

ORIGINAL

Prevalence of Asthma and Severity of Allergic Rhinitis Comparing 2 Perennial Allergens: House Dust Mites and *Parietaria judaica* Pollen

A Sala-Cunill,^{1,2} J Bartra,³ G Dalmau,⁴ R Tella,⁵ E Botey,⁶ E Raga,⁷ A Valero,³
on behalf of *#

¹Allergy Section, Internal Medicine Department, Hospital Universitari Vall d'Hebron, Universitat Autònoma de Barcelona, Barcelona, Catalonia, Spain

²Allergy Research Unit, Allergy Department, Institut de Recerca Vall d'Hebron, Universitat Autònoma de Barcelona, Barcelona, Spain

³Allergy Unit, Pneumology and Allergy Department, Hospital Clinic-IDIBAPS, Barcelona, Catalonia, Spain

⁴Allergy Unit, Hospital Universitari Joan XIII Tarragona, Catalonia, Spain

⁵Allergy Unit, Hospital Universitari Josep Trueta, Girona, Catalonia, Spain

⁶Allergy Unit, Hospital Universitari Dexeus, Barcelona, Catalonia, Spain

⁷Allergy Unit, Hospital Plató, Barcelona, Catalonia, Spain

*Comitè d'Al·lèrgia Respiratòria de Catalunya, Spain. O Asensio de la Cruz, JL Eserverri Asín, E Güell Figueras, R Muñoz, A Puiggròs Casas, A Roger Reig, MM San Miguel Moncín, A Torredemer Palau

#Researchers in alphabetic order: E Alcoceba, P Amat, M Baltasar, M Basagaña, V Cardona, M Cerdà, L Ferré, V Gàzquez, V Gonzalez, R Guspí, S Lara, M Lluch, Ll Marquès, N Rubira, M Rueda, R Serra, J Simón

■ Abstract

Background: Allergic rhinitis (AR) is an increasingly prevalent worldwide disease that has a considerable impact on quality of life and health care costs. Asthma and AR may be part of the same disease, with AR leading to an increased risk of asthma.

Objectives: To assess the prevalence of asthma in patients with AR due to house dust mites (HDMs) or *Parietaria judaica* and analyze the characteristics of asthma and AR in each group.

Methods: Cross-sectional, multicenter study with recording of demographic and clinical characteristics. All patients had AR confirmed by symptoms and a positive skin prick test to HDMs or *P. judaica*. They were classified according to the severity and frequency of AR following the Allergic Rhinitis and its Impact on Asthma (ARIA) and modified ARIA criteria and according to the severity of asthma following the Global Initiative for Asthma criteria.

Results: We studied 395 patients (226 in the HDM group and 169 in the *P. judaica* group) with a mean (SD) age of 43 (15.3) years. Using the modified ARIA criteria, we detected more severe and persistent AR in the *P. judaica* group than in the HDM group (44.5% vs 24.8%, $P < .001$). Nevertheless, there were no statistically significant differences between the groups in terms of the severity or prevalence (50% in HDM vs 47.9% in *P. judaica*, $P = .685$) of asthma.

Conclusion: AR due to *P. judaica* pollen, which behaves like a perennial allergen, is associated with the same prevalence of asthma and with more severe rhinitis than AR due to HDMs.

Key words: Rhinitis. Parietaria. House dust mite. Asthma. ARIA. GINA. Allergy. Pollen. Monosensitized.

■ Resumen

Antecedentes: La rinitis alérgica (RA) es una enfermedad de prevalencia creciente en todo el mundo, con un importante impacto en la calidad de vida, generando un elevado coste sanitario. La rinitis y el asma pueden ser consideradas como parte de una misma enfermedad y por tanto, la RA puede conducir a un incremento del riesgo de desarrollar asma.

Objetivos: Evaluar la prevalencia de asma en pacientes con RA por ácaros del polvo doméstico (APD) y en pacientes con RA por *Parietaria judaica* y evaluar las características de la rinitis y del asma en cada grupo.

Métodos: Estudio multicéntrico, transversal. Se registraron las características demográficas y clínicas de todos los pacientes. Todos los pacientes tenían RA confirmada por síntomas y pruebas positivas a APD o a *Parietaria judaica*. Los pacientes se clasificaron según la gravedad y la frecuencia de la rinitis siguiendo los criterios del ARIA y ARIA modificada y la gravedad del asma según los criterios de la GINA.

Resultados: Se incluyeron un total de 395 pacientes, 226 en el grupo de APD y 169 en el grupo de la *Parietaria judaica*, con una media de edad de $43 \pm 15,3$ años. La clasificación ARIA modificada nos permitió detectar que el grupo de *Parietaria* presentaba una rinitis más persistente y grave comparado con el grupo de APD (44,5% versus 24,8%, $p < 0,001$). Sin embargo, no se obtuvieron diferencias estadísticamente significativas entre la gravedad y la prevalencia (50% en APD vs 47,9% en *Parietaria*, $p = 0,685$) del asma en los dos grupos.

Conclusiones: La RA por polen de *Parietaria judaica*, que se comporta como un alérgeno perenne, puede causar la misma prevalencia de asma y una rinitis más grave que APD.

Palabras clave: Rinitis. Parietaria. Ácaros del polvo doméstico. Asma. ARIA. GINA. Alergia. Polen. Monosensibilizado.

Introduction

Allergic rhinitis (AR) is a symptomatic disorder of the mucous membrane of the nose induced by an immunoglobulin (Ig) E-mediated inflammation of the membranes lining the nose following allergen exposure [1].

AR has a considerable impact on quality of life and social and health care costs, and is becoming increasingly prevalent worldwide [2]. Between 10% and 25% of the world's population has AR, and in Spain, the figure is 22%. The figures for the prevalence of asthma are 1% to 6% in the world and 6% in Spain [1,3,4].

In recent years, many studies have suggested that AR and asthma may be part of the same disease and that AR may be associated with an increased risk of asthma [5-11]. It has been shown that between 20% and 50% of patients with AR have asthma [12,13].

In Spain, the most prevalent allergens are house dust mites (HDMs) and pollen. *Parietaria judaica* is the fourth most common pollen in the Mediterranean area and can be considered a perennial allergen as it causes hay fever from February through to November. The prevalence of sensitization to HDMs and pollen in patients with AR in Spain is 40% and 52% respectively; 7% of pollen-allergic patients are sensitized to *P judaica* [4].

Few studies have assessed the prevalence of asthma in patients with AR, but a multicenter, cross-European study by Leynaert et al [14] found that 22% and 16% of patients with AR due to HDMs and pollen, respectively, have asthma. To our knowledge, no studies have assessed or compared the prevalence of asthma in patients with rhinitis due to HDMs or the perennial allergen *P judaica* [15].

Although the prevalence and burden of AR is increasing, there is a lack of recent epidemiological data for Spain. One recent study examined the profile and treatment of Spanish patients with AR due to grass pollens and HDMs [16], but no studies have compared a perennial pollen with HDMs using the original and modified Allergic Rhinitis and its Impact on Asthma (ARIA) classification.

The aim of the present study was to assess and compare the prevalence of asthma in patients with AR due to HDMs and *P judaica*, with a focus on clinical characteristics.

Methods

Study Design and Ethics

An observational cross-sectional multicenter study was performed. All adult patients attending allergy departments at different centers in Catalonia, Spain from January 2009 to January 2010, with a diagnosis of AR due to HDMs or *P judaica*, were included. Allergy specialists were randomly selected from public and private clinics throughout Catalonia and asked to participate in the study.

The specialists who agreed to participate were asked to recruit the first 15 patients who met the following inclusion criteria: an age of between 18 and 65 years, first consultation (with the investigator), a suspected diagnosis of AR (with or without asthma) due to *P judaica* or HDMs based on clinical presentation and prior history, and allergic sensitization confirmed by a positive skin prick test and/or specific IgE levels of over 0.7 kU/L to *Dermatophagoides* species or *P judaica*. The study did not interfere with the patients' normal care.

Data were collected using a standard form, and subsequently entered into a database for statistical processing. All patients signed an informed consent form. The study was evaluated and approved by the ethics committee at Hospital Universitari Joan XXIII, in Tarragona, Catalonia.

Demographic Characteristics and Atopic Features

For each patient, age, sex, nationality, place of birth, place of residence, and personal and first-degree family history of atopic diseases (atopic dermatitis, rhinitis, asthma, urticaria, food allergy, hymenoptera allergy, mastocytosis, and angioedema) were recorded, and a thorough medical history taken.

Skin Prick Tests

Thirteen aeroallergens (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, platanus, olive, cypress, grass, *P. judaica*, dog and cat dander, ragweed, birch, *Alternaria alternata* and *Chenopodium album*) from Leti, S.A (Spain), all standardized using biological units and representing the most relevant inhalant allergens in AR and asthma according to previous reports from Spain [17] were used for skin prick tests in all the centers that participated in this study. A prick test was considered positive when the patient developed a wheal larger than a histamine wheal or larger than 3 × 3 mm. Patients with a positive skin prick test to both HDMs and *P. judaica* were excluded.

Clinical relevance was measured in patients who presented symptoms following exposure to high concentration of these allergens, HDM and *P. judaica*.

Diagnosis of Allergic Rhinitis

A diagnosis of AR was established when patients had a positive skin prick test with clinically relevant symptoms to *P. judaica* or HDMs. The investigators assigned the frequency and severity of symptoms according to the original [1] and modified [7] ARIA classification systems.

Diagnosis of Asthma

Asthma was diagnosed based on the criteria of the Global Initiative for Asthma (GINA) [18]. All patients with asthma were then classified using the GINA definitions.

Statistical Analysis

Data were collected and analyzed with SPSS version 17 (SPSS Inc). The sample size was calculated to achieve a precision of 5% with a 95% CI. Continuous variables are reported as means (SD). Categorical data were compared as the number of cases and percentages using the χ^2 and Fisher exact tests. A *P* value of .05 or lower indicates statistical significance.

Results

Patients Characteristics

A total of 395 patients (61.6% women and mean [SD] age of 43 [15.3] years) were included. The sociodemographic characteristics are shown in Table 1. Men and women were evenly represented across all groups.

Twenty-nine specialists agreed to participate in the study. These investigators provided data for 435 patients (15 patients per specialist), although after validation of the data, 395 patients had evaluable data (40 patients were excluded for not meeting the inclusion criteria). Seventy-nine percent of the patients were recruited from public clinics. Fourteen private and public clinics participated in the study. All regions of Catalonia were represented: 53% of patients were from Barcelona, 27% from Tarragona, 11% from Lleida, and 9% from Girona.

AR due to HDMs was more common in younger patients (18-44 years) than in older patients (45-65 years), with a statistically significant difference (70% vs 30%; *P*=.005), whereas AR due to *P. judaica* was more common in older patients (64% vs 36%, *P*=.001).

Patients living in an urban location had a significantly higher frequency of AR to HDMs (62%) than to *P. judaica* (36%) (*P*=.003). Conversely, *P. judaica* sensitization was more common in patients living in a rural environment (*P*=.002).

Most of the patients (80.7%) were monosensitized, as shown in Table 1.

AR Characteristics According to the ARIA classification

The characteristics of AR according to the ARIA classification are summarized in Table 2. In both groups, moderate-severe persistent AR was the most common type of rhinitis. However, in the *P. judaica* group, the proportion of patients with this type of AR was significantly higher than in the HDM group (*P*<.001).

Table 1. Patients' Sociodemographic Characteristics^a

	All Patients (n=395)	Patients Sensitized to House Dust Mites (n=226)	Patients Sensitized to <i>Parietaria Judaica</i> (n=169)	<i>P</i> Value
Sex				
Male	152 (38.4)	88 (39)	64 (38)	.795
Female	243 (61.6)	138 (61)	105 (62)	.695
Age, y				
18-44	218 (55.2)	158 (70)	60 (36)	.005
45-65	177 (44.8)	68 (30)	109 (64)	.001
Residence				
Urban	201 (50.8)	140 (62)	61 (36)	.003
Rural	194 (49.2)	86 (38)	108 (64)	.002
Monosensitized	319 (80.7)	190 (84)	129 (76)	.098

^aData are shown as number (%) of patients unless otherwise specified.

Table 2. Characteristics of Allergic Rhinitis According to ARIA Classification^a

	All Patients (n=395)	Patients Sensitized to House Dust Mites (n=226)	Patients Sensitized to <i>Parietaria Judaica</i> (n=169)	P Value
Frequency of symptoms				
Intermittent	148 (37.4)	99 (43.8)	49 (28.9)	< .001
Persistent	247 (62.5)	127 (56.2)	120 (71.1)	.002
Severity of symptoms				
Mild	108 (27.4)	79 (34.9)	29 (17.1)	<.001
Moderate/severe	287 (72.6)	147 (65.1)	140 (82.9)	<.001
Frequency and severity of symptoms				
Mild intermittent	32 (8.1)	20 (8.8)	12 (6.9)	.059
Mild persistent	76 (19.3)	59 (26.2)	17 (10.1)	<.001
Moderate/severe intermittent	107 (27.3)	70 (30.9)	37 (22)	<.001
Moderate/severe persistent	180 (45.7)	77 (34.1)	103 (61)	<.001

Abbreviation: ARIA, Allergic Rhinitis and its Impact on Asthma.

^aData are shown as number (%) of patients unless otherwise specified.

Table 3. Characteristics of Allergic Rhinitis According to the Modified ARIA Classification^a

	All Patients (n=395)	Patients Sensitized to House Dust Mites (n=226)	Patients Sensitized to <i>Parietaria Judaica</i> (n=169)	P Value
Frequency of symptoms				
Intermittent	148 (37.4)	99 (43.8)	49 (28.9)	<.001
Persistent	247 (62.5)	137 (56.2)	120 (71.1)	.002
Severity of symptoms				
Mild	108 (27.4)	79 (34.9)	29 (17.1)	<.001
Moderate	129 (32.6)	72 (31.9)	57 (33.8)	.089
Severe	158 (40)	75 (33.2)	83 (49.1)	<.001
Frequency and severity of symptoms				
Mild intermittent	32 (8.1)	20 (8.8)	12 (6.9)	.059
Mild persistent	76 (19.3)	59 (26.2)	17 (10.1)	<.001
Moderate intermittent	89 (22.5)	60 (26.5)	29 (17.1)	<.001
Moderate persistent	40 (10.2)	12 (5.3)	28 (16.6)	<.001
Severe intermittent	27 (6.8)	19 (8.4)	8 (4.8)	.094
Severe persistent	131 (33.1)	56 (24.8)	75 (44.5)	<.001

Abbreviation: ARIA, Allergic Rhinitis and its Impact on Asthma.

^aData are shown as number (%) of patients unless otherwise specified.

AR Characteristics According to the Modified ARIA Classification

The characteristics of AR according to the modified ARIA classification are summarized in Table 3. When patients were classified according to the severity of symptoms, there were no differences between the 2 groups in terms of the prevalence of moderate AR, but in the *P. judaica* group severe symptoms were significantly more common than in the HDM group ($P<.001$).

However, when we separated both groups taking into account the frequency and severity of symptoms, severe persistent AR was the most common type of AR in the *P. judaica* group, with a statistically significant difference compared with the HDM group ($P<.001$). By contrast, moderate intermittent AR was the most common type of AR in the HDM group, and was significantly more common than in the *P. judaica* group ($P<.001$).

Table 4. Prevalence and Severity of Asthma According to the Global Initiative for Asthma Criteria^a

	All Patients (n=395)	Patients Sensitized to House Dust Mites (n=226)	Patients Sensitized to <i>Parietaria Judaica</i> (n=169)	<i>P</i> Value
Asthma diagnosis	194 (49.1)	113 (50)	81 (47.9)	.685
Severity of asthma				
Intermittent	125 (64.5)	70 (61)	55 (67.7)	.456
Mild persistent	48 (24.8)	29 (26.5)	19 (23.3)	.208
Moderate persistent	16 (8.2)	11 (9.8)	5 (6)	.087
Severe persistent	5 (2.5)	3 (2.7)	2 (3)	.567
Prevalence of asthma according frequency and severity of rhinitis				
Mild Intermittent rhinitis	28 (7.1)	23 (20.3)	5 (6.2)	.002
Moderate/severe intermittent rhinitis	45 (11.3)	26 (23)	19 (23.5)	.765
Mild persistent rhinitis	17 (4.4)	10 (8.8)	7 (8.6)	.853
Moderate/severe persistent rhinitis	104 (26.3)	54 (47.9)	50 (61.7)	.035

^aData are shown as number (%) of patients unless otherwise specified.

Prevalence of Asthma and Characteristics

Overall, 194 patients (49.1%) were diagnosed with asthma according to the GINA criteria. The characteristics of the severity of asthma according to these criteria are shown in Table 4. There were no statistically significant differences between the 2 groups in terms of the prevalence of asthma (50% in the HDM group vs 47.9% in the *P. judaica* group, $P=.685$) or the severity (Table 4).

Nevertheless, asthma was more common in patients with persistent and moderate/severe AR in both groups (26.3%), as shown in Table 4, but the differences were not significant when compared with the prevalence of asthma in patients with other types of AR ($P=.058$).

Discussion

In this study of 395 patients seen by specialists throughout Catalonia, Spain, we observed that 50% of 226 patients with AR due to HDMs and 47.8% of 169 patients with AR due to *P. judaica* had asthma.

To our knowledge, this is the first study to compare the prevalence of asthma and the characteristics of AR between patients with AR due to HDMs or a perennial pollen such as *P. judaica*. We also believe it to be the first study to compare the characteristics of AR according to both the original and the modified ARIA classification systems, thereby adding value to our study. We observed that assessing the severity of AR using the modified ARIA system provided more information and different results. The most common type of AR according to the original ARIA classification in both groups was moderate/severe persistent AR (34.1% in the HDM group and 61% in the *P. judaica* group), but using the modified ARIA system, it

was severe persistent AR (44.5%) in the *P. judaica* group and moderate intermittent rhinitis in the HDM group (26.5%). These results highlight the importance of assessing the characteristics of AR using both systems.

Although few studies have assessed the prevalence of asthma in AR patients or compared AR due to HDMs and AR due to seasonal pollens, it is well known that indoor allergens are more closely associated with a higher prevalence of asthma than pollens. In a recent Spanish study by Valero et al [16] comparing AR due to grass pollen and due to HDMs, while no statistically significant differences were observed between the frequency and severity of rhinitis in the 2 groups, the prevalence of asthma was higher in the HDM group than in the grass pollen group. The authors also observed that rural residence was more closely associated with grass pollen allergy and that urban residence was more closely associated with HDM allergy. A study published by Boulet et al [19] also described the prevalence of rhinitis and asthma in patients with sensitization to indoor allergens (HDMs and molds) and pollens (grass, tree and ragweed). In the pollen allergy group, 74% of patients had rhinitis, 14% had asthma, and 12% had both rhinitis and asthma. In the indoor allergen group, the respective percentages were 55%, 27%, and 24%. In another multicenter, cross-European study by Leynaert et al [12], 22% of patients with AR due to HDMs had asthma compared with 16% of those with AR due to pollen (grass, ragweed, birch, olive, *P. judaica*). Leynaert et al also observed that the percentage of monosensitized patients was very low: 8.2% in the HDM group and 8.4% in the pollen group. The value of the findings from our study is greater, because most of the patients (80%) were monosensitized. In another study, by Arshad et al [20], the prevalence of asthma was 50% in patients with AR due to HDM and 32% in those with AR due to grass pollen. The above data are consistent with our finding that 50%

of patients with AR due to HDMs had asthma. Nevertheless, we detected a higher prevalence of asthma in our pollen group, possibly because the other studies analyzed seasonal pollens, while we analyzed *P judaica*, which behaves like a perennial allergen and can produce more severe and persistent rhinitis.

The results of our study support findings from other studies that have shown that patients with persistent and severe rhinitis have an increased risk of asthma. In a study by Leynaert et al [14], the risk of asthma was found to be highest (odds ratio=11) in patients with perennial AR. In another prospective study spanning 10 years, Linna et al [21] found that 19% of all children had asthma and that this disease was significantly more common in patients with persistent AR than in those with seasonal AR ($P<.01$). Marogna et al [22] also found that patients with moderate/severe AR (22%) had a higher prevalence of asthma compared with those with mild AR (11.6%).

The above findings support the theory that AR and asthma may be part of the same disease, with severe AR resulting in an increased risk of asthma, as has been described in many studies [12, 22-25].

Methodological limitations inherent to the study design must be pointed out. The first is selection bias. We included patients with AR from all parts of Catalonia, but the majority of patients from Girona, Lleida, and Tarragona were from public hospitals while those from Barcelona were from public and private clinics. The highest proportion of patients with AR due to *P judaica* was in Tarragona and Girona while the lowest proportion was in Barcelona. Therefore the groups might not be homogeneous in terms of disease severity. Another limitation is that not all patients were monosensitized. However, in the 19% of patients who were sensitized to other pollens, the effects were not clinically relevant. Finally, the lack of a statistically significant difference between the prevalence of asthma in patients with AR due to HDM or *P judaica* ($P=0.058$) might be due to the small size of the groups analyzed. The results, however, possibly indicate a tendency towards an association between severe rhinitis and a higher prevalence of asthma.

In summary, AR due to *P judaica*, a pollen that behaves like a perennial allergen, is associated with a similar prevalence of asthma as AR due to HDMs and with more severe rhinitis.

Acknowledgments

This work was supported by the Catalan Society of Allergy and Clinical Immunology (SCAIC) and the Spanish Ministry of Science and Innovation, Instituto de Salud Carlos III (grant CM09/00212 to ASC). We also thank Anthony Curran and Adrian Curran for English language editing.

References

- Bousquet J, Van Cauwenberge P, Khaltaev N. Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol*. 2001,108:S147-334.
- Canonica GW, Bousquet J, Mullol J, Scadding GK, Virchow JC. A survey of the burden of allergic rhinitis in Europe. *Allergy*. 2007,62 Suppl 85:17-25.
- Bauchau V, Durham SR. Prevalence and rate of diagnosis of allergic rhinitis in Europe. *Eur Respir J*. 2004,24:758-64.
- Alergológica 2005. Factores epidemiológicos, clínicos y socioeconómicos de las enfermedades alérgicas en España en 2005. SEAIC. Madrid; 2006.
- Koh YY, Kim CK. The development of asthma in patients with allergic rhinitis. *Curr Opin Allergy Clin Immunol*. 2003,3:159-64.
- Bousquet J, Van Cauwenberge P, Bachert C, Canonica GW, Demoly P, Durham SR, Fokkens W, Lockey R, Meltzer EO, Mullol J, Naclerio RM, Price D, Simons FE, Vignola AM, Warner JO; European Academy of Allergy and Clinical Immunology (EAACI); Allergic Rhinitis and its Impact on Asthma (ARIA). Requirements for medications commonly used in the treatment of allergic rhinitis. *European Academy of Allergy and Clinical Immunology (EAACI), Allergic Rhinitis and its Impact on Asthma (ARIA)*. *Allergy*. 2003,58:192-7.
- Valero A, Ferrer M, Sastre J, Navarro AM, Monclus L, Martí-Guadano E, Herdman M, Dávila I, Del Cuervo A, Colás C, Baró E, Antépara I, Alonso J, Mullol J. 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.
- Bousquet PJ, Combescure C, Neukirch F, Klossek JM, Mechin H, Dures JP, Bousquet J. Visual analog scales can assess the severity of rhinitis graded according to ARIA guidelines. *Allergy*. 2007,62:367-72.
- Ciprandi G, Cirillo I. The lower airway pathology of rhinitis. *J Allergy Clin Immunol*. 2006,118:1105-1109.
- Serrano C, Valero A, Picado C. Rhinitis and asthma: one airway, one disease. *Arch Bronconeumol*. 2005,41:569-578.
- Leynaert B, Neukirch C, Kony S, Guenegou A, Bousquet J, Aubier M, Neukirch F. Association between asthma and rhinitis according to atopic sensitization in a population-based study. *J Allergy Clin Immunol*. 2004,113:86-93.
- Leynaert B, Neukirch F, Demoly P, Bousquet J. Epidemiologic evidence for asthma and rhinitis comorbidity. *J Allergy Clin Immunol*. 2000,106:S201-205.
- Bousquet J, Vignola AM, Demoly P. Links between rhinitis and asthma. *Allergy*. 2003,58:691-706.
- Leynaert B, Bousquet J, Neukirch C, Liard R, Neukirch F. Perennial rhinitis: An independent risk factor for asthma in nonatopic subjects: results from the European Community Respiratory Health Survey. *J Allergy Clin Immunol*. 1999,104:301-4.
- Bozkurt B, Karakaya G, Kalyoncu AF. Seasonal rhinitis, clinical characteristics and risk factors for asthma. *Int Arch Allergy Immunol*. 2005,138:73-9.
- Valero A, Justicia JL, Anton E, Dordal T, Fernandez-Parra B, Lluch M, Montoro J, Navarro AM. Epidemiology of allergic rhinitis caused by grass pollen or house-dust mites in Spain. *Am J Rhinol Allergy*. 2011,25:e123-8.
- Crystal-Peters J, Crown WH, Goetzel RZ, Schutt DC. The cost of productivity losses associated with allergic rhinitis. *Am J Manag Care*. 2000,6:373-8.
- Bousquet J. Global initiative for asthma (GINA) and its objectives. *Clin Exp Allergy*. 2000,30 Suppl 1:2-5.
- Boulet LP, Turcotte H, Laprise C, Lavertu C, Bedard PM, Lavoie A, Hébert J. Comparative degree and type of sensitization to common indoor and outdoor allergens in subjects with allergic rhinitis and/or asthma. *Clin Exp Allergy*. 1997,27:52-9.

20. Arshad SH, Tariq SM, Matthews S, Hakim E. Sensitization to common allergens and its association with allergic disorders at age 4 years: a whole population birth cohort study. *Pediatrics*. 2001,108:E33.
21. Linna O, Kokkonen J, Lukin M. A 10-year prognosis for childhood allergic rhinitis. *Acta Paediatr*. 1992,81:100-2.
22. Marogna M, Falagiani P, Bruno M, Massolo A, Riva G. The allergic march in pollinosis: natural history and therapeutic implications. *Int Arch Allergy Immunol*. 2004,135:336-42.
23. 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.
24. Bugiani M, Carosso A, Migliore E, Piccioni P, Corsico A, Olivieri M, Ferrari M, Pirina P, de Marco R; ISAYA (ECRHS Italy) Study Group. Allergic rhinitis and asthma comorbidity in a survey of young adults in Italy. *Allergy*. 2005,60:165-70.
25. Annesi-Maesano I. Epidemiological evidence of the occurrence of rhinitis and sinusitis in asthmatics. *Allergy*. 1999,54 Suppl 57:7-13.

■ *Manuscript received August 2, 2012; accepted for publication, October 9, 2012.*

■ **Anna Sala Cunill**

Paseo Vall d'Hebron 119-129
08035 Barcelona, Spain
E-mail: annasala7@gmail.com