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# Prevalence of IgE-mediated cow milk, egg, and peanut allergy in young Singapore children 

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#### Abstract

Background: The rising prevalence of food allergy reported in the United States, UK, and Australia may be attributable to the rise in peanut allergy prevalence. The food allergy prevalence in other parts of the world such as Asia is, however, less well documented. Objective: This study aimed to evaluate the prevalence of cow's milk, egg, and peanut allergies in a general population of Singaporean children below 30 months of age. Methods: A total of 4,115 children from the general population who attended well-baby visits between 2011 and 2015 completed standardized questionnaires to elicit a convincing history of food allergy to estimate the population prevalence of food allergies. Results: The prevalence of a convincing history of cow's milk allergy was $0.51 \% ~(95 \%$ confidence interval [CI], 0.3-0.7), hen's egg allergy $1.43 \%$ ( $95 \%$ CI, 1.1-1.8), and peanut allergy $0.27 \%(95 \% \mathrm{CI}, 0.12-0.42)$. Of the 15 of 59 children with a convincing history of hen's egg allergy who consented, 12 ( $80 \%$ ) had corroborative positive skin prick tests. Conclusion: The prevalence of food allergy, in particular peanut allergy, in children below 2 years of age is lower in this South East Asian population than reported in Western cohorts. Further research should focus on deciphering differential risk factors for food allergy across different geographical locations.


Keywords: Food allergy; Cow’s milk; Egg; Peanut; Child; Asia

## INTRODUCTION

Allergic diseases such as food allergy are among the most common noncommunicable diseases (NCDs) in children worldwide [1]. Trends in asthma, allergic rhinitis, and atopic dermatitis have shown a global increase over the past few decades [2]. More recently, a similar rise in food allergy has been observed, which has been referred to as the second wave

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Conflict of Interest
The authors have no financial conflicts of interest.

## Author Contributions

Conceptualization: Alison Joanne Lee. Formal analysis: Wern-Ee Tang, Yew-Cheong Tung, Yehudi Yeo, Keith Tsou, Lynette Pei-Chi Shek, Le-Ye Lee, Hugo Van Bever, Bee-Wah Lee. Investigation: Alison Joanne Lee. Methodology: Yiong-Huak Chan. Project administration: Elizabeth Huiwen Tham, Jian-Yi Soh, Cesar Brence Labastida, PingPing Wang, Michelle Mei-Ling Tan. Writing - original draft: Alison Joanne Lee, Elizabeth Huiwen Tham, Bee-Wah Lee. Writing - review \& editing: Elizabeth Huiwen Tham, Hsin Yue Cheng, Bee-Wah Lee.
of the allergy epidemic [3]. This rise is likely attributable to the increase in peanut allergy prevalence occurring mainly in the Western world, which in school-age children in the United States (US) as well as in Australian infants is now as high as 3\% [4, 5].

It is also possible that the perceived increase in food allergy prevalence may be due to increased awareness, interest, and reporting of food allergy; as well as digitalization of health records which has enabled more comprehensive collection and archival of clinical data repositories. However, differences in methodologies remain the greatest challenge in prevalence data collection, especially as gold-standard food challenges are resource and time-consuming.

Nonetheless, marked differences in regional prevalence have provided greater insights into the environmental role in the aetiology of food allergy [6]. For example, Jewish children in the United Kingdom had a 10-fold higher rate of peanut allergy than Jewish children in Israel [7]. This information was the foot-stool in establishing a timely introduction of peanut as a means of preventing peanut allergy in the affected population [8].

Emerging data in Asia highlights regional differences in food allergy despite ethnic similarities. Cow's milk and egg are 2 of the most common food allergens in young children across Asia $[1,9]$, where the overall prevalence of milk and egg allergies are comparable to those reported in the Western populations [10]. This is with the exception of the Australian HealthNuts study, where the prevalence of challenge-proven egg allergy was $8.9 \%$ in 12 -month -old Australian infants [5]. Interestingly, wheat allergy is one of the main causes of food-anaphylaxis in both Japan and Korea [11]. The relative low prevalence of peanut allergy in Asia contrasts with the high prevalence in the Western world. For example, there is a high prevalence of peanut allergy in US children [3\%] [4] as well as Australian children at 4 years (1.9\%) [12] and 10-14 years (2.7\%) [13], but less than $1 \%$ in most parts of Asia [9, 10, 14-17].

This study aimed to evaluate the prevalence of cow's milk, egg, and peanut allergies and the associated risk factors in children below 30 months of age in the general population in Singapore using standardized methodologies to allow comparisons with published data from populations where similar studies were performed.

## MATERIALS AND METHODS

A cohort of children in Singapore aged between 11 and 30 months was evaluated over 3.5 years between November 2011 and June 2015. Children were recruited from 5 major vaccination centres - 3 outpatient government medical centres from the National Healthcare Group of polyclinics and 2 well-baby neonatal clinics at the only 2 children's government hospitals in Singapore (Departments of Paediatrics and Neonatology, National University Hospital, and KK Women's and Children's Hospital). Caregivers who brought their children for routine vaccinations were approached and invited to join phase I of the study consisting of a survey questionnaire on food allergy (Supplementary material: Questionnaire).

The survey included questions on the child's demographics, birth, maternal diet, breastfeeding, food introduction, and a section to assess if their child had symptoms suggestive of cow's milk, hen's egg, or peanut allergy. These questions regarding specific symptoms of allergy were adapted from a validated questionnaire developed by Sicherer
et al. $[18,19]$ to ascertain the presence of immediate type (IgE mediated) food allergy. Socioeconomic status was assessed by asking respondents for total monthly family income, which was categorized as $<\$ 3,500, \$ 3,500-\$ 5,499, \$ 5,500-\$ 7,499$, and $>\$ 7,500$, corresponding to the bottom 20th decile, bottom 20th-40th decile, 40th-50th decile, and top 50th decile respectively, according to the Singapore Department of Statistics, 2012 [20]. The answers were entered directly by the surveyor into the SurveyMonkey ${ }^{\circledR}$ program using touch screen tablets.

A convincing history of IgE-mediated food allergy was defined as meeting the following 3 criteria - firstly, a reaction within 2 hours of intake; secondly, any of the following symptoms of urticaria, skin rash, angioedema, vomiting, diarrhoea, abdominal pain, low blood pressure, difficulty breathing, or wheezing; and thirdly, avoiding the food of concern at the time of survey. Anaphylaxis was defined as per the National Institute of Allergy and Infectious Disease and the Food Allergy and Anaphylaxis Network's guidelines [21] - when any one of the following criteria were fulfilled: (1) Acute onset of an illness with involvement of the skin, mucosal tissue, or both and at least one of the following: respiratory compromise or reduced blood pressure or associated symptoms of end-organ dysfunction. (2) Two or more of the following (involvement of skin-mucosal tissue, respiratory compromise, reduced blood pressure or associated symptoms or persistent gastrointestinal symptoms) that occur rapidly after exposure to a likely allergen for that patient, or (3) reduced blood pressure after exposure to a known allergen for that patient.

Those who met the above-mentioned criteria for convincing IgE-mediated food allergy were invited to join phase II of the study that comprised a skin prick test (SPT), which was performed by a trained research coordinator or nurse and included hen's egg white, hen's egg yolk, cow's milk, soy, and peanut commercial extracts (GREER, Greenville, SC, USA), as well as a positive control (histamine dihydrochloride $10 \mathrm{mg} / \mathrm{mL}$ ) and negative control ( $0.9 \%$ normal saline). A wheal size of 3 mm greater than the diluent (negative) control was considered as a clinically significant positive result. SPTs were not carried out within 6 weeks of an anaphylactic reaction.

Statistical analysis was performed using IBM SPSS Statistics ver. 22.0 (IBM Co., Armonk, NY, USA). Statistical significance was set at $p<0.05$. The risk predictors for egg allergy, cow's milk allergy, and peanut allergy were determined using logistic regression.

Ethics approval was given by the Institutional Review Board (2012/00719), National University of Singapore. Written consent was taken from all participants by a study team member.

## RESULTS

A total of 4,115 participants completed the questionnaire survey of which $89.3 \%$ were Singaporean or permanent residents. The remaining children, although born outside Singapore, were from families who had lived in Singapore for 5 years or more. Patient demographics are shown in Table 1.

## Convincing history of food allergy

The prevalence of convincing history of food allergy, and SPT results outlined in Fig. 1. Based on convincing history alone, the overall prevalence of cow's milk allergy was $0.51 \%$ ( 21 of

Table 1. Demographics and prevalence of egg, milk, and peanut allergy of study population

| Variable | Surveyed population | Egg allergy | Cow's milk allergy | Peanut allergy |
| :---: | :---: | :---: | :---: | :---: |
| Total | 4,115 (100) | 59 (100) | 21 (100) | 11 (100) |
| Egg allergy* | 59 (1.4) | - | $5(23.8)^{\dagger}$ | 2 (18.2) |
| Cow's milk allergy ${ }^{*}$ | 21 (0.5) | $5(8.5)^{\dagger}$ | - | 2 (18.2) |
| Peanut allergy* | 11 (0.3) | 2 (3.4) | 2 (9.5) | - |
| Demographics |  |  |  |  |
| Age (mo), median $\pm$ IQR | $17 \pm 5.0$ | $16 \pm 7.0$ | $18 \pm 6.0$ | $18 \pm 6.0$ |
| Male sex | 2,181 (53.0) | 29 (49.2) | 13 (61.9) | 5 (45.5) |
| Singaporean or Singapore PR | 3,630 (88.2) | 51 (86.4) | 21 (100) | 11 (100) |
| Ethnicity |  |  |  |  |
| Chinese | 2,179 (53.0) | 26 (44.1) | 11 (52.4) | 4 (36.4) |
| Malay | 980 (23.8) | 18 (30.5) | 5 (23.8) | 4 (36.4) |
| Indian | 558 (13.6) | 6 (10.2) | 3 (14.3) | 2 (18.2) |
| Caucasian | 11 (0.3) | 9 (15.3) | 0 (0) | 0 (0) |
| Eurasian | 15 (0.4) | 0 (0) | 0 (0) | 0 (0) |
| Others | 180 (4.4) | $0(0)^{\dagger}$ | 2 (9.5) | 1 (9.1) |
| Total household income per month ${ }^{\ddagger, \S}$ |  |  |  |  |
| <\$3,500 | 980 (23.8) | 13 (24.8) | 8 (38.1) | 3 (27.3) |
| \$3,500-5,499 | 1,115 (27.1) | 17 (28.3) | 1 (4.8) | 2 (18.2) |
| \$5,500-7,499 | 826 (20.1) | 11 (20.9) | 4 (19.0) | 0 (0) |
| >\$7,500 | 1,024 (24.9) | 17 (26.0) | 8 (38.1) | 5 (45.5) |
| Birth weight (kg), median $\pm$ IQR | $3.1 \pm 0.6$ | $3.1 \pm 0.6$ | $3.2 \pm 0.5$ | $2.95 \pm 0.3$ |
| Gestation ${ }^{\text {® }}$ |  |  |  |  |
| Term 37-42 weeks | 3,679 (89.4) | 49 (83.1) | 19 (90.5) | 10 (90.1) |
| Preterm < 37 weeks | 358 (8.7) | 8 (13.6) | 1 (4.8) | 1 (9.1) |
| Postterm >42 weeks | 53 (1.3) | 2 (3.4) | 1 (4.8) | 0 (0) |
| Not sure | 11 (0.3) | 0 (0) | 0 (0) | 0 (0) |

Values are presented as number (\%) unless otherwise indicated.
IQR, interquartile range; PR, Permanent Resident.
*Food allergy was determined by a convincing history based on 3 criteria. Firstly, a reaction within 2 hours of intake; secondly, any of the following symptoms of urticaria, skin rash, angioedema, vomiting, diarrhoea, abdominal pain, low blood pressure, difficulty breathing, or wheezing; and thirdly, avoiding the food of concern at the time of survey. ${ }^{\dagger} p<0.05$, significant results in multivariate analysis (see Table 4). ${ }^{\ddagger}$ Denotes average household income deciles according to Singapore Department of Statistics, 2012. 〈\$3,500: 20th decile; \$3,500-\$5,499: 40th decile; $\$ 5,500-\$ 7,499$ : 40th decile; $>\$ 7,500$ : top 50th decile. ${ }^{\text {SPercentages of subjects do not add up to } 100 \% \text { due }}$ to missing data.


Fig. 1. Study flow diagram. Convincing food allergy was defined as meeting 3 criteria - firstly, a reaction within 2 hours of intake; secondly, any of the following symptoms of urticaria, skin rash, angioedema, vomiting, diarrhoea, abdominal pain, low blood pressure, difficulty breathing, or wheezing; and thirdly, avoiding the food of concern at the time of survey.

4,115; $95 \%$ confidence interval [CI], $0.3-0.7$ ) with mean age at first reaction $6.00 \pm 4.85$ months. The prevalence of hen's egg allergy was $1.43 \%$ ( 59 of $4115 ; 95 \%$ CI, 1.1-1.8) and mean age at first reaction was $9.00 \pm 3.59$ months. The prevalence of peanut allergy was $0.27 \%$ (11 of 4,115; $95 \%$ CI, $0.12-0.42$ ) with mean age at first reaction $8.0 \pm 4.9$ months.

At the time of the questionnaire administration, only 1,962 (47.7\%) of the cohort had ever been exposed to peanuts or peanut products. Within the subgroup of subjects with previous peanut exposure, $0.56 \%$ ( 11 of $1962 ; 95 \% \mathrm{CI}, 0.12-0.42$ ) had a convincing history of peanut allergy. In subjects with reported cow's milk and egg allergy, a subanalysis of only children with prior exposure showed similar findings (data not shown), as the majority of the population ( $92.1 \%$ for cow's milk and $96.7 \%$ for any form of egg) had been exposed by the time of survey.

The overall prevalence of a convincing history of anaphylaxis to any of these 3 foods was $0.19 \%$. Anaphylaxis was reported in $14.2 \%(n=3)$ of those with a convincing history of cow's milk allergy and $8.5 \%(\mathrm{n}=5)$ with hen's egg allergy. None of those surveyed had peanut anaphylaxis.

## SPT-proven food allergy

A total of $25.4 \%(\mathrm{n}=15)$ of reported egg allergic patients consented for skin prick testing. The prevalence of egg allergy, as evaluated by a convincing history and corroborative allergen sensitization, was thus $0.29 \%$ ( 12 of 4,115 ) in this cohort, and the prevalence of challengeproven egg allergy was $0.12 \%$ ( 5 of 4,115 ), including the patient who developed anaphylaxis.

## Risk factors for food allergy

Risk factors for food allergy in this population are described in Tables 2 and 3. There were 1,429 subjects ( $34.7 \%$ ) with a family history of allergic disease and 554 ( $13.5 \%$ ) had a family history of food allergy. Multivariate analysis (Table 4) demonstrated that a history of eczema was strongly associated with a convincing history of cow's milk allergy (adjusted odds ratio [OR], 5.09; 95\% CI, 1.51-17.15; $p=0.009$ ) as well as egg allergy (adjusted OR, $3.41 ; 95 \% \mathrm{CI}$, $1.60-7.30 ; p=0.002$ ). A positive family history of atopic disease or food allergy was also a significant risk factor for egg allergy. Non-Chinese ethnicity, smoking, and supplementation of vitamin D during pregnancy were also positively associated with egg allergy. A convincing history of cow's milk allergy was a risk factor for developing egg allergy, and vice versa. The rates of peanut allergy were too low to perform a multiple logistic regression. There were no associations between egg and cow's milk allergy and the timing of introduction of allergenic foods, pet ownership, presence of siblings, and childcare attendance.

## DISCUSSION

This is one of the largest population-based studies in Asia with comprehensive evaluations of cow's milk, egg, and peanut allergy in children below 30 months of age. Based on convincing history alone, the reported prevalence of cow's milk, hen's egg, and peanut allergy were $0.51 \%, 1.43 \%$, and $0.27 \%$ respectively. Within the subgroup with documented prior peanut consumption, the prevalence of reported peanut allergy was $0.56 \%$. These data support the notion that food allergy rates are truly low in this region.

Within the Asian region, most food allergy prevalence studies have been based on convincing history alone [10]. A Chinese study showed similar rates for egg allergy (1.4\%) but higher

Table 2. Risk factors of food allergy - lifestyle and family history

| Variable | Surveyed population ( $n=4,115$ ) | Egg allergy ( $\mathrm{n}=59$ ) | Cow's milk allergy ( $\mathrm{n}=21$ ) | Peanut allergy ( $\mathrm{n}=11$ ) |
| :---: | :---: | :---: | :---: | :---: |
| Mode of delivery $\ddagger$ |  |  |  |  |
| Normal vaginal delivery | 2,693 (65.4) | 41 (69.5) | 13 (61.9) | 6 (54.5) |
| Caesarean section | 1,416 (34.4) | 18 (30.5) | 8 (38.1) | 5 (45.5) |
| Foods/supplements during pregnancy |  |  |  |  |
| Egg | 3,881 (94.3) | $53(89.8)^{\dagger}$ | 20 (95.2) | 9 (81.8)* |
| Cow's milk | 3,574 (86.9) | 50 (84.7) | 19 (90.5) | 10 (90.9) |
| Soy | 3,618 (87.9) | 51 (86.4) | 20 (95.2) | 10 (90.9) |
| Peanut | 2,838 (69.0) | 41 (69.5) | 16 (76.2) | 6 (54.5) |
| Tree nuts | 3,046 (74.0) | 44 (74.6) | 19 (90.5) | 8 (72.7) |
| Shellfish | 3,063 (74.4) | 45 (76.3) | 15 (71.4) | 8 (72.7) |
| Fish | 3,870 (94.1) | 56 (94.9) | 20 (95.2) | 9 (81.8) |
| Probiotics | 1,273 (30.9) | 20 (33.9) | 8 (38.1) | 3 (27.3) |
| Fish oils | 2,529 (61.5) | 32 (54.2) | 13 (61.9) | 8 (72.7) |
| Vitamin D | 2,342 (56.9) | 37 (62.7) ${ }^{\dagger}$ | 15 (71.4) | 7 (63.6) |
| Folic acid | 3,791 (92.1) | 54 (91.5) | 18 (85.7) ${ }^{\dagger}$ | 10 (90.9) |
| Furred pet ownership | 529 (12.9) | 4 (6.8) | 19 (90.5) | 2 (18.2) |
| Smoking exposure (in or outside the house) | 1,573 (38.2) | $26(44.1)^{\dagger}$ | 16 (76.2) | 5 (45.5) |
| Only child | 1,627 (39.5) | 19 (32.2) | 8 (38.1) | 3 (27.3) |
| No. of siblings, median $\pm$ IQR | $1.0 \pm 1.0$ | $1.0 \pm 1.0$ | $1.0 \pm 1.0$ | $1.0 \pm 2.0$ |
| Attends child care services | 453 (11.0) | 6 (10.2) | 3 (14.3) | 1 (9.1) |
| Personal or family history of atopy |  |  |  |  |
| Atopic dermatitis | 576 (14.0) | $30(50.8)^{\dagger}$ | $9(42.9)^{\dagger}$ | 8 (72.7) |
| Wheeze | 593 (14.4) | 10 (16.9) | 6 (28.6) | 3 (27.3) |
| Ever had a wheeze | 182 (4.4) | 4 (6.8) | 1 (4.8) | 1 (9.1) |
| Recurrent (more than 2 episodes) |  |  |  |  |
| Allergic rhinitis | 852 (20.7) | 18 (30.5) | 7 (33.3) | 5 (45.5) |
| Family history of food allergy | 554 (13.5) | 16 (27.1) ${ }^{\dagger}$ | 2 (9.5) | 5 (45.5) |
| Family history of atopic conditions | 1,429 (34.7) | $36(61.0)^{\dagger}$ | 10 (47.6) | 9 (81.8) |

Values are presented as number (\%) unless otherwise indicated.

* $Q R$, interquartile range.
$* p<0.05$, significant results in univariate analysis. ${ }^{\dagger} p<0.05$, significant results in multivariate analysis (see Table 4). ${ }^{\ddagger}$ Percentages of subjects do not add up to $100 \%$ due to missing data.
rates of cow's milk allergy (1.9\%) in preschoolers [22]. A South Korean study reported the prevalence of egg and cow's milk allergy to be $2.8 \%$ and $1.7 \%$ in children aged 1 year [23], while the prevalence of caregiver-reported immediate egg and cow's milk allergy were higher in Japan at $5.3 \%$ and $2.1 \%$ respectively in children of the same age [24]. A more recent study in primary school children aged 7 to 10 years in China, India, and Russia using the EuroPrevall screening questionnaire also showed generally low rates of food allergy [25]. With food allergy defined as having both allergy symptoms and IgE sensitization, the rates of egg allergy was $0.20 \%, 0.04 \%, 0.10 \%$, and $0.05 \%$ in Hong Kong, Guangzhou, Tomsk, and India respectively. The prevalence of cow's milk allergy was also generally low, with the highest being $0.04 \%$ in Shaoguan and $0.05 \%$ in Tomsk.

With the exception of Australia, the prevalence of cow's milk and egg allergy across the globe are comparable with the Asian data. The Australians have the highest prevalence of challenge-proven egg allergy $(8.9 \%)$ so far in 1-year-old children [5]. A follow-up at age 4 years showed a decline in egg allergy rates to $1.2 \%$ [12]. After Australia, the next highest prevalence rates of cow's milk and egg allergy in children were in the United Kingdom [26] and the US $[27,28]$. In the UK Isle of Wight cohort, the prevalence of convincing cow's milk allergy was $1.6 \%$ to $3.5 \%$, and for egg allergy $1.1 \%$ to $1.4 \%$ in children aged 1 to 2 years [26]. Self-reported food allergy rates in children below 2 years of age in the US were $2 \%$ for cow's milk allergy and $1 \%$ for egg allergy [27, 28]. There are currently no available challenge-proven food allergy data from the US.

Table 3. Risk factors of food allergy - feeding history

| Variable | Surveyed population ( $n=4,115$ ) | Egg allergy ( $\mathrm{n}=59$ ) | Cow's milk allergy ( $\mathrm{n}=21$ ) | Peanut allergy ( $\mathrm{n}=11$ ) |
| :---: | :---: | :---: | :---: | :---: |
| Breastfeeding§ |  |  |  |  |
| At any point | 3,765 (91.5) | 56 (94.9) | 20 (95.2) | 11 (100) |
| <6 Months | 1,740 (42.3) | 21 (35.6) | 8 (38.1) | 5 (45.5) |
| $\geq 6$ Months | 1,976 (48.0) | $35(59.3)^{\dagger}$ | 12 (57.1) | 6 (54.5) |
| Never breast fed | 307 (7.5) | 3 (5.1) | 1 (4.8) | 0 (0.0) |
| Age when formula milk introduced (mo)§ |  |  |  |  |
| <6 Months | 2,807 (68.2) | 34 (57.6) | 12 (57.1) | 8 (72.7) |
| 6 Months or more | 911 (22.1) | 19 (32.2) | 12 (57.1) | 2 (18.2) |
| Not started | 236 (5.7) | 4 (6.8) | 1 (4.8) | 1 (9.1) |
| Not sure | 83 (2.0) | 1 (1.7) | 0 (0) | 0 (0) |
| Main type of milk feeding in first 6 months of life§ |  |  |  |  |
| Breast milk | 1,177 (28.6) | 21 (35.6) | 9 (42.9) | 4 (36.4) |
| Mixed (formula and breast milk) | 2,432 (59.1) | 34 (57.6) | 11 (52.4) | 7 (63.6) |
| Formula | 465 (11.3) | 3 (5.1) | 1 (4.8) | 0 (0) |
| Age when solids introduced ${ }^{\text {® }}$ |  |  |  |  |
| <4 Months | 49 (1.2) | 1 (1.7) | 0 (0.0) | 0 (0.0) |
| 4-6 Months | 2,654 (64.5) | 35 (59.3) | 13 (61.9) | 4 (36.4) |
| >6 Months | 1,248 (30.3) | 21 (35.6) | 7 (33.3) | 7 (63.6) |
| Not weaned yet | 21 (0.5) | 1 (1.7) | 0 (0) | 0 (0) |
| Not sure | 62 (1.5) | 0 (0) | 0 (0) | 0 (0) |
| Age of egg introduction§ |  |  |  |  |
| <4 Months | 31 (0.8) | 0 (0) | 0 (0) | 0 (0) |
| 4-6 Months | 810 (19.7) | 13 (22.0) | 4 (19.0) | 2 (18.2) |
| >6 Months | 3,110 (75.6) | 46 (78.0) | 16 (76.2) | 9 (81.8) |
| Not introduced yet | 80 (1.9) | 0 (0) | 1 (4.8) | 0 (0) |
| Not sure | 57 (1.4) | 0 (0) | 0 (0) | 0 (0) |
| Age of peanut introduction§ |  |  |  |  |
| <12 Months | 326 (7.6) | 7 (11.9) | 2 (9.5) | 6 (54.5) |
| 12 Months of more | 993 (24.1) | 14 (23.7) | 7 (33.3) | 5 (45.5) |
| Not started | 2,037 (49.5) | 29 (49.2) | 11 (52.4) | 0 (0) |
| Not sure | 53 (1.3) | 1 (1.7) | 0 (0) | 0 (0) |
| Has taken more than 1 course of antibiotics | 815 (19.8) | 22 (37.3) | 8 (38.1)* | 1 (9.1) |

[^0] 100\% due to missing data.

Table 4. Multivariate analysis of risk factors* for food allergy

| Variable | Adj OR | $95 \% \mathrm{Cl}$ | Adj $p$ value |
| :--- | :---: | :---: | :---: |
| Cow's milk allergy |  |  |  |
| Reported eczema in child | 5.09 | $1.51-17.15$ | 0.009 |
| Taking folic acid in pregnancy | 0.10 | $0.01-0.79$ | 0.029 |
| Egg allergy - convincing history | 28.44 | $4.21-191.90$ | 0.001 |
| Egg allergy |  |  |  |
| Breastfeeding $\geq 6$ months $^{\dagger}$ | 0.30 | $0.13-0.66$ | 0.003 |
| Non-Chinese ethnicity | 4.66 | $1.3-16.68$ | 0.018 |
| Reported eczema in child | 3.41 | $1.60-7.30$ | 0.002 |
| Family history of food allergy | 2.32 | $1.06-5.00$ | 0.034 |
| Family history of atopy | 3.85 | $1.75-8.33$ | 0.001 |
| Smoking - any members of household | 4.44 | $1.16-17.01$ | 0.030 |
| Eating egg in pregnancy | 0.23 | $0.061-0.89$ | 0.033 |
| Taking vitamin D in pregnancy | 4.42 | $1.00-19.55$ | 0.050 |
| Cow's milk allergy - convincing history | 11.73 | $2.16-63.62$ | 0.004 |

Adj, adjusted; OR, odds ratio; CI, confidence interval.
*Variables included in the multivariate logistic regression model are nationality, ethnicity, gender, maternal diet during pregnancy (egg, cow's milk, peanut, treenut, soy, fish, shellfish), maternal intake of supplements during pregnancy (folic acid, vitamin D, probiotics, fish oils), birth type, gestation, breast feeding (ever breast fed and duration), birth order (1st child), formula and solid food (milk formula, any solid, egg, peanut) introduction, personal history of eczema, 2 or more wheezes, allergic rhinitis, family history of food allergy or allergic conditions, pet ownership, smoking, childcare, income and antibiotic use. ${ }^{\dagger}$ Breastfeeding < 6 months as reference group.

In contrast, the EuroPrevall birth cohort had lower rates of challenge-proven egg and cow's milk allergy across 9 European countries. The adjusted prevalence of challenge-proven cow's milk allergy in children below 2 years of age was $0.54 \%$ ( $95 \%$ CI, $0.41-0.70$ ) and ranged from $<0.3 \%$ to $1 \%$ between centres [29]. The prevalence of challenge-proven egg allergy in the same cohort was $1.23 \%$ ( $95 \%$ CI, $0.98-1.51$ ) and ranged between $0.07 \%$ and $2.18 \%$ [30]. These prevalence rates are comparable to the questionnaire-based rates in our study. Most (6 out of 9) European countries included in the study, including Germany, Italy, and Poland, reported very low rates of cow's milk and egg allergy ( $<1.0 \%$ ). In Greece, cow's milk and egg allergy were almost nonexistent ( $0.07 \%$ ) and egg allergy was only $0.1 \%$.

The prevalence of peanut allergy ( $<1 \%$ ) in the Asian populations has been consistently low, despite differing methodologies [10]. The prevalence of peanut allergy by convincing history in children below 2 years of age in this study was only $0.27 \%$. As self-reported symptoms tend to overestimate the true disease prevalence, the true peanut allergy prevalence is likely to be even lower. In addition, none of these allergic children reported symptoms suggestive of anaphylaxis, suggesting that the peanut allergy phenotype might be relatively mild in Singapore. This low prevalence is consistent with 2 previous studies in Singapore which reported peanut allergy prevalence of just $0.1 \%$ to $0.3 \%$ in children below 4 years of age [9] and $0.64 \%$ in $4-6$ year olds [14]. Similarly, a Korean study showed a peanut allergy prevalence of just $0.22 \%$ in 6-7 year olds [31], while that in Hong Kong and India were found to be only $0.10 \%$ and $0.03 \%$ respectively [25].

The challenge-proven peanut allergy rates in Western cohorts in the UK and Australia range between $1.2 \%$ and $3.1 \%$ [5,32], exceeding the self-reported peanut allergy rates in Singapore and Korea. While there are no challenge-proven studies from the US, the prevalence of a convincing history of peanut allergy in young children below 2 years of age was $1.4 \%$ (28), which is 5 times higher than we have found in our study. Hence, guidelines which have been published in the US and Europe on early peanut exposure for the primary prevention of peanut allergy [33, 34] may not be as applicable to the Asian region [35].

Environmental influences on epigenetics may play a role in modulating the differences in peanut allergy prevalence between populations. The Australian HealthNuts study reported the prevalence of challenge-proven peanut allergy to be $6.7 \%$ in infants with one parent born in East Asia, and $7.7 \%$ in infants with both parents born in East Asia. They also found that Asian children born in Australia to ethnic Asian parents were more likely to have challenge-proven peanut allergy (adjusted OR, 2.67; 95\% CI, 2.28-3.27) than those who were born in Asia and then subsequently migrated to Australia [36]. The reverse has also been shown to be true in an observational study in Singapore, where migrants born in Western countries were at higher risk of peanut allergy (adjusted OR, 3.47; 95\% CI, 1.35-8.93) in 4-6 year olds as well as 14-16 year olds (adjusted OR, 5.56; 95\% CI, 1.74-17.76) compared with those who had been born in Asia [14]. It appears that dietary differences alone cannot explain these differences as demonstrated in an earlier Singapore birth cohort study [9] and more studies focusing on environmental risk factors for food allergy in South East Asia are required to ascertain protective mechanisms.

Strengths of this study included the large unselected population-based sample, which allowed for accurate estimations of reported food allergy. Although the SPT rate in those who were cow's milk and peanut allergic limited our ability to assess specific allergen sensitization-proven prevalence, for those who did undergo the procedure, the test was positive in $84 \%$ of those with a convincing history of cow's milk, egg or peanut allergy.

In conclusion, based on a convincing history, the prevalence of IgE-mediated cow's milk, egg, and peanut allergy was established to be low in infants and toddlers in this developed South East Asian population. Consistent with other Asian populations, the reported prevalence of peanut allergy is approximately 10 times lower than in some Western cohorts. Further studies are needed to determine risk factors underpinning these differences in similarly urbanised populations. This is a necessary step in understanding causality and determining prevention in populations where food allergy is still escalating.

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## SUPPLEMENTARY MATERIAL

Supplementary questionnaire can be found via 10.5415/apallergy.2022.12.e31

## Supplementary questionnaire

The Prevalence and Natural History of Cow's Milk and Hen's Egg Allergy in Singapore

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[^0]:    Values are presented as number (\%).
    ${ }^{*} p<0.05$, significant results in univariate analysis. ${ }^{\dagger} p<0.05$, significant results in multivariate analysis (see Table 4). §Percentages of subjects do not add up to

