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The prevalence and temporal trends of food allergy among preschool children in Northern Thailand between 2010 and 2019

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ABSTRACT

Background: Although recent studies suggest that the prevalence of food allergy (FA) has not changed, the data from developing countries are limited. This study aimed to investigate time trends in the prevalence of FA among preschool children in 2010 and 2019 in Northern Thailand.

Methods: Two cross-sectional studies were performed, 9 years apart (2010 and 2019), using the same methods, in children aged 3–7 years living in Chiang Mai, Thailand. Parent-reporting questionnaire surveys were conducted. Families with children reporting FA were invited to undergo further investigations with skin prick testing, serum specific IgE, and oral food challenge (OFC). The prevalence of parent-reported FA, food sensitization, and OFC-confirmed FA were compared between the 2 periods.

Results: A total of 1013 out of 1146 questionnaires (452/546 in 2010 and 561/600 in 2019) were returned. The response rate was 88.4%. The prevalence of parent-reported food allergy in 2019 was significantly lower than that in 2010 (5.5% vs 9.3%; $p = 0.02$). However, there was no significant change in the prevalence of OFC-confirmed FA (0.9% vs 1.1%; $p = 0.75$). Three leading causative foods of parent-reported FA were cow's milk, shrimp, and eggs. Shrimp was still the most common OFC-confirmed food allergen. Atopic dermatitis was the most significantly parent reported factor associated with FA.

Conclusion: The overall prevalence of FA among preschool children in Northern Thailand had not increased during the past decade. There was no significant difference in the prevalence of OFC-confirmed FA between 2010 and 2019.

Keywords: Children, Food allergy, Time trends, Prevalence, Thailand

INTRODUCTION

Food allergy (FA) is an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food. The clinical spectrum of FA ranges from mild skin irritation to severe life-threatening anaphylaxis.[1,2] Over the past few decades, FA has become a public health issue that has impact on quality of

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life in terms of difficulty in diet preparation, daily activity management, and psychological and financial problems for patients and their caregivers, especially children and adolescents. The affected children and their parents have many challenges in managing their daily activities.[1–4]

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) does not always imply clinical reactivity. The accurate diagnosis of FA should be based on an oral food challenge (OFC).[1,2] Accuracy of FA diagnosis is important in informing the management, follow-up plan, and treatment of the individuals.

It has been suggested that the prevalence of FA has increased, representing a "second wave" of the allergy epidemic.[3,5] The published data of increased hospital admission for food-induced anaphylaxis,[6–9] referrals for allergy services,[10] reports of self-reported- or doctor-diagnosed FA,[11] and auto-injector epinephrine prescriptions support the perception of the increase in prevalence.[12] However, the recent comparison data from cross-sectional surveys and birth cohorts from the developed countries show that the prevalence of FA remain stable or have decreased.[13–16] Moreover, a repeated cross-sectional study, using the same methodology of OFC-proven outcomes shows that the prevalence of FA in infants from Chongqing, China significantly increased from 3.5% in 1999 to 7.7% in 2009 ($p = 0.017$), but there was no significant difference found in 2019 (11.1%).[17]

In Thailand, 2 studies have reported on the prevalence of FA. The first study[18] published in 2005, surveyed children aged 6 months to 6 years in Bangkok. The parent reported and OFC confirmed FA rates were 6.2% and 0.45%, respectively. Another study[19] was conducted in 2010 in Chiang Mai, the largest province in Northern Thailand. The FA prevalence in preschool children was 13.1% and 1.1%, from parent reported and OFC confirmed FA, respectively. Although these studies differed in study population and areas, they might imply that the prevalence of FA among young children in Thailand has risen over the last decade. Moreover, we observed an increase in the number of patient referrals to our allergy service due to food reaction complaints from 4.7% to 10.5% in 2013 and 2019, respectively (unpublished data).

To determine whether the prevalence of FA has increased, repeated cross-sectional studies using the identical area, methodology, and population are needed. Here we investigate the prevalence and characteristics of FA among children aged 3–7 years in Chiang Mai, Thailand in 2019, and compared the results with our previous survey held in 2010.[19]

METHODS

This is a repeated cross-sectional study performed in preschool children ages 3–7 years, studied in the same kindergartens with the same study frame and methods, to investigate the time trends in the prevalence of FA. The study was performed from January to December 2019. The methods were described in the previous study.[19] In brief, the subjects were selected by multistage random sampling from 9 kindergartens in the Muang District, Chiang Mai Province, Thailand. Each child was given a standard questionnaire to be completed by his/her parents. The questionnaire included the child's demographic data, feeding history during infancy, and the history of FA and atopic diseases of both the child and the family. For FA history, the parents were asked to specify the trigger foods, time of onset, and details of their symptoms. Parents of children who were suspected of FA were further phone interviewed of their clinical history and time-course related to FA by a pediatric allergist (PR).

The definitions of FA were as follows: "ever had FA", the occurrence of FA at least once in the child's lifetime; and "current FA", the 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 (Fig. 1).

The SPT was carried out using commercially available extracts of a standard food allergen (ALK

Abelló, USA). In addition to the SPT, the prick-to-prick skin test (PTP) using selected cooked foods was performed using a lancet either on the back or forearm. The sIgE to each specific causative food was measured using ImmunoCAP (Thermo Fisher) as described previously.[19]

The open OFC tests[19,20] were conducted in the Chiang Mai University Hospital under the supervision of allergists and trained nurses with close observation for any adverse signs and symptoms. Tests were performed when the children were completely well and had discontinued any antihistamine medication for at least 7 days before the challenge. In patients with positive test results it was suggested that culprit foods were avoided, and they were scheduled for follow-up. If no immediate reaction occurred it was suggested that parents observed the children and recorded any reactions, follow up being by telephone 3 days afterward. A challenge to a different food was conducted at least 2 weeks after the first challenge.

The sample size was estimated before recruitment from a 13% prevalence of parent-reported FA in the previous study[19] with a 3% margin of error. The recruitment sample size was at least 475. With an approximately 25% adjustment for a non-response rate of parents, 600 questionnaires were distributed to nine kindergartens which was the same cohort as in 2010.[19]

The analyses were performed using SPSS version 23.0 (SPSS, Chicago, IL, USA). Results are expressed as mean ± SD, percentages, or 95% CI of responses to each question. The prevalence of responses was compared using the chi-square test or Fisher's exact test as appropriate. The odds ratio (OR) and 95% CI were calculated to analyze the factors associated with "ever had FA". Covariates with $p < 0.2$ on the univariate analysis were included in the multivariate analysis. $p < 0.05$ for two-sided tests was considered to be statistically significant. To compare prevalence with the previous study, a comparison of proportion using the chi-squared test was used.

This study was reviewed and approved by the Research Ethics Committee of the Faculty of Medicine, Chiang Mai University Hospital, Chiang Mai University (001/2562). Written informed consent was obtained from the parents of all participants. The study was registered with the Thai Clinical Trials Registry (No TCTR20210604005).

RESULTS

In the 2010 survey, a total of 452 out of 542 completed parent-report questionnaires were returned (participation rate, 82.8%). The results of the survey were described in our previous publication.[19] In the present survey, a total of 561 out of 600 completed questionnaires were returned (participation rate, 93.5%). The demographic characteristics of the children who completed questionnaires in both surveys are shown in Table 1. There were significant differences in the age of participants, age of solid food introduction, and personal history of asthma or recurrent wheezing. Due to the national breastfeeding promotion policy and a health education drive for solid food introduction at 4–6 months of age, solid food introduction in the 2019 survey occurred when children were significantly younger and there were fewer children in the partially breast-fed group.

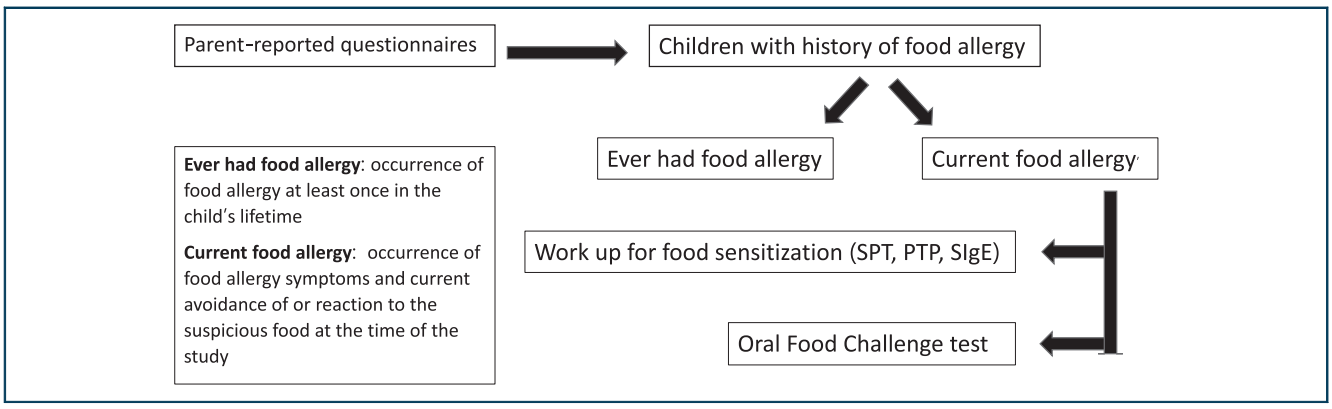

Fig. 1 Process for food allergy surveys (2010 and 2019)

Additionally, the transformation of pre-school education in Thailand in 2009–2010 leading to an earlier start in kindergarten at 3 years old significantly affected the number of younger age of participants in the 2019 survey.

In the present survey, 49 children (8.7%; 95% CI: 6.6–11.4) were reported as "Ever had FA" and 31 children (5.5%; 95% CI: 3.7–7.5) were reported as "Current FA". Types of food that caused FA are listed in Table 2. The 3 most recognized causative foods were cow's milk, shrimp, and hen's egg (47%, 33%, and 18%, respectively). Cow's milk and hen's egg were the most common culprits in the participants first presenting symptoms at less than 1 year of age. Onset of shellfish allergy tended to occur when children were older. Ten children (20.4%) reported having more than one causative food.

Thirty-eight children (77.6%) had a skin reaction (hives, rash, itching, and swelling of lips and face), the most common clinical manifestation followed by gastrointestinal symptoms (34.7%) as shown in

Demographic data, n (%)	2010 study (N = 452)	2019 study (N = 561)	*P-value*
Sex; Male	234 (51.8)	284 (50.6)	*0.700*
Age (years), mean ± SD	5.3 ± 1.0	4.8 ± 0.5	*<0.001*
3 to <4	63 (13.9)	139 (24.8)	*<0.001*
4 to <5	97 (21.5)	155 (27.6)	*0.026*
5 to <6	152 (33.6)	210 (37.4)	*0.198*
6 to 7	136 (30.1)	57 (10.2)	*<0.001*
Breast-feeding up to 4 months			
Ever breast-fed	430 (95.1)	530 (94.5)	*0.672*
Breast-fed only	300 (66.4)	388 (69.2)	*0.345*
Partially breast-fed	99 (21.9)	68 (9.6)	*<0.001*
Formula fed	52 (11.5)	100 (17.8)	*0.005*
Age of solid food introduction			
<4 months	138 (30.5)	39 (7.0)	*<0.001*
≥4–6 months	107 (23.7)	394 (70.2)	*<0.001*
>6 months	207 (45.8)	128 (22.8)	*<0.001*
Personal allergic history	202 (44.7)	259 (46.2)	*0.634*
Asthma/recurrent wheezing	16 (3.5)	95 (16.9)	*<0.001*
Allergic rhinitis	128 (28.3)	177 (31.6)	*0.255*
Atopic dermatitis	118 (26.1)	122 (21.7)	*0.102*
Paternal allergic history	84 (18.6)	96 (17.1)	*0.535*
Asthma	7 (1.5)	14 (2.5)	*0.265*
Allergic rhinitis	63 (13.9)	71 (12.7)	*0.576*
Food allergy	12 (2.6)	8 (1.4)	*0.164*
Atopic dermatitis	2 (0.4)	7 (1.2)	*0.166*
Maternal allergic history	85 (18.8)	106 (18.9)	*0.978*
Asthma	9 (2.0)	12 (2.1)	*0.911*
Allergic rhinitis	69 (15.3)	74 (13.2)	*0.317*
Food allergy	12 (2.6)	6 (1.1)	*0.072*
Atopic dermatitis	5 (1.1)	12 (2.2)	*0.180*
Allergic history in siblings	33 (7.3)	38 (6.8)	*0.757*
Asthma	5 (1.1)	7 (1.2)	*0.882*
Allergic rhinitis	31 (6.9)	22 (3.9)	*0.033*
Food allergy	3 (0.9)	9 (1.6)	*0.326*
Atopic dermatitis	6 (1.3)	4 (0.9)	*0.540*

Table 1. Characteristics of study participants

Foods n (%)	*Parent-reported 'ever had FA' n = 49 (8.7%)	Parent-reported 'Current FA' n = 31 (5.5%)	sensitization (positive SPT/SIgE) n = 11 (2.0%)	Children challenged n = 19 (3.4%)	Positive OFC n = 5 (0.9%)
Cow's milk	23 (46.9)	22 (70.9)	5 (45.5)	7 (36.8)	1 (20.0)
Shrimp	16 (32.7)	14 (45.2)	5 (45.5)	9 (47.4)	2 (40.0)
Hen's egg	9 (18.4)	4 (12.9)	1 (9.1)	1 (5.3)	0 (0)
Fish	3 (6.1)	3 (9.7)	1 (9.1)	2 (10.5)	1 (20.0)
Wheat	3 (6.1)	3 (9.7)	0 (0)	1 (5.3)	1 (20.0)
Mollusk	3 (6.1)	3 (9.7)	0 (0)	2 (10.5)	0 (0)
Ant's egg	3 (6.1)	3 (9.7)	1 (9.1)		
Squid	2 (4.1)	1 (3.2)	1 (9.1)		
Soy	1 (2.0)	1 (3.2)	0 (0)		
Peanut	1 (2.0)				
Watermelon	1 (2.0)	1 (3.2)	0 (0)	1 (5.3)	0 (0)
Pork	1 (2.0)				
Radish	1 (2.0)	1 (3.2)		1 (5.3)	0 (0)

Table 2. Children with reported- or confirmed-food allergy in 2019 study (N = 561). *Ten children reported allergy to more than one food. Ten children underwent challenge to more than one food. FA, food allergy; OFC, oral food challenge; SPT, skin prick test; sIgE, serum specific IgE*

Table 3. There was no difference in reported clinical symptoms of food allergy between the 2010 and present surveys. Anaphylaxis was reported in six children (1.1% of 561 participants). Shrimp and hen's eggs were found to be the causes of these severe reactions.

Nineteen out of 31 children who had "current FA" (61.3%) underwent SPT, sIgE, and OFC. Eleven children (1.9%; 95% CI: 0.9–3.2) were sensitized to foods according to either SPT or sIgE. Almost half of the children were sensitized to cow's milk and shrimp. Three children (0.5%) were sensitized to more than 1 food. There was a girl with a history of anaphylaxis after ingestion of ant's egg (*Oecophylla smaragdina* or weaver ants), showing positive results on the PTP test, but the OFC was not conducted.

Reactions	2010 (n = 59) n (%)	2019 (n = 49) n (%)	*P-value*
Skin reactions	48 (81.4)	38 (77.6)	*0.540*
Hives, rash, itching	46 (78.0)	38 (77.6)	*0.961*
Swelling of lips and face	14 (23.7)	9 (18.4)	*0.505*
Gastrointestinal symptoms	20 (33.9)	17 (34.7)	*0.931*
Nausea and vomiting	11 (18.6)	10 (20.4)	*0.815*
Abdominal pain	7 (11.9)	2 (4.1)	*0.147*
Diarrhea	13 (22.0)	8 (16.3)	*0.458*
Respiratory symptoms	7 (11.9)	8 (16.3)	*0.512*
Congested nose/runny nose	5 (8.5)	3 (6.1)	*0.637*
Chest tightness or wheeze	2 (3.4)	6 (12.2)	*0.083*
Anaphylaxis	2 (3.4)	6 (12.2)	*0.083*

Table 3. Clinical manifestation of reported food allergy

Five children (0.9%; 95% CI: 0.2–1.6) had positive OFC. Fish (*Oreochromis niloticus*), shrimp (*Litopenaeus vannamei*), giant river prawn (*Macrobrachium rosenbergii*), cow's milk, and wheat were the confirmed causes. There were two children with positive reactions to specific species of shrimp by OFC, *M. rosenbergii* and *L. vannamei*, respectively. All children with positive OFC had only mild immediate skin reactions (urticarial and perioral rashes). No adverse reaction was observed at the three-day follow-up. Time-lapse after the introduction of food to symptoms range from five to 40 minutes. No severe reactions requiring epinephrine injection occurred during the procedures. Four out of 5 children with a history of cow's milk allergy with cow's milk sensitization passed OFC. A child with a history of egg anaphylaxis, presented no symptoms during OFC, despite the existing evidence of sensitization through sIgE.

Associated factors with "Ever had FA" are demonstrated in Table 4. Significant factors in the univariate logistic regression analysis were partially breastfed during birth to 4 months of age (OR 2.00; 95% CI 0.95–4.23; $p = 0.07$), personal history of atopic dermatitis (OR, 3.69; 95% CI, 2.02–6.74; $p < 0.001$), and atopic history of a first-degree relatives (OR, 1.86; 95% CI, 1.03–3.36; $p = 0.04$). Only a personal history of atopic dermatitis was a significant factor on the multivariate logistic regression model (OR, 3.52; 95% CI, 1.89–6.58; $p < 0.001$). Analysis of an association with infant feeding pattern includes formula-fed, age of complimentary food, cow's milk, and egg introduction, were non-significantly associated with parent-reported FA.

The prevalence of parent-reported FA, food sensitization and OFC-proven FA between 2010 and 2019 are compared in Table 5. Prevalence of parent-reported "ever had FA" and "current FA" statistically significantly declined in 2019 (13.1% vs. 8.7%; $p = 0.024$ and 9.3% vs. 5.5%; $p = 0.020$ in 2010 and 2019, respectively). However, the prevalence of OFC-confirmed FA remained stable (1.1% vs. 0.9%; $p = 0.749$). As regards the comparison of FA rates classified by age and type of food, there was no difference in prevalence of "current FA" within each age group and in the prevalence of cow's milk and hen's egg allergy over the time. However, the prevalence of shellfish

Factor	Unadjusted OR (95% CI)	*p-value*	Adjusted OR (95% CI)	*p-value*
Family income ≤500,000 THB/year	1.38 (0.74–2.57)	*0.361*		
Parental education <bachelor degree	1.26 (0.63–2.50)	*0.580*		
No sibling	1.10 (0.56–2.04)	*0.872*		
Breast-fed only ≥4 months	0.75 (0.41–1.38)	*0.420*		
Partially breast-fed	2.00 (0.95–4.23)	*0.007*	1.97 (0.90–4.27)	*0.090*
Personal history of atopic diseases	3.21 (1.69–6.12)	*<0.001*		
Asthma	1.48 (0.73–3.00)	*0.312*		
Allergic rhinitis	1.56 (0.86–2.84)	*0.151*	1.01 (0.51–2.01)	*0.972*
Atopic dermatitis	3.69 (2.02–6.74)	*<0.001*	3.52 (1.89–6.58)	*<0.001*
First degree relatives' history of atopic history	1.86 (1.03–3.36)	*0.004*	1.54 (0.80–3.00)	*0.123*
Paternal atopic history	1.45 (0.71–2.96)	*0.320*		
Maternal atopic history	1.63 (0.83–3.19)	*0.187*		
Sibling atopic history	1.25 (0.42–3.68)	*0.567*		
Age of introducing complementary food				
<4 months	0.86 (0.27–2.90)	*1.00*		
>6 months	0.98 (0.84–1.97)	*1.00*		

Table 4. Factors associated with parent-reported food allergy in 2019 study (N = 561). *THB, Thai Baht (1 US dollar equivalents to 31.125 THB at June 10, 2021)*

N (%; 95%CI)	2010 (N = 452) n (%)	2019 (N = 561) n (%)	*P-value*
Parents-reported 'Ever had FA'	59 (13.1; 9.9–16.2)	49 (8.7; 6.6–11.4)	*0.024*
Cow's milk	18 (4.0)	23 (4.1)	*0.936*
Hen's egg	8 (1.8)	9 (1.6)	*0.806*
Shellfish	18 (4.0)	20 (3.6)	*0.740*
Parent- reported 'Current FA'	42 (9.3; 6.6–12.0)	31 (5.5; 3.7–7.5)	*0.020*
Cow's milk	9 (2.0)	22 (3.9)	*0.081*
Hen's egg	4 (0.9)	4 (0.7)	*0.720*
Shellfish	17 (4.8)	17 (3.0)	*0.137*
3 to <4 years old	7/63 (11.1)	6/139 (4.3)	*0.069*
4 to <5 years old	8/97 (8.2)	8/155 (5.2)	*0.381*
5 to <6 years old	11/152 (7.2)	14/210 (6.7)	*0.853*
≥6 years old	16/136 (11.7)	3/57 (5.3)	*0.174*
Food sensitized FA	*NA*	11 (1.9%; 0.9–3.2)	*NA*
OFC-Confirmed FA	5 (1.1; 0.1–2.1)	5 (0.9; 0.2–1.6)	*0.749*
Cow's milk	0	1 (0.2)	*0.342*
Hen's egg	0	0	*1.0*
Shellfish	4 (0.9)	2 (0.4)	*0.007*

Table 5. Comparison of food allergy prevalence in 2010 and 2019

allergy had significantly decreased (0.9% vs. 0.4%; $p = 0.007$).

DISCUSSION

This population-based study has demonstrated that the prevalence of parent-reported "ever had FA" and "current FA" among preschool children in Thailand significantly declined from 2010 to 2019. However, the prevalence of OFC-confirmed FA did not change significantly. The significant recognized factor for FA in the children in this study is the presence of atopic eczema.

FA affects between 1% and 10% of the population.[1,3] Diagnosis of FA is a challenge as regards determining the true prevalence due to heterogeneity of the studies and limitations including the natural course of the disease, diagnostic procedure, and other bias pertinent to recognition and participation. An accurate diagnosis of FA should be based on an OFC.[1-3] Studies of FA prevalence confirmed by OFC are limited due to their being difficult and time-consuming. There are discrepancies between the self-reported prevalence of FA, food sensitization rate, and OFC prevalence. Several studies have shown that only approximately one-tenth to one-third of suspected cases of FA are found to be true FA.[3,19] Therefore, the high frequency of parent-reported FA is expected to be an over perception. Adding weight to this, in this study, approximately 26% (5/19) of the present subjects who underwent OFC had a positive result. According to the present results, the prevalence of parent-reported FA and food sensitization were five-fold, and two-fold more than OFC-confirmed FA (5.5%, and 2.0% vs 0.9%, respectively). Nevertheless, given that only 61% of children (19/31) who reported current FA underwent OFC in the present study, the true prevalence of confirmed FA would be higher than that reported.

The prevalence of FA has been comprehensively studied in recent years. For over a decade, FA prevalence was thought to be increasing.[3,5] There is published evidence to support an increasing prevalence from many countries around the world.[11] In an Australian community-based retrospective analysis of clinical- or SPT diagnosis of FA in children it was claimed there was an urgent need for a systematic epidemiology review study in light of an obvious increase in the prevalence of FA of more than four-fold over 12 years from 1995 to 2006.[10] Repeated cross-sectional studies using OFC-proven FA conducted in 1999 and 2009 in children less than 2 years old from China demonstrated a dramatic increase

in prevalence from 3.5 to 7.7% ($p = 0.02$) over a period of 10 years.[11] In contrast, several developed countries provided recently published evidence of stable prevalence. There are recent reports from large repeated cross-sectional studies that have demonstrated that the prevalence of food sensitization in the United States,[16] the United Kingdom,[14,21] Canada[22] and Australia[13] had remained stable since the 1990s. One study is a repeated cross-sectional report, using identical sampling methodologies and definitions from developing countries which illustrated no change in confirmed FA prevalence. It supports the study of time trends of FA in Chinese infants, which has shown that the prevalence of FA increased rapidly after the 1990s and gradual stabilized after 2010.[17]

Environmental factors, lifestyles, and dietary habits play critical roles in allergen sensitization and food allergy development. Rapid economic development, environmental changes, increase in hygiene, topical sensitization, cesarean section, and delayed introduction of allergenic foods may explain this rising trend in the prevalence of FA in developing countries.[5,11] Thailand, being a high-middle income country with a gradual increase in gross domestic product, has a living environment and lifestyle that has not changed much. This may elucidate the reason of stabilized prevalence of FA during the past decade.

Interestingly, although the number of patients seeking advice regarding FA in our allergy service was increasing, the trend of this community-based parents-reported "Ever had FA" and "current FA" rate declined. This lower rate could be due to the better education for caregivers, primary care physicians, and general pediatricians on FA management during the infancy period. Moreover, this may also reflect increased awareness, increased diagnosis accuracy by primary care physicians, or increased severity of reactions, and therefore referrals for FA assessment, rather than only increased prevalence.[13,22]

Details regarding prevalence in each kind of food has been evaluated. Peanut allergy has prominently increased in some Asian countries, especially Singapore.[23] This study shows that peanut allergy remains rare in Thailand while allergy to shellfish which is an important food in the Asia-Pacific region, has increased.[23] Allergens in shrimp are more potent triggers than those in mollusks and fish. Specific allergy to species of shrimp was identified.[24] It is noteworthy that the reported prevalence of shellfish allergy is high in tropical/subtropical regions where allergic sensitization to house dust mite is also frequent. The tropomyosin in dust mites is a major cross-reactive allergen involved in triggering IgE-mediated hypersensitivity to shrimp.[25] This might contribute to the high shellfish-allergy rate among the population. One specific causative food found in Northern Thailand was ant eggs, a favorite dish in the area. Incidence of this allergy was reported in our previous study (6.8%)[19] and the present study (6.1%). According to the anaphylaxis data in our center, ant eggs are one of the leading causes of food-induced anaphylaxis in 2.7% of children and 1.1% of adults.[26] Taken together these data possibly imply that there are specific FA patterns in specific regions due to differing resources, geographical locations, lifestyles, dietary and genetic backgrounds.

Manifestations of allergic reactions range from mild to severe reactions.[1] Most of the children in our study had mild cutaneous symptoms. The severity of symptoms can be time- and dose-related.[20] Some infants naturally outgrow their FA, especially in the case of allergy to cow's milk and eggs. Our study showed an example of children who had a history of being allergic to certain foods but on investigation passed the OFC to cow's milk and eggs. This could be the explanation between the discrepancy of the prevalence of parent-reported "ever had FA", "current FA", and OFC-confirmed FA.

In many epidemiological studies, atopic eczema is a strong risk factor for IgE-mediated FA, particularly in relation to hen's egg and peanut allergy.[27] Skin barrier dysfunction is postulated to play an important role in the initiation of allergic sensitization and subsequent progression to FA.[27,28] It was in line with these present findings that a significant association of parent-reported FA and child's atopic eczema was demonstrated.[29] Half of our children reported pruritic eczema as a symptom of suspected FA. To prevent FA, early peanut introduction to high-risk infants yields a prominent result to decrease the

prevalence of peanut allergy.[30] However, the efficacy of early introduction of other foods is controversial.[31] Although during the study period, there was a change in pattern of solid food introduction in Thailand, we did not find any association between early food introduction and parent-reported prevalence of FA to cow's milk and hen's egg.

There are several limitations to this study, the first being since this is a cross-sectional study, recall bias may occur. Another limitation is several subjects refused further investigation for a variety of reasons therefore FA could not be verified. The majority of the non-participants had anxiety about severe reactions and some parents did not want to waste their time on investigations. There were a few differences in participant characteristics including the mean age, and solid food introduction due to changes in the national health and education policy. These may well affect the study results. There was also a chance of bias due to open OFC, but this may be acceptable in young children due to its lower psychological impact.

In the future, other aspects may be considered for an epidemiological FA study in Thailand. As the prevalence of atopic diseases in urbanized area is increasing and farm living seems to be a protective factor, a study in different areas in the country could be carried out. Furthermore, the pattern of FA among unique specific foods in the Asia-Pacific area has not yet been studied. More in depth laboratory investigations and pattern recognition would be of interest in the future.

In summary, the present study demonstrated that the overall prevalence of FA among preschool children in Northern Thailand is not showing an increasing trend during the past decade. Atopic dermatitis is a prominent factor in the prediction of FA by parent-reporting. Increased knowledge of FA amongst caregivers and easier accessibility to allergists might have impact on the prevalence and pattern of parent-reported FA. Follow-up of natural resolution in the case of each food should be done to avoid unnecessary food avoidance. Patterns of FA in each country differ due to genetic, cultural, and geological locations and region-specific evaluation of FA in different areas should be considered.

Abbreviations

FA: food allergy, IgE: immunoglobulin E, OFC: oral food challenge test, PTP: prick-to-prick skin test, SPT: skin prick test, sIgE: serum specific immunoglobulin E.

Ethics statement

This study was reviewed and approved by the Research Ethics Committee of the Faculty of Medicine, Chiang Mai University Hospital, Chiang Mai University (001/2562). Written informed consent were obtained from the parents of all participants. The study was registered with the Thai Clinical Trials Registry (No TCTR20210604005).

Availability of data and materials

The datasets generated during the current study are available from the corresponding author upon reasonable request.
The study was reviewed and approved by the Research Ethics Committee of the Faculty of Medicine, Chiang Mai University Hospital, Chiang Mai University (001/2562). Written informed consent were obtained from all participants' parents. The current study was registered at the Thai Clinical Trial Registry (No TCTR20210604005).

Author contributions

(i) Concept and Design: Pisuttikan Rangkakulnuwat and Mongkol Lao-Araya; Analysis and Interpretation of Data: Pisuttikan Rangkakulnuwat and Mongkol Lao-Araya (ii) Drafting the Article: Pisuttikan Rangkakulnuwat (iii) Final Approval of the Version to be Published: Pisuttikan Rangkakulnuwat and Mongkol Lao-Araya.

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Consent for publication

All authors agreed to the publication of this work.

Declaration of competing interest

The authors declare that they have no competing interests.

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