



Original Article

Prevalence of food allergy among preschool children in northern Thailand

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Abstract *Background:* The epidemiology and clinical spectrum of food allergies (FA) confirmed by oral food challenge tests (OFC) in the Southeast Asian countries are limited. The aim of the present study was to examine the prevalence and characteristics of FA among preschool children in northern Thailand.

Methods: Five hundred and forty-six children aged 3–7 years living in Chiang Mai, Thailand participated in this study. A cross-sectional parent questionnaire survey was conducted. Families with children reporting FA were invited to undergo further investigations with skin prick testing, serum specific IgE, and OFC.

Results: A total of 452 out of 546 questionnaires (82.8%) were returned. Forty-two children (9.3%) were reported to have FA. The five leading allergic foods reported were shrimp, cow's milk, fish, chicken eggs, and ant eggs. The most commonly reported symptom was a skin rash (78.0%), followed by abdominal pain and vomiting (31.1%). Anaphylaxis was found in two children (3.4%), from ant eggs allergy. Eighteen children underwent OFC; five of them were positive to shrimp, fish, and crab. Either skin prick test or serum-specific IgE was positive in these children. Factors associated with parent-reported FA included personal and family history of atopic dermatitis.

Conclusions: The prevalence of IgE-mediated FA confirmed on OFC was $\geq 1.11\%$ (95% confidence interval: 0.41–2.98%). The most common causative food was shrimp. Ant eggs were a unique food allergen causing severe reactions in preschool children in northern Thailand.

Key words children, food allergy, food challenge, prevalence, Thailand.

Food allergy (FA) is an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food.¹ The clinical spectrum of FA ranges from mild skin irritation to severe life-threatening anaphylaxis. Currently, an avoidance of causative food remains the only mainstay management of FA.^{1,2} Hence, the affected children and their parents experience difficulty in managing their daily activities.

The majority of FA is mediated by immunoglobulin E (IgE), but sensitization to a specific food as confirmed on skin prick test (SPT) or serum-specific IgE (SIgE) do not always imply clinical reactivity. The accurate diagnosis of FA should be based on an oral food challenge (OFC).^{1–6} Studies of FA prevalence confirmed by OFC are scarce due to their being difficult and time consuming.^{7–9} There are discrepancies between the self-reported prevalence of FA and the OFC prevalence.^{7,9} A study in the USA by Bock that followed children from birth to 3 years of age demonstrated a parent-reported FA of 28%, but only 8% were positive on OFC.¹⁰ In one meta-analysis, including data from 51 studies, the overall prevalence of parent-reported FA

in children was 12%. This compares to a much lower value of 3% when assessed on reported FA symptoms and sensitization or OFC.⁹

The epidemiology and clinical spectrum of FA have been extensively studied in the USA, Europe and Australia, but such data in Asia, especially Southeast Asia, are limited.⁸ Moreover, the previous studies reported on the different kinds of causative food allergen among different regions. Several unique food allergens among Asian countries have been reported.⁸ Therefore, there is a need for data on the local prevalence and clinical spectrum of FA in this area.

Chiang Mai is the largest province in northern Thailand where health-care services in the urban area are sufficient. Access to an allergist, however, is limited. Most patients with FA are managed by general practitioners. Diagnosis of FA in clinical practice is usually based on clinical history, while use of confirmed allergy tests such as SIgE, SPT or OFC is not routine. In Thailand, there had been only one epidemiological study of FA among 6-month-old to 6-year-old children in Bangkok. The prevalence of FA was 6.25% on FA questionnaire and 0.45% on OFC. Cow's milk and eggs were common causative foods among young children, whereas shrimp was the most common reported cause in older children.¹¹

The aim of the present study was to determine the prevalence and clinical features of parent-reported and OFC-confirmed FA

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among preschool children living in Chiang Mai, Thailand. We also investigated the possible associated factors of FA.

Methods

Subjects

This was a cross-sectional study that was performed in 2010 in Muang District, Chiang Mai Province. The subjects were selected by multistage random sampling. Nine kindergartens were selected randomly from a complete list of kindergartens in the district provided by the local education department. Three different classes were randomly selected from each school. All children ($n = 546$) in the selected classes were approached and given a detailed questionnaire to be completed by their parents. Children whose parents gave informed consent by returning the completed self-report questionnaire ($n = 452$; participation rate, 82.8%) were enrolled.

A sample size was calculated to estimate a 95% confidence interval (95%CI) for a prevalence of FA of approximately 10% with a 3% margin of error. A final sample size of at least 540 children was calculated after adjusting for a non-response rate of 40% of parents.

This study was approved by the Research Ethics Committee, Faculty of Medicine, Chiang Mai University.

Questionnaire

Each child was given a standard questionnaire to be complete by his/her parents. The questionnaire including the child's demographic data, number of siblings, feeding history during infancy, the child's and the family's history of atopic diseases. The presence of family history of atopic disease was confirmed if his/her parents and sibling had doctor-diagnosed asthma, allergic rhinitis, atopic dermatitis, or FA. For FA history, the parents were asked to specify the trigger foods, time of onset and details of their symptoms. Parents were also asked whether their child currently avoided that causative food. The last question requested consent for the child's participation in further investigations.

The questionnaire contained simple and brief questions in order to increase participation, ensure comprehensibility, and to provide accurate answers. The questionnaire was validated and pre-tested on a pilot group of 20 parents with or without FA.

Definitions of FA

Parents were asked about the occurrence of food allergy in their children. The definitions of FA were as follows: 'ever had FA', occurrence of FA at least once in the child's lifetime; 'current FA', occurrence of FA symptoms and current avoidance of or reaction to the suspicious food at the time of the study.

Children who were reported to have current FA were invited to participate in further diagnostic investigations, including SPT, SIgE, and OFC.

Skin test procedure and SIgE

The SPT were carried out using commercially available extracts of standard food allergen (ALK Abelló, Port Washington, NY, USA). As well as the SPT, the prick-to-prick skin test (PTP) using selected cooked foods were performed using straight sur-

gical needles either on the back or forearm.^{12,13} One mg/mL histamine and glycerinated phenol-saline SPT were used as positive and negative controls, respectively. The wheal diameter was the mean of the largest wheal diameter and diameter orthogonal to it. Wheal reactions ≥ 3 mm than the negative control were considered positive reactions.⁴ The SIgE to each specific causative food was measured using ImmunoCAP (Phadia, Uppsala, Sweden) according to the manufacturer's instructions. The SIgE was considered positive if >0.35 IU/mL.¹⁴

Food challenge procedure

The OFC were performed when the children were completely well and had discontinued antihistamine for at least 7 days before the challenge. The open OFC tests were conducted in the hospital under the supervision of an allergist with close observation for any adverse signs and symptoms. The introduction of suspected foods was started at ≤ 1 g according to the previous history. For children with suspected cow's milk allergy, one drop of cow's milk was placed on the inner lips first. If no reaction occurred the following dose was increased gradually every 15–30 min, until the usual daily dose was reached (in total 280 mL of cow's milk; 30 g of fish, shrimp, beef, crab; 10 g of cocoa). The child was observed for at least 4 h following the last dose of the challenge. The OFC was considered positive if clinical reactions were noted.^{3,5,6} Emergency resuscitation equipment and drugs were available in case of emergency. The parents of the child were asked to observe any adverse reaction for at least 3 days and notify the study physician immediately if unexpected or severe reactions occurred. A challenge to a different food was conducted at least 2 weeks after the first challenge.

Statistical analysis

All analyses were performed using SPSS version 13.0 (SPSS, Chicago, IL, USA). Results are expressed as mean $\pm$ SD, percentages, or 95%CI of responses to each question. The prevalence of responses was compared using χ^2 test or Fisher's exact test as appropriate. The odds ratio (OR) and 95%CI were calculated to analyze the associated factors of 'ever had FA'. Covariates with $P < 0.2$ on univariate analysis or which were considered biologically relevant were included in multivariate analysis. $P < 0.05$ for two-sided tests was considered to be statistically significant.

Results

Four hundred and forty-six of 552 questionnaires (82.8%) were completed and returned. Table 1 summarizes the demographic characteristics of the children who completed questionnaires. Fifty-nine parents (13.05%; 95%CI: 9.94–16.17) and 42 parents (9.29%; 95%CI: 6.61–11.98) reported that their children had ever had FA and had current FA, respectively. Types of food that caused FA are listed in Table 2. Among the 13 types of foods that were reported, cow's milk was the most commonly reported to ever cause FA (30.5%), while shrimp was the most common cause of current FA (33.3%). Table 3 lists the clinical manifestations and frequency of reactions in children who had ever had FA, in descending order, as: skin reactions, swelling of lips and face,

Table 1 Subject data ($n = 452$)[†]

Variable	<i>n</i> (%)
Sex	
Male	234 (51.8)
Female	218 (48.2)
Age (years), mean $\pm$ SD	5.3 $\pm$ 1.0
3 to <4	63 (13.9)
≥ 4 to <5	97 (21.5)
≥ 5 to <6	152 (33.6)
≥ 6 to 7	136 (30.1)
Breast-feeding up to 4 months of age	
Breast-fed only	300 (66.4)
Partially breast-fed	99 (21.9)
Formula fed [‡]	52 (11.5)
Age of solid food introduction	
<4 months	138 (30.5)
4–6 months	107 (23.7)
>6 months	207 (45.8)
Food allergy	
Parent-reported 'ever had FA'	59 (13.1)
Parent-reported 'current FA'	42 (9.3)
Presence of any allergic diseases	202 (44.7)
Asthma	16 (3.5)
Allergic rhinitis	128 (28.3)
Atopic dermatitis	118 (26.1)
Paternal allergy history	
Asthma	7 (1.5)
Allergic rhinitis	63 (13.9)
Atopic dermatitis	2 (0.4)
Food allergy	12 (2.6)
Maternal allergy history	
Asthma	9 (2.0)
Allergic rhinitis	69 (15.3)
Atopic dermatitis	5 (1.1)
Food allergy	12 (2.6)
Allergy history in siblings	
Asthma	5 (1.1)
Allergic rhinitis	31 (6.9)
Atopic dermatitis	3 (0.6)
Food allergy	6 (1.3)

[†]Completed questionnaires only. [‡]Breast-fed to <1 month of age. Ever had FA, occurrence of FA ever in the child's lifetime; current FA, occurrence of FA symptoms and current avoidance of or reaction to the suspicious food at the time of the study. FA, food allergy.

gastrointestinal symptoms, and respiratory symptoms. The time to onset of reaction ranged from <1 min to 24 h after food consumption (median, 40 min; interquartile range, 20–120 min). Most reported reactions (40/54, 74%) occurred early <1 h after food consumption; six reactions (11%) occurred at >4 h. Two children (3.4%) reported anaphylaxis caused by ant eggs (*Oecophylla smaragdina*). The symptoms were urticaria, angioedema, and chest tightness, which required emergency treatment.

Twenty-one OFC were performed in 18 children. The SPT, PTP, and SIgE were done in all of them. The details of all children who underwent SPT, PTP, SIgE, and OFC with positive OFC results are given in Table 4. FA was confirmed in five children: three to shrimp, one to fish, and one to both shrimp and crab. All of the positive challenge reactions were confined to within the mucocutaneous system. No severe life-threatening reactions occurred during OFC. The total time to reaction ranged

from 1 min to 3 h. The SIgE were positive in all, except for one child who reacted to fish, but this child had a wheal reaction of 13 mm in diameter on PTP. One child had positive OFC and SIgE to both shrimp and crab. One child was challenged with two different species of shrimp due to her complaint of a specific type of shrimp allergy. This child had positive OFC only to freshwater shrimp (*Macrobrachium lanchesteri*) but negative OFC to sea-water shrimp (*Panaeus monodon*). She also had positive SIgE to shrimp but negative skin test on commercial SPT and cooked shrimp PTP. In the present study, five children out of a total 452 children were confirmed to have FA, therefore the estimated prevalence of FA among this group was 1.11% (95%CI: 0.14–2.07%). All of them had positive results to either skin test or SIgE, with suggested IgE-mediated reactions.

The associated factors for 'ever had FA' are given in Table 5. Significant factors that were found on univariate logistic regression analysis were personal history of atopic diseases (OR, 2.09; 95%CI: 1.20–3.64; $P = 0.011$), personal history of atopic dermatitis (OR, 2.58; 95%CI: 1.47–4.57; $P = 0.001$), history of atopic disease in first-degree relatives (OR, 3.30; 95%CI: 1.38–7.94; $P = 0.004$), and history of atopic dermatitis in first-degree relatives (OR, 7.07; 95%CI: 1.72–29.10; $P = 0.01$). Both a personal history of atopic dermatitis, and that of a first-degree relative with atopic dermatitis were still statistically significant after being adjusted for in the multivariate logistic regression model. History of atopic disease was not included in the multivariate analysis because of the association between atopic dermatitis and atopic disease.

Discussion

This population-based study has demonstrated that the prevalence of parent-reported 'ever had FA' and 'current FA' were 13.1% and 9.3%, respectively. Among the current FA, the leading causative foods were shrimp, cow's milk, fish, chicken eggs, and ant eggs. The prevalence of FA, as confirmed by OFC, was 1.1%. The confirmed causative foods were shrimp, fish, and crab. Most of these children (78%) presented with mucocutaneous reactions. History of anaphylaxis was described in two children (3.4%), caused by ant eggs. Factors associated with parent-reported FA included personal and family history of atopic dermatitis.

According to previous studies, the prevalence of self/parent-reported FA was between 3% and 35%.⁹ The prevalence of FA varies in different countries and according to survey methodologies. Studies in Asian countries estimated that the rate of questionnaire-based FA was 1.2–8.1%.^{11,15–19} In Thailand, only one epidemiological study of FA in Bangkok, reported in 2005, gave a prevalence rate of parent-reported FA, and that was 6.25%,¹¹ which is lower than the present rate. This might indicate that FA has increased in prevalence. A recent study of the time trend of FA from the same hospital using the same methodology in China performed in 1999 and 2009, found a significant increase in FA rate from 3.5% to 7.7%.¹⁸ This might not be applicable to the present study, however, due to the differences in questionnaire, method, and population.

The most reliable method to diagnose FA is OFC. The discordance between self/parent-reported FA and OFC-confirmed FA

Table 2 Type of foods and no. children with food allergy

Food	Parent-reported 'ever had FA' <i>n</i> (%), (<i>n</i> = 59)	Parent-reported 'current FA' <i>n</i> (%), (<i>n</i> = 42)	Children challenged <i>n</i> (%), (<i>n</i> = 18) [†]	Positive challenge <i>n</i> (%), (<i>n</i> = 5) [‡]
Cow's milk	18 (30.5)	9 (21.4)	5 (27.8)	0
Shrimp	15 (25.4)	14 (33.3)	8 (44.4)	4 (80.0)
Chicken eggs	8 (13.6)	4 (9.5)		
Fish	5 (8.5)	5 (11.9)	3 (16.7)	1 (20.0)
Crab	4 (6.8)	3 (7.1)	1 (5.6)	1 (20.0)
Ant eggs	4 (6.8)	4 (9.5)		
Wheat	4 (6.8)	1 (2.4)		
Beef	2 (3.4)	2 (4.8)	2 (11.1)	0
Chocolate	2 (3.4)	2 (4.8)	1 (5.6)	0
Insect	2 (3.4)	2 (4.8)		
Coconut	1 (1.7)	1 (2.4)		
Squid	1 (1.7)	1 (2.4)		
Mollusk	1 (1.7)	1 (2.4)		

Ever had FA, occurrence of FA ever in the child's lifetime. Nine children reported more than one food. Current FA, occurrence of FA symptoms and current avoidance of or reaction to the suspicious food at the time of the study. Seven children reported more than one food. [†]Two children underwent challenge to two foods. One child was challenged with freshwater and seawater shrimps. [‡]One child had positive challenge with two foods. FA, food allergy.

has been described in various reports.^{7,10,11,18,19} Several studies have shown that only approximately one-third of suspected FA are found to be true allergy.²⁰ In accordance with this, approximately 28% (5/18) of the present subjects who underwent OFC had a positive result. According to the present results, the prevalence of parent-reported FA was ninefold more than OFC-confirmed FA (9.3% vs 1.1%). Given that only 43% of children (18/42) who reported current FA underwent OFC in the present study, the true prevalence of confirmed FA would be higher than that reported.

Table 3 Clinical manifestations of reported food allergy (*n* = 59)

Reactions	<i>n</i> (%)
Skin reaction (hives, rash, itching)	46 (78.0)
Swelling of lips and face	14 (23.7)
Nausea or vomiting	11 (18.6)
Abdominal pain	7 (11.9)
Diarrhea	13 (22.0)
Congested or running nose	5 (8.5)
Chest tightness or wheeze	2 (3.4)
Anaphylaxis [†]	2 (3.4)

[†]Considered if there were two or more organ systems involved.

The population surveys from France and the UK showed that milk, eggs, and peanuts were the main reported food allergens in children aged 2–6 years old.^{21,22} Milk and eggs were the most common food allergens in most reports, while shellfish allergy was found to be common in Asian countries.²³ Shellfish, especially shrimp, was the leading food allergen in the present pre-school population. This finding is in agreement with several previous surveys among Hong Kong and Bangkok children.^{11,16} In the present study, one child was allergic to both shrimp and crab. The cross-reaction between multiple species of shellfish is not rare due to a very high homology of tropomyosin.^{23,24} Moreover, we found a child who was allergic to freshwater shrimp (lancheester's freshwater prawn, *M. lanchesteri*) but not to seawater shrimp. This supports a recent study by Jirapongsananuruk *et al.*, which demonstrated a species-specific shrimp allergy to freshwater shrimp (*M. rosenbergii*) and seawater shrimp (*P. monodon*).²⁵ We did not find any report of *M. lanchesteri* allergy in the medical literature, but this child did not undergo OFC to different species of freshwater shrimp to confirm the cross-reaction between them. This is the first report of ant eggs (*O. smaragdina*) allergy. Ants of species *O. smaragdina* are known as weaver ants. They are distributed throughout tropical

Table 4 Positive oral food challenge

No	Sex	Age (years)	Food	SPT	PTP	SIgE	Time to onset	Reactions
1	F	4.8	Shrimp	5	7	35.9	30 min	Lips swelling/itching
2	M	6.4	Shrimp	3.5	5	9.11	3 h	Urticaria
			Crab	3.5	7	8.53	1 h	Urticaria
3	F	5.4	Shrimp (seawater)	0	0	7.69		Negative
			Shrimp (freshwater)		0		2 h	Urticaria
4	M	4.8	Shrimp	10	8.5	8.13	10 min	Urticaria
5	M	6.7	Fish	0	13	0.30	1 min	Lips swelling/itching

PTP, prick-to-prick skin test with the respective cooked food (wheal size in mm); SIgE, specific IgE concentration to the respective food on fluorescence enzyme immunoassay using the Phadia ImmunoCAP-system (IU/mL); SPT, skin prick test with the respective food commercial extracts (wheal size in mm).

Table 5 Factors associated with parent-reported food allergy ($n = 59$)

Factor	Unadjusted OR (95%CI)	$P^{\dagger}$	Adjusted OR (95%CI)	$P^{\ddagger}$
History of infant feeding				
Breast-fed for ≥ 4 months	1.24 (0.71–2.14)	0.48		
Age of solid food introduction ≤ 4 months	1.10 (0.60–2.01)	0.88		
Personal history of atopic disease [§]	2.09 (1.20–3.64)	0.011		
Asthma	0.95 (0.21–4.29)	1.00		
Allergic rhinitis	1.61 (0.91–2.86)	0.12	1.29 (0.70–2.39)	0.42
Atopic dermatitis	2.58 (1.47–4.53)	0.001	2.23 (1.22–4.08)	0.01
History of atopic disease [§] in first-degree relatives [¶]	3.30 (1.38–7.94)	0.004		
Father	1.33 (0.68–2.59)	0.47		
Mother	1.46 (0.76–2.81)	0.28		
Siblings	1.24 (0.49–3.09)	0.62		
Asthma	1.12 (0.32–3.91)	0.75		
Allergic rhinitis	1.39 (0.78–2.47)	0.29		
Atopic dermatitis	7.07 (1.72–29.10)	0.01	5.63 (1.31–24.24)	0.02
Food allergy	0.79 (0.23–2.70)	1.00		

[†]Univariate logistic regression model. [§]Multivariate logistic regression model. [§]Allergic rhinitis, asthma, atopic dermatitis, or food allergy. [¶]Father, mother, and siblings. CI, confidence interval; OR, odds ratio.

Asia, Australasia, and some Pacific islands. Ant eggs including larvae are considered a delicacy and have been eaten by humans in various cultures in Australia and Southeast Asia, especially in the northern and north-eastern part of Thailand.²⁶ They are used as ingredients in soups, salads, fried dishes, and sometimes eaten raw together with spices. It is a common cause of anaphylaxis in clinical practice in northern Thailand. Among four children with a reported allergy to ant eggs, two of them had anaphylactic reactions. Because of their experience of severe reactions and of the food being easy to avoid, their parents refused to participate further in skin testing or OFC. This kind of food was not noted in the previous report in Bangkok children.¹¹ In addition, we did not find any reported peanut allergy, which is common in Western countries. This is in accordance with many studies that have found that peanut allergy appears to be rare in Asia.^{7,8,17,19}

The prevalence of cow's milk, chicken egg and wheat allergy was high in 'ever had FA' and declined in current FA. All children who reported having cow's milk allergy and who underwent OFC, were negative. This supports the finding that most cow's milk, egg, and wheat allergy in young children will be outgrown.^{1,2} In contrast, shellfish allergy in the present children seems to be persistent, and the prevalence of positive OFC was higher.

Epidemiologic studies have provided data on the risk factors for developing FA, which include genetic risks, association with atopy, breast-feeding period, and timing of solid food introduction.^{1,7,17} The present study indicated that personal and family history of atopy, especially atopic dermatitis, were the associated factors of FA.

The limitation of the present study is that a large number of parents who reported FA refused further investigation. This may be due to anxiety regarding the severe reaction they might experience. In contrast, some parents might consider the investigations to be a waste of their time because the previous FA reactions were mild. Another limitation is a recall bias due to the nature of the study design.

In conclusion, the present study has demonstrated a discrepancy between parent-reported and confirmed FA. From the

limited number of OFC, the overall prevalence of IgE-mediated FA in 3–7-year-old preschool children in northern Thailand was 1.1%. Personal and family history of atopic disease, especially history of atopic dermatitis, might be the predictors of FA. Ant eggs, a unique allergenic food, were the leading cause of severe allergic reactions in northern Thailand. The culture and dietary factors might be important in this situation. Therefore, a re-evaluation of the list of allergy-causing foods in different countries is required.

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