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# Growth of children with food allergies in Singapore

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## ABSTRACT

**Background:** Although it is known that children with food allergies are at risk of impaired growth, this has not been well studied in South-East Asia.
**Objective:** The aim of this cross-sectional study is to survey the growth of children with food allergies in Singapore and the factors impacting it.
**Methods:** Anthropometric data, demographic data, type of food allergy, foods eliminated, and atopic comorbidities were recorded. Malnutrition was defined using World Health Organization standards (≤-2 *z*-score for weight-for-height [WH], weight-for-age [WA], and height-for-age [HA]).
**Results:** Seventy-four patients (51% male) were recruited over 1 month, with median age at diagnosis of 8 months (interquartile range [IQR], 4–13 months) and at data collection of 25 months (IQR, 14–48 months). Sixty-two (84%) had IgE-mediated allergy, 8 (11%) mixed IgE and non-IgE, and 4 (5%) non-IgE-mediated allergy. Food exclusions: 55% one food, 27% two foods, 8% three to four foods, and 10% ≥5 foods. Only 1% were underweight (WA ≤ -2 *z*-score) and 3% had WA ≥ +2 *z*-score. Having a mixed type food allergy significantly reduced WA ($p = 0.023$). WA was significantly lower for those referred to the dietitian ($p = 0.027$). 5.4% were stunted (HA ≤ -2 *z*-score). Factors significantly associated with stunting were underlying eczema ($p = 0.03$) and having an IgE-mediated ($p = 0.03$) or mixed type food allergy ($p = 0.002$). One point four percent (1.4%) were undernourished (WH ≤ -2 *z*-score) and 1.4% were overweight (WH ≥ +2 *z*-score). Multivariate regression analysis found that children with mixed type food allergies were significantly shorter (*z*-score -1 lower). Children had a lower WA if they had skin involvement as part of their symptom presentation.
**Conclusion:** This is the first survey documenting growth in children with food allergy in Singapore. Eczema, IgE-mediated and mixed type allergies are associated with poorer growth rates in these children. Early, individualised nutritional intervention is recommended for all children with food allergy.

**Keywords:** Child; Food allergy; Food elimination; Growth; Singapore

Asia Pacific allergy

## INTRODUCTION

The prevalence of food allergy in children is on the rise worldwide and this has been described as an unanticipated "second wave" of the allergic epidemic [1]. The mainstay of management remains an elimination of the allergenic food. These are most commonly cow's milk, hen's egg, peanuts, tree nuts, shellfish, wheat, soya and fish, many of which contribute significantly towards the nutritional status of a growing child [2]. Although it is known that children with food allergies are at risk of growth impairment, there is paucity of data on growth status and its relation to the type of allergy, foods eliminated, and allergic comorbidities in South-East Asia. Isolauri et al. [3] demonstrated lower growth parameters in cow's milk allergic children with atopic dermatitis, when compared to healthy controls. A more recent survey in the United Kingdom by Meyer et al. [4] which included children under dietetic care for either IgE or non-IgE mediated food allergies, indicated that even with dietetic input, about 10% were stunted. Poor nutritional status has been shown to impact hospital stay, cognitive skills and growth [5]. In particular, stunting in children who are undernourished in early childhood has been associated with poorer cognitive function later in life [6]. The aim of this cross-sectional study is to survey the growth of children with food allergies in Singapore and the factors impacting it. This study is part of an international multicentre survey on growth in children with food allergies (submitted for publication).

## MATERIALS AND METHODS

### Study design

Over a 6-week period (April to May 2016), consecutive patients attending the allergy clinics in KK Women's and Children's Hospital, with a known or newly diagnosed food allergy, had their data collected anonymously by members of the study team. Data collected included age, sex, type of food allergy (IgE, non-IgE, or mixed), foods eliminated, atopic comorbidities, whether the child was receiving dietetic advice, and anthropometric data. The inclusion criteria were children aged between 0 to18 years old with any food allergy diagnosed by (1) a history consistent with an IgE-mediated food allergy and confirmed through either skin prick testing or specific IgE testing or oral food challenge; or (2) in the case of non-IgE mediated allergies, diagnosed through an elimination diet followed by reintroduction with resolution and reappearance of clinical symptoms. Children with nonallergic comorbidities, or those whose food allergies have not been confirmed as per inclusion criteria, were excluded from the study. The data and analysis used in this study were different from that of the international study.

### Statistical analysis

The standards for malnutrition provided by the World Health Organisation (WHO) were used for data analysis [7]. The WHO Anthro software ver. 3.2.2 was used to convert growth parameters to *z*-scores for weight-for-age (WA), height-for-age (HA), and weight-for-height (WH). Malnutrition was defined as a WA (underweight), WH (wasting), and HA (stunting) of ≤-2 *z*-scores. Data was analysed with R version 3.2.3 (R Core Team, 2015, Vienna). Categorical variables are presented as frequencies and continuous data are presented as medians and interquartile ranges. The Mann-Whitney *U* test was used to compare *z*-scores between binary variables and the Spearman correlation test was used to study the relationship between *z*-scores and number of foods excluded. Regression analysis, with WA, HA, and WH as primary outcome variables, was also performed, to assess the influence of type of food


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allergy, number and type of food eliminated, age of diagnosis, dietitian involvement, system involvement (in allergic reactions), on growth.

### Ethical approval

The study is approved by the Institutional Review Board of KK Women's and Children's Hospital.

## RESULTS

Seventy-four children were recruited, with 51% being male. The median age at diagnosis of a food allergy was 8 months (interquartile range [IQR], 4–13 months), and at data collection was 25 months (IQR, 14–48 months). The clinical characteristics of these patients are summarised in **Table 1**. The majority of these children (84%) had IgE-mediated food allergies. Fifty-five percent excluded only 1 food in their diet, while the rest excluded 2 or more foods. The most commonly excluded foods were hen's eggs, cow's milk, peanuts, and tree nuts. Almost all of the patients (95%) had allergic skin manifestations such as urticaria or angioedema. Nineteen percent of these children had allergic gastrointestinal manifestations, usually in the form of vomiting. Only 9% had respiratory involvement in the initial allergic presentation. Most of these children (76%) had eczema as an atopic comorbidity. A very small proportion of these children (5%) had been seen by a dietitian at the point of data collection.

Data from the whole cohort indicated that 1% was underweight (WA ≤ -2 *z*-score), 5% were stunted (HA ≤-2 *z*-score), 1% was undernourished (WH ≤ -2 *z*-score) and 3% were overweight (WH > 2 *z*-score). Univariate analysis (**Table 2**) indicated that WA was significantly lower for

**Table 1.** Clinical characteristics

| Characteristic | No. (%) |
|---|---|
| Type of allergy | |
| IgE-mediated | 62 (84) |
| Non-IgE mediated | 4 (5) |
| Mixed | 8 (11) |
| No. of foods excluded | |
| 1 Food | 41 (55) |
| 2 Foods | 20 (27) |
| 3–4 Foods | 6 (8) |
| ≥5 Foods | 7 (10) |
| Type of foods | |
| Egg | 45 (61) |
| Cow's milk | 27 (36) |
| Peanuts and tree nuts | 28 (38) |
| Soy | 7 (9) |
| Fish | 5 (7) |
| Shellfish | 5 (7) |
| Wheat | 3 (4) |
| System Involvement | |
| Skin | 70 (95) |
| Gastrointestinal | 14 (19) |
| Respiratory | 7 (9) |
| Atopic comorbidity | |
| Eczema | 56 (76) |
| Allergic rhinitis | 21 (28) |
| Asthma | 6 (8) |
| Seen by dietitian | 4 (5) |
| Not seen by dietitian | 70 (95) |


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**Table 2.** Univariate analysis of factors affecting growth

| Variable | Weight-for-age when | | | Height-for-age when | | | Weight-for-height when | | |
|---|---|---|---|---|---|---|---|---|---|
| | Yes | No | *p* value | Yes | No | *p* value | Yes | No | *p* value |
| Type of allergy | | | | | | | | | |
| IgE | −0.41 | −0.91 | 0.110 | −0.61 | −1.52 | 0.032* | −0.14 | 0.08 | 0.922 |
| Non-IgE allergy | 0.08 | −0.55 | 0.619 | −0.26 | −0.66 | 0.454 | 0.32 | −0.12 | 0.731 |
| Mixed allergy | −1.15 | −0.32 | 0.023* | −1.69 | −0.56 | 0.002* | −0.07 | −0.08 | 0.866 |
| Food eliminated | | | | | | | | | |
| Egg | −0.44 | −0.44 | 0.559 | −0.69 | −0.54 | 0.279 | −0.12 | 0.05 | 0.571 |
| Cow's milk | −0.64 | −0.32 | 0.176 | −0.61 | −0.66 | 0.200 | 0.08 | −0.14 | 0.804 |
| Peanuts | −0.25 | −0.64 | 0.071 | −0.56 | −0.66 | 0.589 | 0 | −0.12 | 0.788 |
| Tree nuts | −0.25 | −0.64 | 0.066 | −0.56 | −0.66 | 0.313 | 0.02 | −0.17 | 0.800 |
| Soy | −0.43 | −0.50 | 0.620 | −0.70 | −0.65 | 0.733 | −0.05 | −0.10 | 0.724 |
| Fish | −0.88 | −0.44 | 0.527 | −0.06 | −0.66 | 0.479 | −0.93 | −0.02 | 0.051 |
| Shellfish | −0.61 | −0.44 | 0.593 | −0.61 | −0.66 | 0.973 | −0.68 | −0.07 | 0.351 |
| Wheat | −0.90 | −0.44 | 0.627 | −1.31 | −0.61 | 0.106 | 0.55 | −0.12 | 0.201 |
| Type of milk replacement (for those eliminating cow's milk) | | | | | | | | | |
| AAF | −0.64 | −0.43 | 0.710 | −1.10 | −0.65 | 0.445 | −0.04 | −0.07 | 0.914 |
| EHF | −0.24 | −0.55 | 0.763 | −0.43 | −0.67 | 0.642 | 0.02 | −0.12 | 0.938 |
| SF | −0.86 | −0.41 | 0.170 | −0.96 | −0.63 | 0.378 | 0.20 | −0.10 | 0.817 |
| System involvement | | | | | | | | | |
| Skin | −0.57 | 0.41 | 0.075 | −0.66 | −0.26 | 0.251 | −0.14 | 0.55 | 0.198 |
| Gastro | −0.42 | −0.55 | 0.575 | −1.08 | −0.63 | 0.471 | 0.23 | −0.14 | 0.716 |
| Respiratory | −0.08 | −0.55 | 0.849 | −0.77 | −0.58 | 0.217 | −0.05 | −0.10 | 0.767 |
| Atopic comorbidity | | | | | | | | | |
| Eczema | −0.62 | −0.04 | 0.075 | −0.69 | −0.14 | 0.037* | −0.07 | −0.02 | 0.379 |
| Allergic rhinitis | −0.28 | −0.60 | 0.803 | −0.66 | −0.63 | 0.955 | −0.06 | −0.12 | 0.817 |
| Asthma | −0.84 | −0.44 | 0.320 | −0.55 | −0.65 | 0.584 | −0.06 | −0.12 | 0.983 |
| Seen by dietitian | −1.67 | −0.43 | 0.027* | −1.42 | −0.61 | 0.122 | −1.31 | −0.06 | 0.104 |

AAF, amino acid-based formula; EHF, extensively hydrolysed formula; SF, soy-based formula.
*$p < 0.05$.

those with mixed type food allergy ($p = 0.023$) and those referred to the dietitian ($p = 0.027$). Factors significantly associated with stunting were underlying eczema ($p = 0.037$) and having an IgE-mediated ($p = 0.032$) or mixed type food allergy ($p = 0.002$). Multivariate regression analysis found that children had a lower WA (*z*-score -1 lower) if they had skin involvement as part of their symptom presentation; while those with mixed type food allergy were significantly shorter (*z*-score -1 lower). Those being seen by a dietitian were also significantly smaller (lower WA and WH).

## DISCUSSION

This is the first survey documenting growth in children with food allergy in Singapore.

We found that 5% of all children surveyed had a HA ≤ -2 *z*-score, which according to the WHO classification, represents stunting. We found a significantly lower HA in children with eczema, IgE-mediated allergy, or mixed IgE- and non-IgE-mediated food allergy. In a large longitudinal cohort study, Beck et al. [8] also found that eczema coexisting with food allergy at 1 year and persistent food allergy at 4 years of age was associated with a lower height and weight. Venter et al. [9] recently reviewed the factors involved in poor growth in children with food allergies, and suggested that impaired growth in atopic children should not be attributed to food avoidance alone, but to a general condition of 'subinflammation,' which unfavourably affects the absorption and utilization of substrates. Indeed, lower

albumin levels have been identified in children with cow's milk protein and atopic dermatitis compared with healthy controls despite similar protein intake, possibly forming the basis for this hypothesis. Another suggestion is that energy and protein requirements may be higher to allow for skin regeneration (due to rapid skin turnover and inflammation) and to compensate for skin losses in allergic children with atopic dermatitis [9–11]. Increased energy expenditure associated with itch and sleep disturbance in this group has also been hypothesised as a factor, but convincing data is lacking. A small study conducted by Hon et al. [12] demonstrated no difference in resting energy expenditure between children with severe-moderate atopic dermatitis and controls. Beck et al. [8] also hypothesized the apparent combined effect on growth of food allergy and eczema could be explained by those children exhibiting a more severe allergic phenotype. Other possible contributory factors include an active inflammatory state, sustained by the release of proinflammatory cytokines such as interleukin-6 and tumour necrosis factor-α [13], use of corticosteroids, sleep disturbances and impaired growth hormone release [9].

Contrary to some studies [14, 15], we found no correlation between the number of foods avoided and reduced growth. Jhamnani et al. [10] also recently reported this lack of association. Beck et al. [8] similarly reported no effect of the number of foods avoided on growth parameters. Meyer et al. [4] found no significant difference in in HA and WH in children avoiding multiple foods but did find an association between WA and children avoiding ≥ 3 foods. Such differences in findings between the various studies are likely due to the heterogeneity of the study designs, differences in population studied and the degree of dietitian's involvement. In our study, we have a fairly young cohort, with primarily IgE-mediated or mixed type allergies, with a low degree of dietitian involvement. The lack of a straightforward association between the number of foods restrictions and growth could further support the hypothesis of persistent intestinal ‘subinflammation,' in children with food allergies. This could be caused by noncompliance to the elimination diet, antigen residues in foods or undiagnosed allergies. In our clinical practice, we also find that the restricted diet often impacts a child's desire and ability to eat and feed themselves. This is often compounded by parental self-perceptions of food allergies in relation to eczema, leading to further restrictions in the diet. A recent Korean study [11] reported that 48.1% of children with atopic dermatitis had experienced previous food restriction prior to individualised nutrition intervention combined with an elimination diet. The mean food-specific IgE levels to the major food allergens (apart from milk) for these children were below the locally used predictive decision points used in determining if food elimination is warranted, indicating unnecessary food avoidance. Negative experiences with food due to an allergic reaction can also create fear of food, with some developing food aversion to varying degrees [16].

In our survey, we found no association between the type of food elimination and growth, contrary to other published data [3, 17, 18]. The most common food avoided in our cohort was egg (61%), followed by cow's milk (36%). The lower level of cow's milk allergy and in our cohort may, in part, explain the lower percentage of children who were both underweight and undernourished compared to other published data [3, 15, 17, 18] where cow's milk allergy was the most common food allergy and where an association had been found between cow's milk allergy and poor growth.

For the 36% eliminating cow's milk from their diet, 7% were on an amino acid formula. Twenty-two percent (22.2%) were on an extensively hydrolysed formula. The majority,

40.7%, were on a soy based infant formula, while the rest (30%) were either breastfed or not on milk replacement. Soy formula is frequently used as a first line formula for children with cow's milk protein allergy above 6 months of age in Singapore, due to the high cost of hypoallergenic formulas. Type of milk replacement was not associated with low WA, HA, or WH in our survey.

Our results indicated that low WA and WH was associated with seeing a dietitian. This was not surprising, and was most likely not a true association, but instead, reflected the present practice of only referring those who were already malnourished. In our survey, only 5% (n = 4), of the cohort were seen by the dietitian. All of those referred had a weight for age *z*-score of <-2. Our results, supported by data from other studies [4, 19], indicate an early dietetic referral is recommended for children with food allergy to maximise nutritional intake before their growth falters, particularly for those with eczema and multiple food allergy. Dietitians are especially aware of the macro and micronutrient requirements required for catch up growth and health, with micronutrients generally known to be of more concern than energy intake in this group. Earlier studies have indicated that when diet is adequately supplemented, with close dietetic and physician follow-up, the extent of food elimination either has no impact on growth or nutritional status, or allows an improvement in growth parameters following dietetic intervention [13, 15]. The practice in our centre has since been changed to allow for earlier dietetic referral for children with food allergies.

Our survey has several limitations. Working in the main tertiary referral centre, we might be seeing a skewed population with more severe forms of food allergies. There was no control group in our study for comparison, as we only captured data of children with food allergies. Future studies with a control group of children with no food allergies are planned. As this was a cross-sectional survey, we were not able to collect growth data at different time points, to allow for follow up on growth patterns or velocities, or to establish the effect of dietetic input on growth.

In conclusion, children with food allergies are at risk of faltering growth. Eczema, IgE-mediated and mixed type allergies are associated with poorer growth rates in these children. Early, individualised nutritional intervention is recommended for all children with food allergy and not only for those with allergies to milk and other more nutritionally important foods. This study has added to the growing data that impaired growth in children with food allergies is multifactorial and further research needs to be performed to establish the interaction between the various factors.

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