

Validation of ARIA (Allergic Rhinitis and its Impact on Asthma) classification in a pediatric population: The PEDRIAL study

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Abstract

Allergic rhinitis (AR) is the commonest chronic disease in children. Allergic Rhinitis and its Impact on Asthma (ARIA) classification based on symptom duration (intermittent vs. persistent) and severity (mild vs. moderate/severe) has not been yet validated in children. Thus our objective was to validate ARIA classification in children, after determining the severity and duration of AR in a pediatric population, using ARIA definitions. Children aged 6–12 with a diagnosis of AR were included in an observational, cross-sectional, multicenter study. Patients were classified according to ARIA guidelines. AR symptoms were assessed using the Total Four Symptoms Score (T4SS). Severity was also evaluated by the patient using a visual analogue scale (VAS). Comparisons were made by means of a statistical analysis. One thousand two hundred and seventy-five children from 271 centers were included. Among them, 59.5% had intermittent and 40.5% persistent AR, while 60.7% seasonal and 39.3% perennial according to dated classification, with significant differences existing between one classification and another; 89.7% had moderate/severe rhinitis. Significantly higher T4SS and VAS scores were obtained in moderate/severe compared to mild AR. In our experience, the current ARIA classification can be considered a valid tool also in children from 6- to 12-yr old.

Allergic rhinitis (AR), even though probably under-diagnosed, is the most common chronic disease in childhood with a prevalence in some regions of up to 40% (1), and it is proven to have a significant impact on children's cognitive performance and quality of life (QoL) (2). The Allergic Rhinitis and its Impact on Asthma (ARIA) recommendations, updated recently (3), proposed a new classification for AR based on duration profile (intermittent/persistent) rather than on seasonal profile, and a further grading of severity (mild and moderate/severe), according to symptom intensity and impairment in patient's QoL. Previous studies in adults have validated ARIA proposals for AR grading (4–6).

Children suffering from AR have also a measurable impairment in health-related QoL (7), demonstrated by decreased school performance, sleep disturbances, emotional

and other psychosocial problems (8, 9). It seems demonstrated that patients with AR managed through a scheme based on international guidelines achieve a significant improvement in symptoms and health-related QoL compared to those evaluated and treated with a non-standardized scheme (10). A proper stepwise approach to children with AR is vital to optimize the risk/benefit ratio of any therapeutic intervention and avoid comorbidities (11, 12). However, to the best of our knowledge, the new ARIA classification has not been validated in children.

The aim of this work was to determine the severity and duration of AR in a pediatric population using ARIA definitions, and to validate this updated classification in children aged 6–12 yr, by evaluating whether different severity degrees imply differences in symptom score or patient's self evaluation impairment.

Material and methods

Study design and patients

An epidemiological, multicenter, cross-sectional study was conducted in Spain, under circumstances of normal clinical practice. A total of 271 centers and 334 investigators (from allergy, otorhinolaryngology and pediatrics centers) participated in the study. Patients were recruited if they fulfilled the following inclusion criteria: (i) 6- to 12-yr old, (ii) a previous diagnosis of AR made by an allergist, (iii) a parental informed written consent, and (iv) children should have not received any treatment for their AR during the 2 wk preceding inclusion at least. Patients were considered suffering from AR if they had (i) suggestive symptoms of rhinoconjunctivitis within the two precedent years or more that should be related to skin prick test results and (ii) at least one positive skin prick test and/or serum-specific IgE to an aeroallergen locally relevant. The children were enrolled within a 3-month period between May and July 2008 and were recruited from all regions of Spain to avoid any geographic or seasonal influence. The study was approved by the Ethical Committee of Hospital Clinic of Barcelona, Spain.

Study outcomes

The case form reports were designed by a multidisciplinary group of expert allergists and ENT specialists from different regions of Spain and were fulfilled by the intervening physician. Demographic data (age, sex, height, and weight), place of residence, and household characteristics, as well as allergen sensitization profile, were obtained. The presence of comorbidities was also evaluated.

Duration of AR was classified according to ARIA guidelines as persistent (symptoms appearing more than 4 days a week and more than 4 wk) or intermittent (symptoms appearing <4 days a week or <4 wk) (3). 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: (i) sleep disturbance, (ii) impairment of daily activities, leisure, and/or sports, (iii) impairment of school performance, and (iv) bothersome symptoms (3). AR symptoms were assessed using the Total Four Symptoms Score (T4SS) by calculating the sum of scores for nasal obstruction, rhinorrhea, nasal itching, and sneezing. Each nasal symptom was scored on a scale from 0 to 3 (0, no symptoms; 1, mild; 2, moderate; 3, severe) resulting in a T4SS ranging from 0 to 12. Severity was also assessed by the patient by means of a visual analogue scale (VAS), from 0 to 100 mm.

Statistical methods

A descriptive analysis of the studied population – in terms of demographic characteristics and distribution of patients according to ARIA classifications – was performed. Statistical analysis included a comparison between different degrees of severity according to ARIA classification, total symptom's score (T4SS), and VAS.

Statistical analysis was carried out by Infocienia Clinical Research, S.L. (Barcelona, Spain), using SAS (Statistical Analysis System) program, version 9.1.3. (SAS Institute Inc., Cary, NC, USA). All variables to analyse were described for the total sample. The number of valid cases (N) was used in all tables, figures, or graphics, as well as in calculating percentages or any other statistical consideration. 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 every 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 0.05 was considered.

Results

Demographic characteristics of the patients

A total of 1275 valid case form reports were included in the study. Mean age of the patients was 9.05 (± 1.93) yrs. The population studied was homogeneous according to gender distribution (girls 41.3%), household characteristics, living environment, or mean body mass index (data not shown). The most frequent sensitizers were pollens (53.2%) and house dust mites (43.5%). The most frequent comorbidities were conjunctivitis (53.6% of children), asthma (49.5%), and atopic dermatitis (40%). The mean duration of AR was 2.54 ± 2.38 yr.

Classification of AR

Classifications of AR according to ARIA guidelines and allergen based are presented in Table 1. Almost 60% of patients suffered from intermittent rhinitis. Most patients suffered from moderate/severe rhinitis. The most frequent forms of AR were moderate/severe intermittent (52.1%) followed

Table 1 Classification of AR following seasonal/perennial classification and following ARIA guidelines in patients aged 6–12 yr*

ARIA classification [n (%)]	Seasonal/perennial classification [n (%)]	
	Seasonal 767 (60.7)	Perennial 497 (39.3)
Intermittent 756 (59.5)	591 (77.1)	159 (32.1)
Persistent 515 (40.5)	176 (22.9)	336 (67.9)

AR, allergic rhinitis; ARIA, Allergic Rhinitis and its Impact on Asthma.

*Chi-squared test $p < 0.0001$ for comparison between ARIA and seasonal/perennial classifications.

Table 2 Concordance of VAS and T4SS with duration and severity of children with AR following ARIA classification

Variable	Intermittent/mild	Intermittent/mod/severe	Persistent/mild	Persistent/mod/severe	p-Value*	Correlation
VAS score						0.45007
N	77	634	39	462	<0.0001	
Mean (SD)	11.48 (11.70)	36.46 (24.14)	12.33 (13.35)	46.31 (24.34)		
Median	10.00	35.00	8.00	47.00		
(P25; P75)	(2.00; 17.00)	(17.00; 52.00)	(2.00; 15.00)	(28.00; 65.00)		
T4SS						
N	88	646	40	466	<0.0001	
Mean (SD)	2.99 (2.14)	6.06 (2.76)	3.70 (2.68)	7.07 (2.48)		
Median	3.00	6.00	3.00	7.00		
(P25; P75)	(2.00; 4.00)	(4.00; 8.00)	(1.50; 6.00)	(6.00; 9.00)		

AR, allergic rhinitis; ARIA, Allergic Rhinitis and its Impact on Asthma; T4SS, Total Four Symptoms Score; VAS, visual analogue scale; SD, standard deviation; (P25; P75), percentile 25 and percentile 75.

*Kruskal–Wallis test.

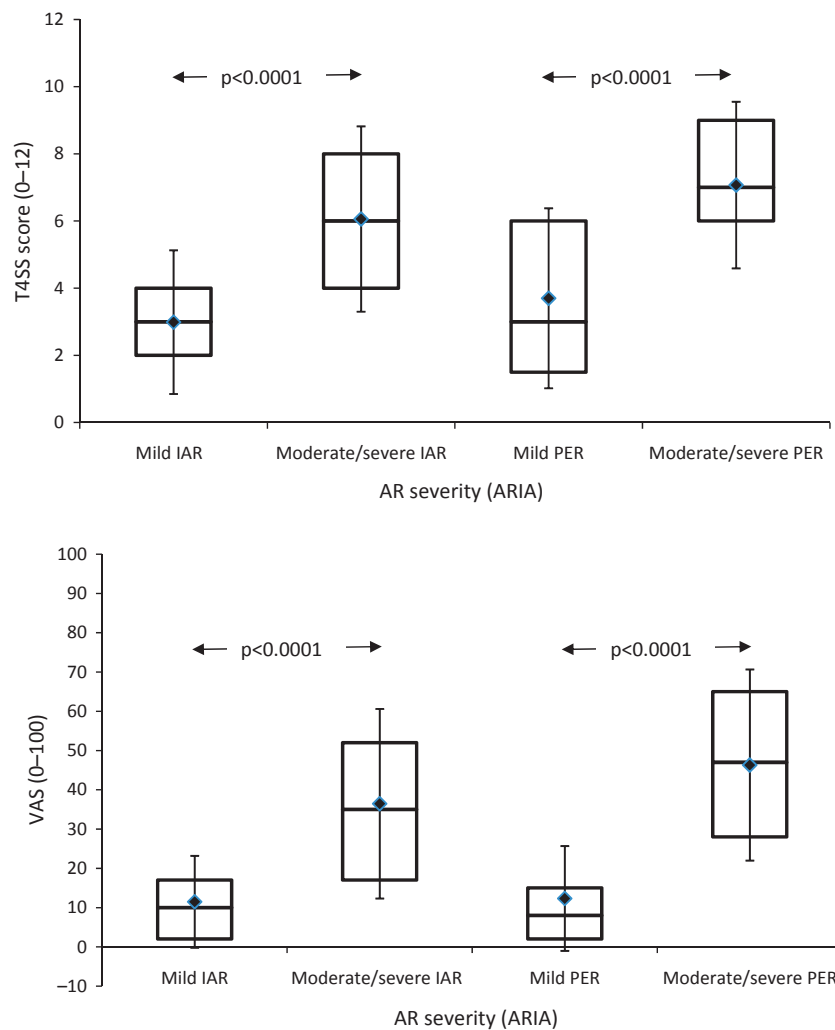


Figure 1 Allergic rhinitis severity assessed using visual analogue scale and T4SS in children classified using ARIA criteria. Data are expressed in median and 25–75 percentiles (boxes) and mean and

standard deviation (diamonds and error bars). ARIA, Allergic Rhinitis and its Impact on Asthma; T4SS, Total Four Symptoms Score.

Table 3 Individual symptoms in children with AR classified according to ARIA guidelines

Variable	Intermittent/mild	Intermittent/mod/severe	Persistent/mild	Persistent/mod/severe	p-Value*
Sneezing					
N	75	599	37	457	<0.0001
Mean (SD)	0.80 (0.96)	1.68 (0.93)	0.95 (0.97)	1.79 (0.89)	
Median	0.00	2.00	1.00	2.00	
(P25; P75)	(0.00; 2.00)	(2.00; 2.00)	(0.00; 2.00)	(2.00; 2.00)	
Rhinorrhea					
N	87	637	40	462	<0.0001
Mean (SD)	0.83 (0.65)	1.56 (0.85)	1.05 (0.75)	1.74 (0.87)	
Median	1.00	2.00	1.00	2.00	
(P25; P75)	(0.00; 1.00)	(1.00; 2.00)	(0.50; 2.00)	(1.00; 2.00)	
Nasal itching					
N	88	636	40	465	<0.0001
Mean (SD)	0.80 (0.78)	1.46 (0.83)	0.93 (0.76)	1.65 (0.86)	
Median	1.00	1.00	1.00	2.00	
(P25; P75)	(0.00; 1.00)	(1.00; 2.00)	(0.00; 1.50)	(1.00; 2.00)	
Nasal obstruction					
N	86	638	39	462	<0.0001
Mean (SD)	0.71 (0.78)	1.55 (0.91)	0.87 (0.77)	1.96 (0.89)	
Median	1.00	2.00	1.00	2.00	
(P25; P75)	(0.00; 1.00)	(1.00; 2.00)	(0.00; 1.00)	(1.00; 3.00)	

AR, allergic rhinitis; ARIA, Allergic Rhinitis and its Impact on Asthma; SD, standard deviation; (P25; P75), percentile 25 and percentile 75.

*Kruskal–Wallis test.

by moderate/severe persistent (37.6%), mild intermittent (7.1%), and mild persistent (3.2%) rhinitis. When patients were classified according to their seasonal or perennial pattern, almost two-thirds of patients suffered from seasonal rhinitis. And when both classifications were compared, a significant difference was observed between them ($p < 0.0001$), indicating that they are not equivalent and cannot be interchanged (Table 1).

Usefulness of ARIA up-to-date classification in children

Considering duration/severity grades, VAS scores and T4SS showed a significant correlation (correlation coefficient 0.45; $p < 0.0001$) (Table 2). To evaluate if ARIA classification was able to accurately discriminate between the four different duration/severity grades in children, we performed an analysis of T4SS and VAS score in the different categories. Significant differences on both T4SS and VAS were obtained between intermittent and persistent AR, as well as between mild and moderate/severe AR (Fig. 1). Furthermore, we observed that symptoms assessed using T4SS were significantly different among the diverse ARIA categories (Table 3), thus remarking their usefulness in grading AR for children.

Usefulness of seasonal/perennial classification in children

In the case of the allergen-based classification for AR, VAS and T4SS showed no significant differences between seasonal and perennial AR, reinforcing the evidence that this classification is not able to categorize properly children suffering

from AR (Table 4). In addition, individual symptoms were not able to discriminate between seasonal and perennial AR, except for the variable nasal obstruction (Table 5).

Discussion

The ARIA guidelines were developed by the World Health Organization to establish an evidence-based protocol for the treatment of AR. Considered a useful point of reference for physicians who treat both adults and children with AR, guidelines have been updated recently (3). Among ARIA

Table 4 Concordance of VAS score and T4SS with allergen-based classification of AR

Variable	Seasonal AR	Perennial AR	p-Value*
VAS score			
N	750	489	0.0597
Mean (SD)	35.89 (25.27)	38.74 (25.69)	
Median	34.0	36.0	
(P25; P75)	(13.0; 54.0)	(17.0; 58.0)	
T4SS			
N	767	497	0.5339
Mean (SD)	6.05 (2.90)	6.14 (2.82)	
Median	6.0	6.0	
(P25; P75)	(4.0; 8.0)	(4.0; 8.0)	

AR, allergic rhinitis; T4SS, Total Four Symptoms Score; VAS, visual analogue scale; SD, standard deviation; (P25; P75), percentile 25; percentile 75.

*Mann–Whitney test.

Table 5 Symptoms in the classification of AR in children according to seasonal/perennial classification

Variable	Seasonal	Perennial	p-Value*
Sneezing			
N	719	474	0.2812
Mean (SD)	1.65 (0.96)	1.61 (0.95)	
Median	2.00	2.00	
(P25; P75)	(1.00; 2.00)	(1.00; 2.00)	
Rhinorrhea			
N	760	492	0.9156
Mean (SD)	1.54 (0.87)	1.54 (0.90)	
Median	2.00	2.00	
(P25; P75)	(1.00; 2.00)	(1.00; 2.00)	
Nasal itching			
N	759	496	0.6755
Mean (SD)	1.45 (0.88)	1.43 (0.86)	
Median	1.00	1.00	
(P25; P75)	(1.00; 2.00)	(1.00; 2.00)	
Nasal obstruction			
N	759	492	0.0236
Mean (SD)	1.55 (0.94)	1.67 (0.99)	
Median	2.00	2.00	
(P25; P75)	(1.00; 2.00)	(1.00; 2.00)	

AR, allergic rhinitis; SD, standard deviation; (P25; P75), percentile 25 and percentile 75.

*Kruskal–Wallis test.

recommendations, a new classification for AR was proposed, given the fact that previous classifications dividing AR into seasonal, perennial, and occupational disease were not fully suitable. The new classification segregates AR according to the duration profile (intermittent/persistent) and severity (mild and moderate/severe), along with the symptom intensity and the impairment in patient's sleep, working, and leisure activities (3).

ARIA experts panel proposal for AR classification has been validated in adults through surveys on patients consult-

ing for AR in clinical practice (4, 5), and the discrimination between patients has been optimized by observational, cross-sectional studies comparing classification based on ARIA items with health-related QoL questionnaires (6).

As stated before, patients with AR managed through a scheme based on international guidelines have in fact a better outcome than those evaluated and treated with a non-standardized scheme (10). In children, ARIA advocates a similar stepwise approach to therapy as in adults, but with properly adjusted doses of pharmacological agents (3). Given the special attention that physicians should pay to any therapeutic intervention in the pediatric population, we think particularly important to accurately classify all children suffering from AR, to maximize therapy's efficacy while minimizing its adverse effects. In this sense, the results of our epidemiological survey on a total of 1275 questionnaires contribute to validate the new ARIA categorization in children aged 6–12.

In our sample, 59.5% of children with AR suffer from intermittent rhinitis and 40.5% from persistent rhinitis. Most (89.7%) of them were classified as moderate/severe, being intermittent moderate/severe AR (52.1%) the most common, followed by persistent moderate/severe AR (37.6%). Our results show that T4SS was significantly different among the diverse categories, with a direct correlation between scores and severity according to ARIA classification; in addition, each ARIA item had a significant discriminating capacity, what confirms the usefulness of the items selected by the ARIA panel in the classification and grading of AR. In the same way, results from VAS in mm adequately correlated with severity according to ARIA items. In other words, ARIA classification by itself was able to discriminate severity grades in children from 6- to 12-yr old in our study.

In addition, we have shown that allergen-based classification and ARIA classification of AR are different also in children from 6- to 12-yr old, and they cannot be interchanged, as already demonstrated in adults (5).

In conclusion, we consider the current ARIA classification as a valid tool also in children aged between 6 and 12 yr.

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