# Food allergy and allergic rhinitis in 435 asian patients – A descriptive review

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**SUMMARY**

**Objective: To describe the prevalence of food allergy in Asian patients with allergic rhinitis.**

**Study Design: A non-randomized prospectively collected patients over a three year period, with complaints of nose congestion, rhinorrhea and/or nasal discharge.**

**Results: There were 435 patients enrolled, 213 children and 222 adults. The children group had a high prevalence of allergen specific IgE to Dermatophagoides pteryonysinus (70%), Dermatophagoides farina (69%), and Blomia tropicalis (55%); followed by dogs (32%), cats (19%) and cockroaches (19%). In the children food allergy category, the top three allergens were egg white (54%), milk (31%) and soya bean (13%). The adult group had results of Dermatophagoides pteryonysinus (71%), Dermatophagoides farina (72%), and Blomia tropicalis (59%); the adult food allergy category, the top 3 allergens were egg white (13%), milk (6%) and soya bean (5%). There was a statistically significant difference in the child and adult group for Dust, D. pteryonysinus, D. farina, B.tropicalis, egg white, wheat, gluten and soya bean. In the age specific child groups, there was an increased in egg food allergy levels, with a peak at the age of five-nine years old and decreasing thereafter (p=0.04). In the children group, the mean Total Nasal Symptom Score (TNSS) was 10.3 (range of 7 to 13); the adult group was similar, with a mean TNSS of 9.8 (range 5 to 12).**

**Conclusion: The prevalence of food allergy in paediatric patients with allergic rhinitis is fairly high and should be considered when treating these children.**

**KEY WORDS:**
*Food Allergy, Allergic Rhinitis*
*Level of evidence: IV*

## INTRODUCTION

Food allergy is an immunological reaction to a food allergen. The term IgE mediated food allergy implies that the immunoglobulin E is involved in the reaction. All other reactions to food, should be referred to as non-allergic food hypersensitivity reactions.[1] Allergic conditions are among the most common childhood medical conditions in the United States.[2] This large disease burden of these allergic conditions results in a significant source of morbidity, mortality and huge healthcare expenditure.[3,4] It is difficult to accurately assess the incidence of these allergic conditions like eczema, asthma and allergic rhinitis; moreover, their incidence and prevalence may be changing due to environmental influences.[5, 6]

Food allergy is increasing throughout Asia and is reported to affect approximately 4 to 5 % of Singaporean school children.[7] The increase has been noted highest in affluent communities adopting the westernized lifestyle, with the westernized countries having highest prevalence.[8] There are very few population based studies on food allergy in Asia; self-reported questionnaires for children less than 12 years old are in the range of 4-5% in Singapore,7 4% in rural China,[9] to as high as 12% in Seoul, Korea[10] and Japan.[11] A meta-analysis reported by Rona et al, reveals the prevalence range between 3-35% around the world.[12]

Allergic reactions can range from skin rash, abdominal bloating, rhinorrhea, sneezing, wheezing, asthma-like symptoms, peri-orbital edema to anaphylaxis. Allergic life threatening conditions like anaphylaxis are not common (but potentially fatal), the milder allergic reactions in the form of eczema, rhinitis and asthma are strongly associated with impairment of quality of life, affecting the patient's mood, daily life, impact on the child's academic performance, decreasing social interaction, and significant economic costs.[13-18]

We conducted this study to assess the incidence of allergies in patients with nasal symptoms, namely allergic rhinitis. This article is meant to investigate the prevalence of inhalant and food allergy amongst 435 Asian adult and child patients with allergic rhinitis that is so often missed and/or forgotten.

## MATERIALS AND METHODS

Non-randomized prospectively collected patients who attended a specialty clinic from January 2013 to December 2015 were recruited into this study. Patients had nasal obstruction, nasal discharge, persistent nasal congestion, and/or post-nasal drip.

The inclusion criteria were age > 2 years, Asian countries (namely Singapore, Malaysia, Indonesia, China, South

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Korea, India, Vietnam, Thailand, Philippines and Hong Kong) no previous nasal surgical treatment or immunotherapy, no family history of nasal polyps or ciliary dysfunction syndromes. Patients who had a clinical diagnosis of sinusitis and/or noted to have nasal polyps on naso-endoscopy and/or had computer tomograms showing sinusitis or polyposis were excluded.

The study protocol and methodology was reviewed and approved by the hospital Ethics Committee / Institutional Review Board (IRB).

All patients underwent a comprehensive clinical assessment including a thorough physical examination, flexible naso-endoscopy, and a blood test for food allergies. Patients completed the Total Nasal Symptom Score (TNSS) and the allergic rhinitis symptom questionnaire (based on the classification of allergic rhinitis according to the ARIA, allergic rhinitis and its impact on asthma).[19]

Examination included height, weight, body-mass index (BMI), and blood pressure, and an endoscopic assessment of the nasal cavity, posterior nasal space, oropharyngeal area, uvula size and thickness, tonsillar size and Mallampati grade. Attention was paid to endoscopic findings of either turbinate hypertrophy, septal deviation and/or nasal polyps. Food allergy testing utilized the 3gAllergy™ (Siemens Healthcare) third generation allergen specific IgE, with a detection sensitive detection limit of 0.1kU/L. This level of sIgE correlates with the likelihood of a clinically significant reaction to that specific food trigger. Sampson et al documented serum positive levels of specific food allergen IgE had a 95% positive predictive value in the diagnosis of food allergy (based on a study of over 100 children).[20]

The allergy blood test panel included a total of 22 allergens, these include dust, three different dust mite species (namely Dermatophagoides pteryonysinus, Dermatophagoides farina, and Blomia tropicalis), fungus (Alternaria alternata), grass (Bermuda grass, Ragweed), cat dander, dog dander, cockroach, wheat, corn, sesame seed, peanut, soya bean, gluten, cacao, egg white, milk, chicken, fish and anchovies.

## STATISTICAL ANALYSIS

All statistical analyses were performed using SPSS23.0 with statistical significance set at $p < 0.05$. Differences in numerical variables between Adult and Child were compared using 2-Sample T test when normality & homogeneity assumptions were satisfied; otherwise Mann Whitney U test was performed. Chi-square or Fisher's Exact test to compare differences in categorical outcomes. One-Way ANOVA or Kruskall Wallis was performed to compare the numerical variables across the 4 age groups with Bonferroni correction on multiple comparisons.

## RESULTS

There were 435 patients collected, both adult and child. There were 213 children (age<18 years old) and 222 adults. In the children group the mean age was 9.2 years old (range of 2 to 18 years of age); whilst in the adult group, the mean age was 35.4 years old with a range of 19 to 64 years old.

The blood results for the children group showed significantly high levels of allergen specific IgE to Dermatophagoides pteryonysinus (70%), Dermatophagoides farina (69%), and Blomia tropicalis (55%); this was followed by dogs (32%), cats (19%) and cockroaches (19%). In the food allergy category, the top 5 allergens were egg white (54%), milk (31%), soya bean (13%), wheat (11%), corn (8%) and sesame seed (8%). (see table I).

The adult group had similar results, though not completely alike; the highest levels of allergen specific IgE were also in Dermatophagoides pteryonysinus (71%), Dermatophagoides farina (72%), and Blomia tropicalis (59%); this was followed by dog (27%), cockroach (25%) and cat (18%). However, in the food allergy category, the top 5 allergens were significantly lower, compared to the child group, being egg white (13%), milk (6%), soya bean (5%), sesame seed (5%) and corn (4%) (see table I).

Comparing the absolute levels of each allergen specific IgE for the adult and child groups, these were statistically significant, Dust ($p<0.01$), Dermatophagoides pteryonysinus ($p<0.0001$), Dermatophagoides farina ($p<0.0001$), and Blomia tropicalis ($p<0.014$). Comparing the absolute levels of each food allergen specific IgE for the adult and child groups, these were statistically significant, egg white ($p<0.0001$), soya bean ($p<0.037$), gluten ($p<0.0001$), fish ($p<0.002$), and wheat ($p<0.018$).

With further stratification of age for the children group, we found a gradual steady increase in the inhalant IgE specific levels from the age groups of 0-4 years old, 5-9 years old, 10-14 years old and 15-18 years of age. This steady increase in inhalant allergy was noted more pronouncedly in the Dermatophagoides pteryonysinus (36.8% to 66.2% to 84.5% to 87.2%), Dermatophagoides farina (39.5% to 63.6% to 84.5% to 89.7%), Blomia tropicalis (13.2% to 44.2% to 79.3% to 84.6%), dog (23.7% to 27.3% to 33.6% to 38.5%), followed by cat (7.9% to 15.6% to 24.2% to 28.2%) (see table II). In the food category, there seemed to be an increasing trend to egg as an allergen with a peak noted in the group of children between the age of five-nine years old, and decreasing thereafter (see table 3); the IgE specific levels for egg were strongly increasing in the groups (47.4% to 68.8% to 51.7% to 33.3%) ($p=0.04$). The other food allergens did not show such a trend and were statistically not significant.

Clinical questionnaires in the children group showed, the mean TNSS was 10.3, with a range of 7 to 13; the adult group was similar, with a mean TNSS of 9.8 (range 5 to 12). The allergic rhinitis symptom questionnaire (based on the classification of allergic rhinitis according to the ARIA, allergic rhinitis and its impact on asthma),[19] showed that 61% of the children (130 out of 213) had "persistent" allergic rhinitis, while 29.1% (62 out of 213) had "moderate to severe" allergic rhinitis, and 21 out of 213 (9.9%) children had "intermittent" allergic rhinitis. The adult group reveals that 38.5% (82 out of 213) had "persistent" allergic rhinitis, while 25.4% (54 out of 213) had "moderate to severe" allergic rhinitis, and 77 out of 213 (36.6%) adults had "intermittent" allergic rhinitis. This TNSS had no correlation with the assayed levels of allergens noted in these patients.

**Table I: Showing the respective mean and percentage values between the child and adult group of food allergy blood tests**

| Allergen | Level (mean) kU/L | | Percentage % (n/N) | | P-value |
|---|---|---|---|---|---|
| | Child | Adult | Child | Adult | |
| Dust | 2.04 | 0.62 | 66 | 58 | 0.010 |
| D. pter | 34.67 | 14.59 | 70 | 71 | 0.000 |
| D.farinae | 28.85 | 12.18 | 69 | 72 | 0.000 |
| B. trop | 5.24 | 2.70 | 55 | 59 | 0.014 |
| A.alternata | 0.07 | 0.03 | 5 | 2 | 0.427 |
| Bermuda | 0.22 | 0.09 | 7 | 10 | 0.389 |
| Ragweed | 0.29 | 0.32 | 9 | 10 | 0.929 |
| Cat | 1.19 | 1.23 | 19 | 18 | 0.957 |
| Dog | 0.81 | 0.85 | 32 | 27 | 0.946 |
| Cockroach | 0.43 | 0.16 | 19 | 25 | 0.249 |
| Wheat | 0.06 | 0.01 | 11 | 3 | 0.018 |
| Corn | 0.06 | 0.01 | 8 | 4 | 0.104 |
| Sesame | 0.06 | 0,07 | 8 | 5 | 0.945 |
| Peanut | 0.58 | 0.01 | 9 | 4 | 0.210 |
| Soya Bean | 0.07 | 0.01 | 13 | 5 | 0.037 |
| Gluten | 0.03 | 0.01 | 5 | 2 | 0.043 |
| Cacao | 0.01 | 0.00 | 2 | 0 | 0.147 |
| Egg white | 0.47 | 0.04 | 54 | 13 | 0.000 |
| Milk | 0.16 | 0.09 | 31 | 6 | 0.351 |
| Chicken | 0.04 | 0.00 | 7 | 0 | 0.201 |
| Fish | 0.03 | 0.00 | 8 | 0 | 0.002 |
| Anchovies | 0.01 | 0.01 | 4 | 4 | 0.977 |

**Table II. Percentage of allergen specific inhalant allergy distributed according to childhood age groups. Statistical significance was not found in any of the groups.**

| Group (age) | n | D. pter (%) | D. far (%) | Blomia (%) | Cat (%) | Dog (%) |
|---|---|---|---|---|---|---|
| 0-4 | 38 | 36.8 | 39.5 | 13.2 | 7.9 | 23.7 |
| 5-9 | 77 | 66.2 | 63.6 | 44.2 | 15.6 | 27.3 |
| 10-14 | 58 | 84.5 | 84.5 | 79.3 | 24.2 | 33.6 |
| 15-18 | 39 | 87.2 | 89.7 | 84.6 | 28.2 | 38.5 |

D.pter = Dermatophagoides pteryonysinus,
D. far = Dermatophagoides farina,
Blomia = Blomia tropicalis

**Table III. Percentage of allergen specific food allergy distributed according to childhood age groups. Statistical significance was only noted in the egg food allergy, between age group of 5-9 years and 10-14 years old (p=0.04)**

| Group (age) | n | Egg (%) | Milk (%) | Soya (%) | Wheat (%) | Peanut (%) |
|---|---|---|---|---|---|---|
| 0-4 | 38 | 47.4 | 42.1 | 15.8 | 10.5 | 15.8 |
| 5-9 | 77 | 68.8 | 37.7 | 6.4 | 10.4 | 3.9 |
| 10-14 | 58 | 51.7 | 27.6 | 20.7 | 10.3 | 13.8 |
| 15-18 | 39 | 33.3 | 12.8 | 10.3 | 10.3 | 12.8 |

## DISCUSSION

As the bowels in human-beings are of an enormous surface area, it is vulnerable to all sorts of substances, bacteria, pathogens, chemicals, and protein that the human ingests. The immune system in the bowel is in the form of mucosa-associated lymphoid tissue (MALT), they protect against pathogenic organisms and toxins, whilst not responding to harmless commensal bacteria and food components. In health, the physical properties of the gut, including gastric acid, digestive enzymes, mucosal integrity and mucus secretion, reduce the penetration of ingested pathogens and food proteins. This immune protection may minimize the amount of potentially allergenic protein absorbed by the gastrointestinal tract, but it is believed that immunologically recognizable dietary protein can still be absorbed and can potentially result in an allergic reaction.

IgE-mediated food allergy results when an immune response that is effective in targeting parasites, instead is mounted against food proteins. Food or other allergic inducing proteins may enter the body by ingestion, inhalation and/or skin penetration. They are taken up by the body's antigen presenting cells and presented to T-helper cells. Cytokines are released and T-helper1 cell effect a response called cell-mediated response, effective against intracellular bacteria and protozoa. When food proteins inappropriately triggers the T-helper2 cell response, the result is a Type 1 hypersensitivity reaction and an IgE-mediated food allergy response that can manifest on the skin, sinus and/or lungs.

Theoretically, any protein can cause sensitization, however, as the food we ingest is fairly consistent throughout the world, the vast majority of these hypersensitivity reactions occur to the same most common food protein allergens.

These common food allergen proteins tend to be water-soluble glycopeptides with higher resistance to proteolytic enzymes, acid, and heat; hence, they are resistant to the acidity of the gastric juices. Sampson et al in 2006, reported that in children, cow's milk, egg, peanut, soy, tree nuts, fish, shellfish, and wheat account for 85% of all non-emergency food allergies.[20] In terms of non-anaphylactic food allergy, Gerez et al[21] in 2005, showed that in 14-15 year old Singaporean children, the prevalence of peanut allergy was only 0.3%, while Chiang et al[22] in 2007, illustrated (with skin prick tests) that the prevalence of peanut sensitization in 3 - 16-year-olds in Singapore could be as high as 27.3%, and is ranked third most common after egg (40%), shellfish (39%), then in fourth was cow's milk (11.8%), sesame (9.3%), wheat (3.7%) and soy (3.2%). In a separate study, Khoo et al[23] suggested that the rate was 12% in those younger than 3 years. Relatively high rates of sensitization have also been recorded among allergic Hong Kong (31% in atopic eczema)[24] and Taiwanese children (36% in atopic eczema).[25] Shek et al conducted a survey in Singapore school children aged 14 to 15 years and showed that the positive responses for convincing shellfish allergy were comparatively high at 3.95% or about 5 times that of US children.[26] In terms of severe anaphylactic food allergy, Liew et al[27] reported in 108 children, that the commonest trigger was peanut (19%), egg (12%), seafood (10%), bird's nest (10%) and cow's milk (6%).

In our series, the children group revealed a very high prevalence of egg food allergy (54%), milk (31%), soya bean (13%), wheat (11%), corn (8%) and sesame seed (8%). These findings were similar to Chiang et al22 in 2007, when they investigated 227 patients with suspected food allergy by performing skin prick test, however, our data was more objective as we had used allergen specific IgE serum levels (some authors believe that skin prick testing may be either be too sensitive or inaccurate with higher variability in readings). Rance et al[27] showed that commercial extracts degrade and lack sensitivity. Unlike serum allergen specific IgE levels, the skin prick test cannot distinguish between sensitization versus true allergy, but there might be a correlation between the size of wheal and the likelihood of true allergy. The size of the wheal generated varies both with the candidate allergen and the population under study, but there have been attempts at standardizing significant 'decision points' for each allergen.[28] Verstege et al found that the sensitivity and specificity of skin prick tests were relatively poor if using a simple positive or negative result, but by correlating the size of wheal with the results of a double-blind placebo-controlled food challenge they were able to identify clinical decision points with 95% specificity for hen's egg and cow's milk.[28] In general, skin prick tests provide rapid means to detect IgE sensitisation and are highly sensitive but only moderately specific in regard to clinical reactivity, i.e. there is a high rate of false positivity. Hence, a negative skin prick test result has more than 95% negative predictive accuracy and is therefore useful for confirming the absence of an IgE-mediated reaction than the presence of one.[29, 30] This was a strong basis for our study using the slightly more expensive but reliable allergen specific IgE serum levels. However, the physician should be cognizant of the fact that between 10%–25% of patients with undetectable serum food allergen specific IgE levels have been reported to have clinically relevant reactions 31 and a physician-supervised food challenge may be needed to confirm the absence of clinical allergy.

Most authors agree that the recognized tests for diagnosing IgE-mediated food allergy are the skin prick test, and serum food allergen-specific IgE antibody levels. The double-blind placebo-controlled food challenge remains the gold standard in food allergy testing, but is not frequently performed due to its inherent safety issues, risks, inconvenience and high cost. In our study, when comparing the actual assay levels of each allergen specific IgE for the adult and child groups, these were statistically significant, dust, Dermatophagoides pteryonysinus ($p<0.0001$), Dermatophagoides farina ($p<0.0001$), and Blomia tropicalis ($p<0.014$). Comparing the actual absolute levels of each food allergen specific IgE for the adult and child groups, these were also statistically significant, egg white ($p<0.0001$), soya bean ($p<0.037$), gluten ($p<0.0001$), fish ($p<0.002$), and wheat ($p<0.018$). When the children group was further stratified according to age, there was no statistical significance in the various food allergens, except for egg as an allergen. There seemed to be an increasing trend to egg as an allergen with a peak noted in the group of children between the age of 5-9 years old, and decreasing thereafter (see table III); the IgE specific levels for egg were strongly increasing in the groups (47.4% to 68.8% to 51.7% to 33.3%) ($p=0.04$). Many authors believe that many of these early onset allergies are associated with the eventual development of tolerance and this leads to a different spectrum of allergies in adults.[32] This could perhaps explain our findings of a much lower prevalence of food allergies in our adult group of patients, with the possibility that the children develop tolerance (the "grow out of it" theory) as they grow into adulthood with fewer food allergies.

**Egg**

In our study, egg food allergy was the highest in both children (54%) and adults (13%). Many authors believe that there could be a few allergens in the egg white, these include ovalbumin, ovomucoid, ovomucin, ovotransferrin and lysozyme.[33] The egg yolk itself may have allergic proteins like, alpha-livitin.[33] There is a theory that there may be reduced allergenic potential of the egg when heat or digestive enzymes are applied to it, this might explain why some children might react to uncooked but not cooked eggs.[34, 35]

Boyano-Martinez et al in a study of 107 children (less than 1-year-old) with atopic dermatitis, and no known egg ingestion showed egg IgE positivity in 67%, and positive to food challenge tests.[36] It is postulated that around two-thirds of children would outgrow their egg sensitivity by the age of 5 years old.[37] In our series of 213 children, we actually had the egg IgE specific levels increasing from the 0-4years age group, peaking at the five-nine years age group and decreasing thereafter.

**Cow's Milk**

Cow's milk contains a fair number of potential protein allergens. The major protein allergens are caseins (alpha-, beta-, and kappa-casein), alpha-lactalbumin (ALA), beta-lacto-globulin (BLG) and bovine lactoferrin. Most authors believe that only 40% to 80% of children with IgE-mediated cow's milk allergy might outgrow their allergy by eight years of age, whereas with non-IgE-mediated cow's milk protein allergy, children will develop tolerance by five years of age.[38, 39] In our series, we also demonstrated this tolerance, as the prevalence decreased with the children's age, and reducing in adulthood.

Avoidance therapy of the cow's milk may seem the best solution, switching to a soy-based milk formula is what most paediatricians would recommend; however, Ahn et al, in Korea, showed that 18% of children with egg allergy also had soy allergy.[40] This would be a confounding factor to consider when making a switch from cow's milk to soy-based milk.

### Soya Bean

There are multiple allergens known in soy; however, it is not definite which ones of these are inciting the allergic reaction and are important for clinical reactions.[41] As soy proteins are widely utilised in processed and manufactured foods, it is not uncommon for children to be exposed to soy proteins. A variety of soy products have elicited allergic reactions, like soybean sprouts, soy milk, yogurt, desserts, flakes, flour, tofu and meat substitutes. Although soy is also a legume (like peanut), cross-reactions between soy and peanut occur only in a minority of cases.[42] A potential source of allergen in soybeans is the lecithin in soybean. Lecithins are important as emulsifiers and stabilisers for the food and pharmaceutical industries. The soy allergy in our series was 13% in the children group and 5% in the adult group.

### Wheat

As with other food allergens, wheat also has a number of potentially allergic proteins. Wheat allergens are mainly the albumins and globulins which are important in atopic eczema, the omega5-gliadins may trigger the rare entity of wheat-dependent exercise-induced anaphylaxis or urticaria and low-molecular-weight glutenin which may trigger anaphylaxis.[43] Unlike egg and cow's milk food allergy, many authors have found that wheat allergy may persist into adulthood more often than suspected.[44]

### Peanut

Whilst peanut allergy is the top food trigger (19%) for anaphylaxis in Singapore,[45] its non-anaphylactic food allergy reaction is reported to be approximately 0.6%.[46] Peanut allergy is still the highest reason for an adrenaline auto-injector (41% of prescriptions) in Singapore.[46] It is believed that the allergenic component of the peanut is found in the protein (not the carbohydrate or fat). Hence, most peanut oils do not contain this allergenic protein (unless they are contaminated with the protein).[42] Eight peanut allergens have been identified, these are arbitrarily termed Ara h 1 to Ara h 8. Most authors believe that most of these peanut allergens are members of the same seed storage protein families.[42] Peanuts belong to the plant family of legumes, which also includes soybeans, green beans, and lentils. However, clinical cross reactivity between peanut and other legumes have only been postulated to be less than 10%. Scholnick et al showed that approximately 20% of preschool children who are allergic to peanuts will outgrow their allergy by the school years.[47] Hence, it is recommended that these children be reassessed when they start school at around 5 years of age onwards.

## CONCLUSION

As the prevalence of food allergy is evidently high in Asian patients with allergic rhinitis, it would be prudent to routinely assess their IgE allergen specific levels and advice these patients avoidance therapy, in order for better clinical outcomes and more satisfied patients.

**Competing interest section – the authors all declare that they have no competing interest**
Author contribution – KPP, conceived the study, collected the patients, analyzed the data, and wrote the article. KAP, EBP, TYNC, JKS – wrote the article, results, conclusion, and methodology. CYH – performed the statistical analysis and wrote the statistical section

**Compliance with Ethical Standards**
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Informed consent was obtained from all individual participants included in the study.

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