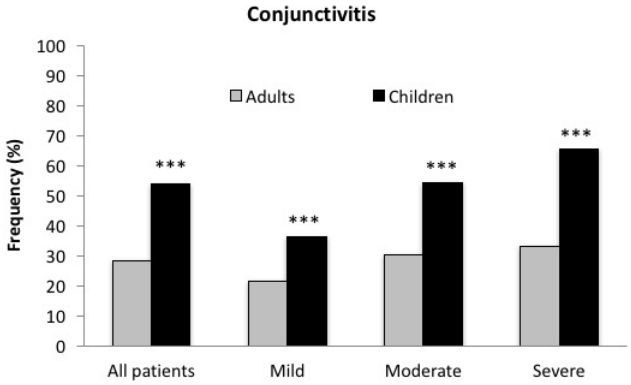

Figure 3. Frequency of conjunctivitis comorbidity in allergic rhinitis (AR) patients according to modified (m-ARIA) severity criteria. ***, p<0.0001 compared to adults with AR.

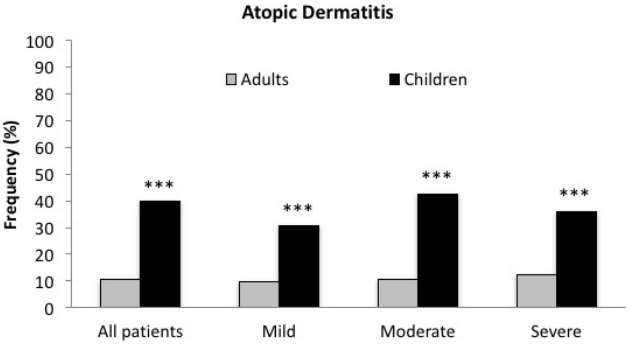

Figure 4. Frequency of atopic dermatitis comorbidity in allergic rhinitis (AR) patients according to modified (m-ARIA) severity criteria. ***, p<0.0001 compared to adults with AR.

Using m-ARIA classification, children had significantly more moderate and severe AR than adults. The higher prevalence of moderate/severe in both populations may be the result of selection bias, as patients were recruited mostly from tertiary centres. But severity clearly affects more the paediatric than adult AR population.

In Spanish children, Ibero et al. [14] analysed 260 children (5-17 years) using the ARIA classification. The study reported 30.7% having intermittent and 69.4% persistent AR. Moderate disease was more frequent (67.7%) than mild (20.8%) or severe (11.6%). Differentially, in the present study children had more intermittent AR than persistent. Findings in severity were however similar to our study. In adult population, we found however more persistent AR in Spanish adults, although Valero et al. [9] has reported PER to be less frequent (36%) than IAR (64%). According to allergen-based classification we found children having slightly more perennial AR than adults (39.3% vs 35.1%). Our study has also shown that this classification is different in children and it cannot be interchanged as it has already been demonstrated in adults [15].

The objective of evaluating VAS, as a useful instrument for assessing AR severity, was to improve the ARIA classification of AR severity. A recent study has been able to categorize the ARIA severity classification using this VAS score [16]. Concerning to prevalence of symptoms, adults reported more symptoms by both T4SS and VAS. While VAS and T4SS measure intensity of symptoms, m-ARIA severity score evaluates the involvement of AR in the patient's quality of life. These two concepts are completely different, so they measure different impacts of disease. This may explain the difference between a greater affection of AR in children according to m-ARIA and higher symptom's intensity (T4SS and VAS) in adults.

Several studies have shown that AR represents a clear risk factor for developing asthma [17] in both adults [18] and children [19] populations. Even severe and persistent nasal symptoms have been previously correlated to an increased risk of asthma in adults [20]. In our study, most AR patients reported at least one comorbidity associated with AR, asthma affecting more children than adults.

It is well known that poor adherence to therapy is a general problem in the management of chronic diseases. In addition, children with AR and concomitant asthma may have reduced compliance with nasal treatment as they may be more affected

by their asthma symptoms. This problem could produce more moderate and severe nasal symptoms in children. In addition, children are less likely to take medications if their symptoms are intermittent.

According to m-ARIA, the increasing severity of AR had a positive association with the presence of asthma with significant differences between adult and children. In a recent study in Danish children a high prevalence of AR among children with allergic asthma was also found [21]. In the PETRA study [14], the most frequently reported AR comorbidities were asthma (55%) and conjunctivitis (32%). The only other concomitant disease with a frequency >10% was atopic dermatitis. In a recent paediatric Spanish study, Ibañez et al. [22] reported half of AR patients being associated with concomitant asthma. These findings were similar from those in our study but different from those of International Study of Asthma and Allergies in Childhood (ISAAC) phase III [23]. In ISAAC Eastern European countries, children (6-7 years) had asthma in 26.2%, conjunctivitis in 48.9%, and atopic dermatitis in 13.3%. However, children between 13 and 14 year had 25.4%, 58.7% and 8% respectively. These findings go in the same direction than those in our study.

The development of asthma in childhood (early onset) is often associated with allergy [18] but in adulthood (late onset) is usually independent of allergy [24]. In our study, adult asthma was the only comorbidity which incidence increased in correlation to AR severity, this finding being more frequent in patients with PER (41.6%) than IAR (31.5%). Asthma prevalence was also higher in moderate/severe (41.1%) compared to mild (34.1%) AR. In an epidemiological study in 2,771 adult AR patients [25], Navarro et al. found that more than one third of patients suffered from asthma while two thirds had conjunctivitis. In our study, children had more conjunctivitis and atopic dermatitis than adults.

The present study has some limitations or weaknesses. 1st) The results may not be representative of the general population since the analysis included two observational, cross-sectional, multicentre studies (children and adults) in two phases where patients were recruited from tertiary centres but not from the general population. 2nd) The effect of treatment on the studied outcomes as well as medication compliance was not investigated since reported data from these two cohorts was only analysed at baseline, after two weeks without any medication.

Conclusion

In conclusion, this real-life large-scale prospective study conducted in Spain, confirms there are clear similarities but also some differences between AR in children and adult, being studied either using classic or new (ARIA) classifications. AR in children was more intermittent and severe, and had less symptoms but more comorbidities (asthma, conjunctivitis, and atopic dermatitis) than in adults.

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Authorship contribution

AV had the initial idea for the study. AI-D performed the statistical analysis and wrote the manuscript. All authors collaborated in the retrieval of data and in the discussion of results. All authors have reviewed and approved the final version of this manuscript.

Conflict of interest

The authors have no conflict of interests to declare for the data content of this study.

References

1. Colás C, Brosa M, Antón E, et al. Estimate of the total costs of allergic rhinitis in specialized care based on real-world data: the FERIN Study. Allergy 2017;72:959-66.
2. Guilemany JM, A García-Piñero, I Alobid, et al. Persistent allergic rhinitis has a moderate impact on the sense of smell depending on both nasal congestion and inflammation. Laryngoscope 2009;119:233-8.
3. Langdon C, JM Guilemany, M Valls, et al. Allergic rhinitis causes loss of smell in children: The OLFAPEDRIAL study. Pediatr Allergy Immunol 2016;27:867-870.
4. Canonica GW, Bousquet J, Mullol J, Scadding GK, Virchow JC. A survey of the burden of allergic rhinitis in Europe. Allergy 2007;62:17-25.
5. Nathan RA. The burden of allergic rhinitis. Allergy Asthma Proc 2007;28:3-9.
6. Morais-Almeida M, Gaspar A, Pires G, Prates S, Rosado Pinto J. Risk factors for asthma symptoms at school age: an 8-year prospective study. Allergy Asthma Proc 2007;28:183-9.
7. Ibañez MD, A Valero, J Montoro, et al. Analysis of comorbidities and therapeutic approach for allergic rhinitis in a pediatric population in Spain. Pediatr Allergy Immunol 2013;24:678-84.
8. Bousquet J, Khaltaev N, Cruz AA, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008. Allergy 2008;63:8-160.
9. Valero A, Ferrer M, Sastre J, et al. A new criterion by which to discriminate between patients with moderate allergic rhinitis and patients with severe allergic rhinitis based on the allergic rhinitis and its impact on asthma severity items. J Allergy Clin Immunol 2007;120:359-65.
10. Valero A, Ferrer M, Baró E, et al. Discrimination between moderate and severe disease may be used in patients with either treated or untreated allergic rhinitis. Allergy 2010;65:1609-13.
11. Jáuregui I, Dávila I, Sastre J, et al. Validation of ARIA (Allergic Rhinitis and its Impact on Asthma) classification in a pediatric population: The PEDRIAL study. Pediatr Allergy Immunol 2011;22:388-92.
12. Montoro J, Del Cuvillo A, Mullol J, et al. Validation of the modified allergic rhinitis and its impact on asthma (ARIA) severity classification in allergic rhinitis children: the PEDRIAL study. Allergy 2012;67:1437-42.
13. Izquierdo-Dominguez A, Valero A, Mullol J. Comparative analysis of allergic rhinitis in children and adults. Curr Allergy Asthma Rep 2013;13:142-51.
14. Ibero M, Justicia JL, Alvaro M, et al. Diagnosis and treatment allergic rinitis in children: results of PETRA study. Allergol Immunopathol 2012;40:138-43.

15. Demoly P, Allaert FA, Lecasble M, Bousquet J; PRAGMA. Validation of the classification of ARIA (allergic rhinitis and its impact on asthma). Allergy 2003;58:672-5
16. Del Cuvillo A, Santos V, Montoro J, et al. Allergic rhinitis severity can be assessed using a visual analogue scale in mild, moderate, and severe. Rhinology 2017;55:34-8.
17. Leynaert B, Neukirch C, Kony S, et al. Association between asthma and rhinitis according to atopic sensitization in a population-based study. J Allergy Clin Immunol 2004;113:86-93.
18. Shaaban R, Zureik M, Soussan D, et al. Allergic rhinitis and onset of bronchial hyperresponsiveness: a population-based study. Am J Respir Crit Care Med 2007;176:659-66.
19. Rochat MK, Illi S, Ege MJ, et al. Multicentre Allergy Study (MAS) group. Allergic rhinitis as a predictor for wheezing onset in school-aged children. J Allergy Clin Immunol 2010;126:1170-5.
20. Guerra S, Sherrill DL, Martinez FD, Barbee RA. Rhinitis as an independent risk factor for adult-onset asthma. J Allergy Clin Immunol 2002;109:419-25.
21. Hoffmann-Petersen B, Host A, Larsen KT, et al. Prevalence of IgE sensitization in Danish children with suspected asthma. Pediatr Allergy Immunol 2013;24:727-33.
22. Ibáñez MD, Navarro A, Sánchez MC. et al. Rhinitis and its association with asthma in patients under 14 years of age treated in allergy departments in Spain. J Investig Allergol Clin Immunol 2010;20:402-6.
23. Mallol J, Crane J, Von Mutius E, et al. The international study of asthma and allergies in childhood (ISAAC) phase three: a global synthesis. Allergol Immunopathol 2013;41:73-85.
24. Shaaban R, Zureik M, Soussan D, et al. Rhinitis and onset of asthma: a longitudinal population-based study. Lancet 2008;372:1049-57.
25. Navarro A, Colás C, Antón E, et al. Epidemiology of allergic rhinitis in allergy consultations in Spain: Alergológica-2005. J Investig Allergol Clin Immunol 2009;19:7-13.

Antonio Luis Valero
Servicio de Neumología y Alergia
Hospital Clínic i Universitari
Institut d'Investigacions Biomèdiques
August Pi i Sunyer (IDIBAPS)
and
CIBER de Enfermedades Respiratorias
(CIBERES)
Barcelona
Spain

Tel: +34 932275540
E-mail: valero@clinic.ub.es

Joaquim Mullol is also a corresponding author (jmullol@clinic.cat)