Original Article

Clinical Features of Allergic Rhinitis and Skin Prick Test Analysis Based on the ARIA Classification: A Preliminary Study in Malaysia

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Abstract

Introduction: Allergic rhinitis (AR) is a prevalent disease worldwide but is still underdiagnosed in many parts of Asia. We studied the clinical profiles of AR patients in our community based on the new ARIA classification and investigated the aetiological allergens using a skin prick test. Materials and Methods: In 2008, 142 newly diagnosed patients with AR were seen and underwent skin prick testing with 90 patients completing the study. Results: Intermittent mild and moderate/severe AR were evident in 10% and 21.1% of the patients, while persistent mild and moderate/severe were seen in 20% and 48.9%, respectively. Rhinitis and asthma co-morbidity occurred in 28.8% with asthma incidence significantly higher in persistent AR ($P = 0.002$). There was no significant association between AR severity, city living and asthma co-morbidity. Nasal itchiness and sneezing were the main presenting complaints and were more common in intermittent AR ($P < 0.05$). Sleep disturbance was associated with moderate-severe AR ($P < 0.05$). Polypoidal mucosa was associated with asthma co-morbidity ($P < 0.05$). Monosensitivity reaction occurred in 12.2% of patients and was associated with fungi sensitivity ($P < 0.05$). Majority of patients were oligosensitive (52.8%) and polysensitive (34.4%) and were significantly associated with moderate-severe persistent AR ($P < 0.01$). The highest positive skin prick reaction and the largest average wheal diameter were for the house dust mites and cat allergen ($P < 0.05$). Conclusion: Our results reflected the AR profiles in our country, which was comparable with typical profiles of the neighbouring country and other Mediterranean countries with a similar temperate climate.

Ann Acad Med Singapore 2010;39:619-24

Key words: Allergic rhinitis, ARIA classification, Malaysia, Skin prick test

Introduction

Allergic rhinitis (AR) is a common disease worldwide and is known to cause serious implications to the physical and mental health status of the individual sufferer. It also impacts significantly on healthcare expenditure. For instance, the direct costs of allergic rhinitis in the United States (US) alone were approximately 2.7 billion dollars a year.[1] Nearly 3.8 million days of both work and school were also lost annually due to the disease.[1]

Despite a major health and financial concern, AR is still underdiagnosed and undertreated in many countries.[2] Epidemiological data on the Asian population are sparse. In Malaysia, published studies only focused on a limited age group and there was no epidemiological study in accordance with the recent ARIA (Allergic Rhinitis and its impact on Asthma) classification.[3] The ARIA guidelines subdivide AR based on the duration/chronicity of symptoms (Intermittent for symptoms <4 days/week or <4weeks/year or Persistent for symptoms >4 days/week and >4 weeks/year) and grading of severity (mild when symptoms do not impair sleep, daily activities and work/school performance or moderate/severe when symptoms impair sleep, daily activities and work/school performance).[2,4] This new classification was found to yield better treatment outcomes for AR patients.[5]

Skin prick test is the most widely used and is regarded as the gold standard diagnostic test in allergy. We aimed to study the clinical profiles of AR patients in accordance with the new ARIA guidelines and to investigate

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common aetiological allergens in our community from a skin prick test.

Materials and Methods

The study was conducted over one year's duration (2008). The source population was from new patients attending the AR clinic in a tertiary referral hospital in Malaysia. All patients aged more than 18 years old with positive history of allergy (3 or more recurrent symptoms of rhinorrhea, sneezing, nasal blockage and nasal itchiness during the last 12 months) were invited to participate in the study. The patient's detailed history and nasal endoscopic examination were carried out, and another appointment was given for the skin prick test 2 weeks later. Those patients who are on antihistamines were asked to stop treatment at least one week prior to the skin prick test. Informed written consent was obtained from all patients. The study protocol was approved by the Research and Ethics Committee of the hospital.

Skin prick test were done by the same investigator. Eight common allergens in our community were used for the skin prick test, namely, Dermatophagoides pteronyssinus (house dust mite), Felis domesticus (domestic cat), Mucor mucedo (fungi), wheat flour, peanut, egg yolk, egg white and chicken meat. Numbered strips (2 cm apart) were applied onto the forearm area. Drops of selected allergen were then placed on the forearm skin next to the numbered strip. A sterile lancet (ALK-Abello skin prick test kit, Bege Alle, 2970 Horsholm, Denmark) was used to prick the skin gently through the drops of allergen. Excess allergen was then wiped off. Histamine (as positive control) and diluents (as negative control) were included in the test. After 20 minutes, the forearm skin was examined and the wheal and flare sizes were measured in 2 perpendicular directions. The presence of a wheal of at least 3 mm and flare of at least 10 mm larger than the negative control were regarded as a positive reaction. Patients with a negative skin prick test were excluded from the study.

The data obtained in this study were classified according to the ARIA guidelines and analysed using SPSS 13 software (Chicago, Illinois). The chi-square test or Pearson correlation was used whenever appropriate to evaluate statistical analysis, where *P* value of less than 0.05 was considered significant.

Results

A total of 142 new patients (90 females, 52 males) with AR were seen in the allergic clinic, HUSM in 2008. Out of this, 90 patients were enrolled into the study. Their age group ranged from 18 to 66 years old with the mean age of 32.6 years. Fifty-five patients (61.1%) are female. The majority of the study population were Malay, which account for 76.7% (n = 69), followed by Chinese at 15.6% (n = 14), Indian at 1.1% (n = 1) and others at 6.6% (n = 6). In terms of occupation, the majority of the study subjects (27.8%) were students, followed by housewives (24.4%), professional workers (13.4%), teachers (10%), retirees (5.6%) and the rest were either odd job workers or unemployed. Sixty-three (70%) of the patients were living in the urban area of Kota Bharu, a city with more than 300,000 total number of inhabitants.

Table 1 summarises the main clinical features of the patients. From history taking, 26 (28.8%) patients have a concomitant history of asthma and were on bronchodilator inhalers. Of these numbers, 24 of them had Persistent AR from the ARIA classification. Asthma co-morbidity was significantly associated with Persistent AR (*P* = 0.002).

Table 1. Clinical Characteristics of the Study Subjects (n = 90)

ARIA Classification		
Mild intermittent[a]	9	(10.0%)
Moderate-severe intermittent	19	(21.1%)
Mild persistent[b]	18	(20.0%)
Moderate-severe persistent	44	(48.9%)
Smoking status		
Active	13	(14.4%)
Former	5	(5.6%)
Never	72	(80%)
Associated morbidity		
Asthma	26	(28.8%)
Dermatitis	8	(8.8%)
Conjunctivitis	12	(13.3%)
Family history of atopy	49	(54.4%)
Trigger allergen (from history)		
Dust	83	(92.2%)
Food	44	(48.9%)
Air-conditioned room	20	(22.2%)
Domestic pet	20	(22.2%)
Drugs	13	(14.4%)
Symptoms		
Nasal itchiness	78	(86.7%)
Sneezing	74	(82.2%)
Rhinorrhea	62	(68.9%)
Nasal blockage	60	(66.7%)
Eye irritation	52	(57.8%)
Sleep disturbance	39	(43.3%)

[a]Intermittent: symptoms <4 days/week or <4 consecutive weeks
[b]Persistent: symptoms >4 days/week or >4 consecutive weeks

Table 2. Prevalence of the Clinical Symptoms According to ARIA Classification

Clinical symptoms	Intermittent (n = 28)		Persistent (n = 62)		Total (n = 90)
	Mild (n = 9)	Moderate-severe (n = 19)	Mild (n = 18)	Moderate-severe (n = 44)	
Nasal itchiness	9	19	16	34	78
Sneezing	9	19	12	34	74
Rhinorrhea	6	12	16	28	62
Nasal blockage	3	8	6	43	60
Eye irritation	8	18	6	20	52
Sleep disturbance	0	13	1	26	39

There was no significant association between AR severity and the presence of asthma (P >0.05). Twenty out of 26 patients were living in the city. However, there was no association between city living and AR with asthma co-morbidity (P = 0.361). More than half of the cases (n = 49 , 54.4%) had positive family history of atopy but there was no association seen between positive family history and the chronicity of AR (P = 0.89) or the severity of the disease (P = 0.22).

Eighty-three (92.2%) of the study subjects admitted that their allergic symptoms were triggered by exposure to a dusty environment. Forty-four patients (48.9%) have food allergies and 20 patients (22.2%) admitted to having an allergy triggered by contact with their domestic pets. The most common (97.7%) food type that triggered allergy was seafood-based particularly, prawn and anchovy sauce, followed by chicken-based food (meat, egg and paste). There was no association seen between the type of trigger allergen and the ARIA classification of the disease (P >0.05).

Nasal itchiness and sneezing were the two main clinical presentations. The mucosal irritation symptoms (nasal/eye itchiness and sneezing) were significantly more common in Intermittent AR (P <0.05) (Table 2). Sleep disturbances were reported mostly by patients with moderate-severe diseases, regardless of the persistent or intermittent types (P <0.001). Among the common endoscopic findings in our patients were inferior turbinate hypertrophy (75.6%), mucoid discharge (55%), mulberry turbinates (22%) and polypoidal nasal mucosa (16%). The presence of a polypoidal mucosa was significantly associated with asthma co-morbidity (P <0.05).

Table 3 summarises the distribution of skin prick test reactivity according to the ARIA classification. Majority fell into Persistent AR (62/90, 68.9%), with the highest within the moderate-severe group (44/90, 48.9%). Of the 90 patients, 12.2 % (n = 11) had positive skin reaction to one reagent (monosensitive) and the majority were those with sensitivity to Mucor mucedo (P <0.05). The majority of our subjects were in the oligosensitive group (53.3%, n = 48) and this comprised mainly of those who were sensitive to the house dust mites and cat (P <0.001). Statistical analysis also showed that the moderate-severe persistent group has the highest positive skin reaction to more than one reagent (oligo-polysensitive) (P <0.01).

Mean diameter of the wheal and the prevalence of positive skin prick test are shown in Table 4. The largest mean diameter was for the house dust mite (3.87 mm) and

Table 3. Distribution of Skin Prick Test Reactivity According to the ARIA Classification

ARIA classification	Positive skin prick test (n = 90)			Total
	One allergen (monosensitive)	2 allergen (oligosensitive)	3 or more allergen (polysensitive)	
Mild intermittent[a]	4	2	3	9 (10.0%)
Moderate-severe intermittent	4	10	5	19 (21.1%)
Mild persistent[b]	2	15	1	18 (20.0%)
Moderate-severe persistent	1	21	22	44 (48.9%)
Total	11 (12.2%)	48 (52.8%)	31 (34.4%)	90 (100%)

[a]Intermittent: symptoms <4 days/week or <4 consecutive weeks

[b]Persistent: symptoms >4 days/week or >4 consecutive weeks

χ^2:14.172, df 3(oligosensitive and polysensitive groups were evaluated as one), P <0.01 Monte Carlo Exact.

the smallest diameter was for the egg white (1.13 mm). The diameter of wheal is correlated with the positivity of the results (P <0.05). House dust mite yielded the highest number of positive results (80.0%), followed by cat (37.8%)

Table 4. Mean Diameter (mm) of Wheal in the Skin Prick Test and the Prevalence of Positive Skin Prick Results (n = 90)

Type of allergen	Wheal diameter Mean (SD)	Positive resultsn (%)	Significance
Cat	1.79 (1.14)	34 (37.8)	χ^2:4.373,df1, P <0.05
Wheat flour	1.39 (0.88)	18 (20.0)	P >0.05
House dust mite	3.87 (2.54)	72 (80.0)	χ^2:134.098,df1, P <0.001
Mucor mucedo	1.51 (0.99)	18 (20.0)	P >0.05
Peanut	1.22 (1.06)	23 (25.6)	P >0.05
Egg yolk	1.23 (0.94)	16 (17.8)	χ^2:5.776,df1, P <0.05
Egg white	1.13 (0.94)	16 (17.8)	χ^2:5.776,df1, P <0.05
Chicken meat	1.16 (0.78)	8 (8.9)	χ^2:19.369,df1, P <0.001

while chicken meat was the lowest at 8.9% (P <0.05).

Discussion

AR is a highly prevalent disease affecting 20% of the general population in developed countries.[6-8] AR is still under-diagnosed and under-treated in many parts of Asia despite a high prevalence of 18% to 44% proposed.[9,10] In Malaysia, a study in the paediatric community showed the overall incidence of rhinitis symptoms at 27%, with a significantly higher prevalence in the 12 to 14 year-old age group (38.2%) than in the 5 to 7 year-old age group (18.2%).[11] Subsequent study in the same population 6 years later found no major changes in the prevalence rate of AR, indicating that the disease remains at a high prevalence rate as before.[3] No data were found for the adult population with AR here. With our country gearing towards a developed nation, we may be facing a higher incidence of AR patients in the near future.

The present study was carried out in a tertiary referral hospital in the North-Eastern part of Malaysia, which caters for almost half a million of population. A total of 142 new adult patients were seen in the AR clinic throughout the year of study. Out of this number, 90 patients (63.4%) are female, reflecting a slight female predominance in our adult AR patients. There were not many studies which have looked into the gender preponderance of AR. A multi-centre epidemiological study showed that the prevalence is approximately equal between men and women.[12] However, they found that in children, AR is more common in boys than in girls. In the geriatric population, rhinitis is less commonly allergic in nature, supported by a study that showed the total and specific serum IgE was significantly decreased with age in 559 patients with atopy.[13] This probably explained why the majority of our AR patients fell into a younger age group with the mean age of 33 years.

The majority of the patients in this study were Malays (76.7%), followed by Chinese and Indians. However, these figures did not reflect the actual ethnic distribution of a predominant Malay race at 90% to 95% in the study area. Thus, the high number of Chinese patients with AR here may suggest that AR is also racially distributed, or otherwise it simply showed that the awareness to seek treatment is higher in the Chinese than the Malay patients. There is no such study yet in Malaysia that compares the racial distribution of the disease so no definitive conclusion can be made from this.

Environmental pollution can trigger the symptoms of AR, thus the type of occupation plays an important role in the control of the disease. The highest number of our patients was students. Students fall into a younger age group of below 25 years old, so a high number of students in this study can be explained by the higher prevalence of AR in the younger age group. Housewife was the second highest occupational group in our study sample. The majority of persistent aero-allergens in our environment were found indoors, and these housewives spent most of their time in the house hence they were more exposed to the allergens. Majority (70%) of our patients lived in the city. Here, although city living does not correlate to the chronicity and severity of our AR patients, other studies in the West have shown that rural residence was negatively correlated with allergen sensitivity, particularly to pollen.[14,15] The difference in the climate and seasonal changes may explain the discrepancy between our result and theirs.

AR and allergic asthma are both atopic diseases, with inherited tendency to develop IgE immune response. Both AR and asthma can be triggered by the same allergen and frequently coexist.[16] Asthma is a clinical diagnosis that incorporates genetic predisposition and clinical symptoms with objective measures of lung function, and in this study, the asthmatic subjects were already confirmed by the respiratory physicians and are already on treatment for it. In our study, 28.8% of our AR subjects had concurrent asthma and there was a significant association between asthma co-morbidity and the chronicity of the disease in the ARIA sub-division (higher in Persistent type). A recent study showed a higher prevalence of asthma co-morbidity at 45.3%, but they only found a significant association between asthma and the older AR classification (seasonal and perennial), and not with the new ARIA classification.[14] Differences in research methodology, criteria of patient selection and sample size may explain the dissimilarity of

the findings. Despite this, our results are consistent with others in that we noted that the severity of the AR according to ARIA classification did not correlate with the presence of asthma symptomatology.[14,17] In our patients with both diseases, rhinitis precedes asthma in 77% of the cases. This finding is also in agreement with another study.[18]

In the present study, 54.4% of the subjects had a similar history of atopy among the family members. Family history of allergy is the single-most important factor for the development of allergic diseases. Adults with a family history of asthma or rhinitis have a two-fold to six-fold risk of developing AR compared with adults without such a family history.[19] Borish[20] in1999 reviewed studies on the inheritance of allergic diseases and summarised that up to 50% of children who have one parent and up to 75% of children who have both parents with atopy could become atopic. Similar to other studies, we also found that positive family history did not correlate to the chronicity and severity of AR.[14,19,20]

Aero-allergens like dust-mites, pollens and animal dander are responsible for many sensitivity reactions in AR patients. The high incidences of asthma co-morbidity in AR patients are partly due to the same sensitivity to these aero-allergens. In our study, we found almost half of the AR patients also had food sensitivity from the history. The most common type of food sensitivity in these patients was towards seafood-based, followed by chicken-based food. Living near the coastal region, seafood with rice is the main diet in the study population and this could be the reason for the high reported seafood sensitivity levels here. Of particular interest, the seafood type that most commonly induced allergy was the anchovy sauce. This is a local favorite sauce eaten by the majority of people in the study area with rice. Food sensitivity in AR patients is less well studied and there were few publications available for analysis and comparison. One study in Southeast Asia showed a high prevalence of crustacean seafood sensitivity in the general population.[21] A high incidence of seafood sensitivity in our AR patients could be better studied using a proper specific seafood derived allergen. Unfortunately, we did not have them in our skin prick study.

The ARIA guidelines were used to define the diagnostic criteria for AR in this study.[2,4] AR is defined as a symptomatic disorder of the nose characterised by one or more of the symptoms of itchiness, sneezing, rhinorrhea and nasal congestion, which are reversible spontaneously or with treatment. Other symptoms may also be present, such as eye and sleep symptoms. Although symptoms of AR are clearly defined, very few studies have analysed the prevalence of each of the symptoms. Aidan et al[22] did a survey on 1000 AR patients assessing the impact of the individual symptoms. They found that most of their patients complaint of nasal blockage (85%), followed by sneezing (63%), eye itchiness (60%), rhinorrhea (56%), watery eyes (51%) and nasal itchiness (41%). We, however, found that the highest presenting symptom in our patients was nasal itchiness, followed by sneezing, rhinorrhea and nasal blockage. Environmental, genetic or different allergen profiles may have contributed to the dissimilarity of the symptoms, as it was shown that these factors influenced the sensitivity reaction even within the same geographical region.[23] In our study, the severity of AR is best represented by the sleep disturbance symptom as it was significantly associated with a more severe AR regardless of the type. This is in accordance with other studies and the ARIA guidelines.[14,24] Our result also agreed with Anastassakis et al[14] who found that mucosal irritation symptoms were more common in the less chronic (seasonal) type of rhinitis. On the other hand, nasal endoscopic examination in our patients revealed a high number with inferior turbinate hypertrophy, mucoid discharge, mulberry turbinates and polypoidal mucosa. These findings indicated the chronicity of our patients' diseases and possibly also reflected poor compliance to the medications and treatments prescribed. Polypoidal mucosa was found significantly associated with asthma co-morbidity in line with Samter's syndrome (P <0.05).[25]

Two-thirds of our AR patients fell into a Persistent type (Tables 1 and 3). This finding seems to agree with studies within Asian and Southern Mediterranean countries with warmer climates.[2,9,26] Our country's constant high temperature and humid conditions resulted in persistently high concentration of indoor and outdoor allergens throughout the year. This will lead to the prevalence of chronic sensitivity reactions in patients with AR. Monosensitivity occurred in 12.2% of our patients, the highest with sensitivity to fungi (P <0.05). This similar result has been reported in a high temperature-high humidity climate study.[14] Possible explanation is that the two areas were similar in terms of being agricultural areas, besides having the same type of climate. Our paddy field may be similarly infected with fungi as the other cotton plantation which might then be responsible for the results. On the other hand, the majority of our patients were the oligo-sensitive type. Dust mites and cat allergen were responsible for the significant number of such patients with oligo-sensitivity (P <0.001). House dust mites and animal dander are the best described persistent indoor allergens and our warm and humid tropical climates are favourable conditions for them to thrive. In our skin prick test, house dust mites had the largest average wheal diameter and the highest positive results among all studied allergens. The prevalence of a positive skin prick test for cat is second highest after house dust mite. Cat allergen is found in the saliva and skin hair follicles. Cat allergen is particularly frustrating because

it readily circulates through an entire home. Almost a quarter of the patients in this study had domestic pets in their home and this can lead to the poor control of rhinitis, hence counselling on this matter should be part of the treatment regime.

Comparing our results with the result from a neighbouring Asian country, we noticed that patients in our study had almost similar allergic profiles in the skin prick test analysis.[9] Their results of skin prick testing have indicated that the leading causes of allergy were indoor allergens (house-dust mites, house dust, cockroaches, dogs and cats). Outdoor allergens like pollens and molds, similar to our findings, returned a low percentage of positive skin prick reactions, and therefore, were considered low in allergenicity. The severity profiles were also similar, with multiple allergen sensitivity occurring in the more severe type of rhinitis. These findings further support the fact that the epidemiology of AR is affected by the genetics of the population, the environmental condition and the geographical milieu.

Conclusion

The overall clinical profiles of our AR patients are comparable to the ones from other high temperature/ humidity countries. Indoor allergens like house dust mites and domestic animal dander were the leading causes of reactivity in the skin prick test, more than the outdoor allergens. ARIA classification gives a good indicator of the disease severity in our study and is useful in the management of AR in our population.

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