

# Clinical manifestation and sensitization of allergic children from Malaysia

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**Background:** An epidemiological rise of allergic diseases in developing countries raises new challenges. Currently a paucity of data exists describing allergy symptomatology and sensitization to common food and aeroallergens in young children from developing countries.

**Objective:** To compare changes in symptomatology, food allergen sensitization and aeroallergen sensitization in a cross-sectional study of children <2 years and 2–10 years.

**Methods:** A total of 192 allergic children (aged <2 years, 35 children; aged 2–10 years, 157 children) underwent specific IgE (>0.35 kU/L) to common food (egg white, cow's milk, cod fish, wheat, peanut, soya, peanut, and shrimp) and house dust mites (*Dermatophagoides pteronyssinus* and *Blomia tropicalis*).

**Results:** In children <2 years, atopic dermatitis (65.7%) was the most common symptom whereas in children 2–10 years it was rhinoconjunctivitis (74.5%). Higher sensitization rate to eggs ( $p < 0.01$ ) and cow's milk ( $p = 0.044$ ) was seen in <2 years group when compared to the 2–10 years group, but no significant differences for shrimp ( $p = 0.29$ ), wheat ( $p = 0.23$ ) and soya ( $p = 0.057$ ). Interestingly, sensitization to peanut ( $p = 0.012$ ) and fish ( $p = 0.035$ ) was significantly decreased in the 2–10 years group. Sensitization to house dust mites ( $p < 0.01$ ) dramatically increased in the older children.

**Conclusion:** Our study supports concept of atopic march from a developing country like Malaysia.

**Key words:** Hypersensitivity; Allergens; Asia; Food; Pyroglyphidae

## INTRODUCTION

Recent decades have witnessed pronounced increasing

prevalence of allergic disease in South East Asia [1]. Atopic march describes a sequential progression of atopic dermatitis and food allergy in infants leading to chronic respiratory

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conditions such as allergic rhinitis and asthma in school aged children. Risk of developing atopic diseases is complex, hence temporal patterns described in the atopic march is typically not a simple progression but influenced by genetic and environmental factors.

Prevalence of food allergy is increasing in developed nations but data from many parts of developing Asia are scant, creating a perception of low prevalence though recent reports indicate otherwise [2]. Asia's diverse cultures and unique eating habits further raise the question if current understanding of food allergy, largely derived from Western populations, are relevant to the region. Indeed, food sensitization with food-specific IgE level proposed predictive values for clinical food allergy, was not replicated in Chinese children [3]. Reactions to egg, peanut, milk, tree nuts, soy, fish, and wheat are common in Asians [3], however epidemiological studies from the region till date have primarily been survey based, lacking objective measures, and focussed on older children when sensitization to certain foods could be outgrown.

In a prospective birth cohort study, food allergen sensitization decreased from 10% to 3%, whilst inhalant allergen sensitization increased from 1.5% to 8%, by 6 years [4]. Despite paucity of similar prospective studies from Asia, co-occurrence of food allergy may accelerate the atopic march in Japanese children [5]. Japanese infants sensitized to house dust mites and co-sensitized to food antigens were at greatest risk for asthma development in a 4 year follow-up period [6].

Most studies to date from Asia were from affluent countries sharing comparable socioeconomic indices as Western Europe which may not accurately reflect the populous developing region. Indeed, geographical location emerged as an independent risk factor for development of allergies and asthma spanning three South East Asian nations [7], hence a need for data from regional emerging economies [8]. This cross-sectional study of sensitization and symptomology patterns of Malaysian allergic children was undertaken to draw parallels with the atopic march and how it applies to our population. We attempt to provide an insight on how sensitization to common food and aero-allergens may evolve in children of a developing Asian country such as Malaysia in comparison to other populations from more developed nations.

## MATERIALS AND METHODS

After approval from the Ethical Review Board, 192 allergic children (aged < 2 years, 35 children; aged 2 to 10 years, 157 children) evaluated at an allergy clinic in Pantai Hospital, Kuala Lumpur were enrolled in this retrospective study. All children with allergic symptoms over a three years span were included. The parents were interviewed based on a standard questionnaire that included self reported clinical history of allergy symptoms (gastroenterological, respiratory, dermatological, otorhinolaryngological, and ophthalmological), family atopy history, home environmental factors and diet of the child. When multiple symptoms were present in the individual, each symptom was considered separately.

Based on clinical assessment by an allergy specialist, sensitization was then confirmed by positive specific IgE (>0.35 kU/L) to common food allergens such as egg white, cow's milk, cod fish, wheat, peanut, soya bean, peanut or shrimp, and house dust mite (*Dermatophagoides pteronyssinus* and *Blomia tropicalis*) by ImmunoCAP (Pharmacia, Uppsala, Sweden). Pollens were not evaluated in this study as they are not a major aero-allergen source in Malaysia.

The chi-square test was used to compare children <2 years and 2–10 years in relation to symptoms, food and dust mite sensitization. A *p* value <0.05 was considered statistically significant (SPSS ver. 11.0, SPSS Inc., Chicago, IL, USA).

## RESULTS

Table 1 summarizes prominent symptoms in the group of children tested for allergy. Except for atopic dermatitis and gastrointestinal complaints, all other symptoms were evidently higher in children aged 2 to 10 years when compared to infants lesser than 2 years old. The frequencies of upper respiratory symptoms such as allergic rhinitis (74.5% vs. 34.3%) and lower respiratory symptoms such as asthma (36.9% vs. 22.9%) were significantly higher in older children compared to the younger group. Gastrointestinal symptom was more commonly seen in children less than 2 years (20%) against children (13.4%) 2–10 years. The frequency of atopic dermatitis was higher in children less than 2 years (65.7%) compared to children 2–10 years (58%); though these were statistically not significant.

Of those tested for food allergens (Table 2), younger children

**Table 1.** Frequency of clinical symptoms in children aged 2 to 10 years compared to infants less than 2 years old

Clinical symptom	Total number of cases	Age (yr)		p value
		<2 (n=35)	2–10 (n=157)	
Atopic dermatitis	114	23 (65.7)	91 (58.0)	0.266
Rhinoconjunctivitis	129	12 (34.3)	117 (74.5)	<0.01**
Asthma/wheezing, bronchitis	66	8 (22.9)	58 (36.9)	0.011*
Urticaria, angioedema	24	3 (8.6)	21 (13.4)	0.380
Gastrointestinal	28	7 (20.0)	21 (13.4)	0.434
Others (adenoids, serous otitis media)	15	0 (0)	15 (9.6)	0.087

Values are presented as number (%).

\* $p < 0.05$ . \*\* $p < 0.01$ . Chi-square test.

**Table 2.** Food allergen sensitization in allergic children aged 2 to 10 years compared to infants less than 2 years old

Food allergen	Specific IgE	Age (yr)		p value
		<2	2–10	
Egg white	Positive	18 (60.0)	39 (26.2)	<0.01**
	Negative	12 (40.0)	110 (73.8)	
Cow's milk	Positive	16 (44.4)	38 (25.7)	0.044*
	Negative	20 (55.6)	110 (74.3)	
Cod fish	Positive	5 (23.8)	8 (6.6)	0.035*
	Negative	16 (76.2)	113 (93.4)	
Wheat	Positive	6 (23.1)	14 (11.8)	0.230
	Negative	20 (76.9)	105 (88.2)	
Peanut	Positive	8 (36.4)	17 (12.6)	0.012*
	Negative	14 (63.6)	118 (87.4)	
Soya	Positive	7 (25.0)	13 (9.8)	0.057
	Negative	21 (75.0)	120 (90.2)	
Shrimp	Positive	1 (7.7)	28 (25.2)	0.290
	Negative	12 (92.3)	83 (74.8)	

Values are presented as number (%).

\* $p < 0.05$ . \*\* $p < 0.01$ . Chi-square test.

<2 years were significantly more likely to be sensitized to egg white ( $p < 0.01$ ), cow's milk ( $p = 0.044$ ), cod fish ( $p = 0.035$ ) and peanut ( $p = 0.012$ ), but not to soya ( $p = 0.057$ ), wheat ( $p = 0.23$ ) or shrimp ( $p = 0.29$ ). Children in the <2 years group had higher sensitization rates for all tested food compared to older children including egg white (60% vs. 26.2%), cow's milk (44.4% vs. 25.7%), cod fish (23.8% vs. 6.6%), wheat (23.1% vs. 11.8%), peanut (36.4% vs. 12.6%) and soya (25% vs. 9.8%) except for shrimp (7.7% vs. 25.2%).

Older children had significantly higher sensitization rates ( $p < 0.01$ ) to *D. pteronyssinus* (63.3% vs. 23.1%) and *B. Tropicalis* (63.2% vs. 16.7%) compared to younger children (Table 3).

## DISCUSSION

Epidemiological studies till date on prevalence of allergic disease from Asia have focused on older children with dearth of data in infants, stratification of symptoms and sensitization trends to common food and aero-allergens.

Atopic dermatitis is generally the first clinical manifestation of the atopic march. The most frequent allergy symptoms include atopic dermatitis in children below 2 years of age (65.7%) and rhinoconjunctivitis (74.5%) in children 2–10 years. Allergy symptomology in Singaporean children during second

**Table 3.** Dust mite sensitization in allergic children aged 2 to 10 years compared to infants less than 2 years old

House dust mite allergen	Specific IgE	Age (yr)		p value
		<2	2–10	
<i>Dermatophagoides pteronnyssinus</i>	Positive	6 (23.1)	93 (63.3)	<0.01**
	Negative	20 (76.9)	54 (36.7)	
<i>Blomia tropicalis</i>	Positive	2 (16.7)	67 (63.2)	<0.01**
	Negative	10 (83.3)	39 (36.8)	

Values are presented as number (%).

\*\* $p < 0.01$ . Chi-square test.

year of life primarily featured chronic itchy rash, wheeze and rhinoconjunctivitis [9], however allergic rhinitis developed after 6 years of age and rarely <2 years of age [10], in concordance to our observation. Kapoor et al. [11] examined the prevalence of allergic rhinitis and asthma in 2,270 children with physician-confirmed atopic dermatitis, and by 3 years of age 66% manifested allergic rhinitis and/or asthma. Asthma in early childhood is difficult to differentiate from other notable causes of symptoms such as viral infections, nonetheless despite an overestimation of asthma symptoms in children <2 years group, significant increase in respiratory manifestation among older children was present. Prognosis of atopic dermatitis may vary due to genetic and environmental influence. Atopic dermatitis incidence was higher in the younger age group but not significant between both age groups. There are no longitudinal studies from Asia to describe the natural course of atopic dermatitis, though 70% were in remission by 5 years of age in a retrospective review of Korean infants; albeit late onset atopic dermatitis unaccounted for [12].

Atopic children are more likely to develop food allergy than nonatopic; upto 37% with atopic dermatitis having IgE-mediated food allergy [13]. Cow's milk and egg were the most common food allergens in Malaysian children, as also noted for the region [14]. Food allergy, particularly cow's milk and egg white protein allergy begins early in life but typically outgrown by 2 to 3 years, whereas clinical sensitivity to peanut persists life-long [15]. Sensitization to all tested food allergens, except shrimp, demonstrated a decreasing trend in older children. As a consequence, cow's milk and egg were less likely to be positive in older children in relation to younger children, suggestive of tolerance development.

Previously recognized, wheat and soya allergy being outgrown by preschool-age, on more recent studies focusing on natural course indicate slower progression towards desensitization by late childhood or adolescence, often trailing clinical oral tolerance

[16-19]. These support our findings of decreasing sensitization in older children but not achieving significance, possibly indicative of a protracted desensitization course.

Data on fish allergy in Asia remains scant. From a pool of 7,850 Singaporean children with suspected food allergy only 10 had fish allergy, raising the notion that despite high consumption, fish allergy in the region may be uncommon [20]. Major allergen parvalbumin in locally consumed tropical fish is highly cross-reactive to cod fish, rendering cod fish IgE commercial testing reliable [20]. The natural course of fish allergy is poorly understood though prevailing consensus is it remains persistent. Surprisingly, we observe a significant drop in fish sensitization among older children, seemingly a propensity to outgrow sensitization in our study population. Regular fish consumption within the first year of life, but not later, attenuates atopic tendencies by age 4 years [21,22]. Breast feeding practices, which finds higher acceptance in developing nations, is further a confounding factor to the beneficial immune modulatory properties of early fish consumption [23]. Fish establishes early into diets of allergic Asian children [2], contrasting to Western practices [23]. Fish allergy was more prevalent in the Philippines (2.29%) compared to Singapore (0.26%) and Thailand (0.29%) on a survey based study in adolescents [24]. Hence role of food processing, dietary habits and cultural practices in fish allergy warrants investigation.

Population based peanut allergy prevalence are generally lower in Asians than Western societies [25]. A higher self-reported peanut but lower shrimp allergy amongst Western born expatriate in comparison to local Asians highlight the stark differences [26]. Nonetheless, peanut sensitized Asian children possess similar clinical and immunological traits as their Western counterparts [27]. We find a sharp drop in peanut sensitization in older children, contrasting with a significant rise in shrimp sensitization. Similar trends have been reported in Singaporean children [2]. This may suggest Malaysian children have a tendency

of outgrowing peanut sensitization, lending support towards mounting evidence that peanut allergy in Asia maybe distinct from the West. It is tempting to implicate genetic, dietary habits and environmental factors for the disparities.

Shellfish allergy has traditionally been perceived as persistent, as suggested also by this study. There are two potential pathways for sensitization to shellfish. First, early introduction of the highly allergenic shrimp paste condiment widely used in the local diet. Secondly, the tropical Malaysian climate promotes abundant exposure to dust mite allergens within the indoor environment. In Malaysian allergic rhinitis children, house dust mite and shrimp are the most common aero- and food-allergens, respectively [28].

Hence cross-reacting tropomyosin of dust mite allergens may impart shellfish sensitization in our population. *B. tropicalis* and *D. pteronyssinus* are the predominant reported house dust mites in Malaysian homes [29]. Prospective studies from Asia demonstrate persistently elevated food specific-IgE and early childhood house dust mite sensitization as risk factors for subsequent asthma development [6]. House dust mite sensitization is associated with asthma and allergic rhinitis in Malaysian school aged children [7]. We find dramatic sensitization increases to *D. pteronyssinus* and *B. Tropicalis* in older children contributing to respiratory symptoms.

Some limitations need to be taken into account including a single institute experience and a cross-sectional study. Allergen testing were based on clinical assessment and response by parents, hence not all children were tested to the allergen panel. While longitudinal studies would eventually need to be carried out, the current study defines commonly associated allergenic sources and offers inimitable insight of childhood sensitization trends from a developing country within the region.

In summary a gradual transition from atopic dermatitis to predominantly respiratory symptoms, a decreasing trend of sensitization to common food allergens contrasting with rising aero-allergen sensitization associated with progression of age, support the atopic march concept in allergic Malaysian children. Development of tolerance to peanut sensitization and an increasing sensitization to shrimp maybe unique features to the region requiring further investigation.

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