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Factor associated with food allergy among preschool children with atopic dermatitis, and resolution of atopic dermatitis

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Abstract

Background: Food allergy (FA) has been reported in one-third of children with moderate-to-severe atopic dermatitis (AD).

Objectives: To identify factor associated with food allergy among preschool children with AD, and to compare AD resolution between preschool children with and without FA.

Methods: A cross-sectional study using database registry and questionnaire interview was conducted at Siriraj Hospital (Bangkok, Thailand) during 2022, and physician-diagnosed AD children aged ≤ 6 years were enrolled.

Results: A total of 110 children (60.9% male, median age: 2.3 years) were included. Of those, 53 and 57 children had AD with and without FA, respectively. Very early-onset AD (≤ 3 months) and moderate-to-severe AD at onset were reported in 43.9% and 26.3% of AD without FA, and in 35.8% and 45.3% of AD with FA, respectively. The most commonly reported FAs were hen's egg, cow's milk, and wheat. Moderate-to-severe AD at onset was found significant associated with FA (aOR: 2.50; p = 0.037). Thirty-one (28.2%) patients experienced completed resolution of AD by 5 years of age. Of those, 19 had AD without FA, and 12 had AD with FA (p = 0.213). The median age at AD resolution was 18 months and 22.5 months in the without and with FA groups, respectively. AD with FA showed a strong trend toward a significantly longer duration to achieving AD resolution after adjusting for onset and severity of AD (aHR: 0.46, p = 0.050).

Conclusion: Preschool AD children with FA were found to have significantly greater AD severity at AD onset and a longer duration to AD resolution compared to AD children without FA.

Key words: atopic dermatitis, food allergy, risk factor, preschool children, resolution

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Abbreviations:

AD	atopic dermatitis
aHR	adjusted hazard ratio
aOR	adjusted odds ratio
AR	allergic rhinitis
AS	asthma
CI	confidence interval
FA	food allergy
HR	hazard ratio
IgE	immunoglobulin E antibody
IQR	interquartile range
OFC	oral food challenge
OR	odds ratio
sIgE	specific immunoglobulin E antibody
SPT	skin prick test

Introduction

Atopic dermatitis (AD), which is also known as atopic eczema, is a chronically relapsing inflammatory dermatosis that is characterized by intense itching and recurrent eczematous lesions.[1-2] AD was reported to affect up to 20% of children globally, and the rate of AD continued to increase during the past decade.[3] In Thailand, the prevalence of AD was reported to range from 11% to 16%.[4-5] The majority of AD infants and children will outgrow their condition by 8 years of age;[6] however, a subgroup of difficult-to-manage patients, namely severe AD or AD associated with food allergy (FA), are at higher risk for experiencing persistent disease.[6-8] Children with AD are also at risk for developing an atopic march, including FA, allergic rhinitis (AR), and asthma (AS).[2,9]

A strong correlation among childhood or adolescent AD, food sensitization, and food allergy was confirmed by a recent systematic review.[8] FA is often reported in one-third of AD children, and particularly in those with moderate-to-severe AD.[10] Therefore, if the patient presents with a convincing clinical history of allergic reactions, testing for food allergy should be considered regardless of AD severity.[11] In contrast, food sensitization is not uncommon in AD children; thus, accurate diagnosis of FA is important to avoid unnecessary food avoidance and an unfavorable outcome.[11-12]

Although the dual-allergen exposure hypothesis has been proposed, a multifactorial etiology that includes environmental factors, such as allergens and microbial agents, may contribute to the development of this complex disease.[7,13-14] Differentiating the clinical features of AD patients between those with and without FA, and identifying the underlying risk factors for FA might help us prevent or better manage FA in AD children.

Accordingly, the aim of this study was to identify factors associated with FA among preschool children with AD, and to compare AD resolution between preschool children with and without FA.

Methods

A cross-sectional study with questionnaire interview was conducted at the Allergy and Dermatology Clinic of the Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand during April to December, 2022. The protocol for this study was approved by the Siriraj Institutional Review Board (COA no. Si 273/2022), and written informed consent to participate was obtained from the parents of all study children.

Study participants

Study participants were identified using International Classification of Diseases 10th revision (ICD-10) codes (i.e., atopic dermatitis/L20, other atopic dermatitis/L20.8, atopic dermatitis, unspecified/20.9, other specified dermatitis/L30.8, and dermatitis unspecified/L30.9) and from the hospital Atopic Dermatitis Centers of Reference and Excellence (ADCARE) – A GA²LEN NETWORK database registered during January 2020 to December 2022.

Patients that were invited to participate this study were allergist and/or dermatologist-diagnosed AD children aged less than or equal to 6 years who were diagnosed using the Hanifin and Rajka criteria.[15] Exclusion criteria were patients with primary immunodeficiency diseases, informed consent cannot be obtained, and lost to follow-up.

Onset, severity, and resolution of atopic dermatitis

Onset of AD was classified as very early-onset if AD occurred before 2 years of age.[16-17] The severity of AD was classified as mild if the SCORing Atopic Dermatitis (SCORAD) score was < 25 or the Eczema Area and Severity Index (EASI) was ≤ 7, and as moderate-to-severe AD if the SCORAD score was ≥ 25 or the EASI was > 7.[18-19] Clinically resolution of AD was defined as no eczema and no use of AD medication for > 6 months.[20]

Food allergy diagnosis and definition criteria

Evaluation for FA was performed in all included AD children. No further allergy testing was performed without any supportive case history, such as clinical history of allergic reaction or refractory AD despite adequate skin care and medical treatment. A diagnosis of FA was made by pediatric allergists if patients met any one of the following 3 definition criteria: (I) immunoglobulin E (IgE)-mediated reaction, which was defined as convincing clinical history of immediate reaction to food allergen with positive skin prick test (SPT) and/or specific IgE (sIgE) to specific food or positive oral food challenge (OFC) test;[21] or, (II) level of sIgE to a specific food > 95% positive decision point (> 70% for wheat and soy) without previous clinical history of ingesting that food;[22-24] or, (III) food-triggered AD, which was defined as positive clinical history of food-induced eczema with positive diagnostic elimination diet (i.e., improvement and worsening of eczema after withdrawal and reintroduction of the causative food, respectively) or positive OFC with delayed reaction (6-48 hours)[25-26] (**Supplementary Table 1** and **Supplementary Table 2**). A SPT result was considered positive if the mean wheal diameter was > 3 mm greater than the negative saline control, and a sIgE level was considered positive if greater than 0.35 kUA/L (ImmunoCAP, Uppsala, Sweden). OFC was performed following the recommendations published in the Adverse Reactions to Foods Committee Work Group Report.[22,27]

Questionnaire interview

The following data were collected during the questionnaire interview with the parents of enrolled children: (i) AD characteristics, including AD onset, duration of disease, severity of AD, and resolution of AD; (ii) demographic data, including current age at study enrolment, gender, and number of siblings; (iii) personal allergic diseases, including physician diagnosis of AR and/or AS; (iv) family history of allergic diseases, including AD, FA, AR, and AS; (v) perinatal factors, including perinatal antibiotic exposure, route of delivery, gestational age, and birth weight; (vi) postnatal factors, including breastfeeding frequency during the first 4-6 months,

age at complementary food introduction, and food diversity at 6 months of age; and, (vii) sociodemographic factors, including smoker in the household, pet at home, and monthly family income. Breastfeeding was classified as exclusive (only breastfed), partial (breastfed and formula milk), or never (formula milk only).[28] Food diversity was classified according to the number of different types of foods introduced to study children (1-6 types). The food types included vegetables or fruits, cereals (including rice), bread, meat, cake, and yogurt.[29] Patient medical records were then reviewed to cross-check and verify as much of the information provided by the parent as possible. A single investigator (ST) conducted all interviews and collected all data in this study.

Statistical analysis

All statistical analyses were performed using SPSS Statistics version 18.0 (SPSS, Inc., Chicago, IL, USA) and Stata version 17 (StataCorp LP, College Station, TX, USA). Categorical data are presented as number and percentage, and were analyzed by Chi-squared or Fisher's exact test, as appropriate. Continuous variables (all of which were non-normally distributed) are presented as median and interquartile range (IQR), and were analyzed using Mann-Whitney U test. All potential risk factors for FA that were identified from our review of the literature[17,30-32] were included in univariable and multivariable logistic regression analysis to identify factors associated with FA in AD children. The results of that analysis are presented as odds ratio (OR) and 95% confidence interval (CI) for univariable analysis, and as adjusted OR and 95%CI for multivariable analysis.

The resolution of AD was compared between children with and without FA. The association between FA and resolution of AD was analyzed using Cox proportional hazards regression, demonstrated in a Kaplan–Meier survival curve. The results of that analysis are presented as adjusted hazard ratio (aHR) and 95%CI after adjustment for onset and severity of AD. A *p*-value less than 0.05 was considered statistically significant for all tests.

Results

A total of 260 children were identified and 110 of them were enrolled into this study (**Supplementary Figure 1**). The demographic and clinical characteristics of overall patients, and compared between AD preschool children with and without food allergy are shown in **Table 1**. Sixty-seven (60.9%) patients were male. The median age at enrollment was 2.3 years (interquartile range [IQR]: 1.2-3.8). Of the 110 enrolled children, 57 (51.8%) had AD without FA, and 53 (48.2%) had AD with FA. Moderate-to-severe AD at the onset of AD was found in 26.3% of AD without FA children, and in 45.3% of AD with FA children (p = 0.038).

Table 1. Demographic and clinical characteristics of overall patients, and compared between AD preschool children without and with food allergy.

Characteristics	Overall patients (N = 110)	AD without food allergy (n = 57)	AD with food allergy (n = 53)	*p*
Male gender	67 (60.9%)	34 (59.6%)	33 (62.3%)	0.779
Current age (yrs)	2.3 (1.2-3.8)	2.2 (1.3-3.4)	2.8 (1.2-4.4)	0.153
Age at AD onset (mo)	4.0 (3.0-7.0)	4.0 (3.0-9.0)	4.0 (3.0-6.0)	0.523
Very early-onset AD (age ≤ 3 mo)	44 (40.0%)	25 (43.9%)	19 (35.8%)	0.391
Very early-onset AD (age < 2 yrs)	103 (93.6%)	51 (89.5%)	52 (98.1%)	0.115
AD severity at onset				**0.038**
- Mild	71 (64.5%)	42 (73.7%)	29 (54.7%)	
- Moderate-to-severe	39 (35.5%)	15 (26.3%)	24 (45.3%)	
Current AD treatment				
- Moisturizer	107 (97.3%)	55 (96.5%)	52 (98.1%)	1.000
- TCS/TCI	48 (43.6%)	21 (36.8%)	27 (50.9%)	0.332
Has sibling(s)	51 (46.4%)	28 (49.1%)	23 (43.4%)	0.547
Other allergic diseases				
- Allergic rhinitis	20 (18.2%)	8 (14.0%)	12 (22.6%)	0.242
- Asthma	3 (2.7%)	1 (1.8%)	2 (3.8%)	0.608

Table 1. (Continued)

Characteristics	Overall patients (N = 110)	AD without food allergy (n = 57)	AD with food allergy (n = 53)	*p*
Family history of allergic diseases				
- Allergic rhinitis	60 (54.5%)	30 (52.6%)	30 (56.6%)	0.676
- Asthma	16 (14.5%)	7 (12.3%)	9 (17.0%)	0.485
- Atopic dermatitis	21 (19.1%)	10 (17.5%)	11 (20.8%)	0.669
- Food allergy	20 (18.2%)	8 (14.0%)	12 (22.6%)	0.242
Absolute eosinophil count†	438.0 (254.0-588.0)	406.0 (196.0-527.0)	513.5 (313.5-796.0)	0.097

Data presented as number and percentage or median and interquartile range
A *p*-value < 0.05 indicates statistical significance
†Data available from 66 children (36 AD children with food allergy and 30 AD children without food allergy)
Abbreviations: AD, atopic dermatitis; mo, months; TCS, topical corticosteroid, TCI, topical calcineurin inhibitor; yrs, years

Among the 53 children who reported being allergic to 1 or more of 8 food allergens, 32.1% had single FA, and 67.9% had multiple FA (**Supplementary Figure 2**). The diagnosis of FA was made based on definition criteria I (IgE-mediated reaction), II (level of sIgE to a specific food > 95% positive decision point), and III (food-triggered AD) in 43.0%, 22.5%, and 34.5% of patients, respectively. A total of 151 food allergens were reported, and the most commonly reported FA was egg white (n = 35, 23.2%), followed by cow's milk (n = 32, 21.2%), egg yolk (n = 30, 19.9%), wheat (n = 29, 19.2%), soybean (n = 8, 5.3%), fish (n = 7, 4.6%), shellfish (n = 5, 3.3%), and peanut (n = 5, 3.3%) (**Figure 1**). The majority of the FA diagnoses for egg, wheat, and seafood were made using definition criteria I, whereas the FA diagnoses for cow's milk and peanut were mainly diagnosed using definition criteria III.

Potential risk factors for FA, including perinatal factors (i.e., perinatal antibiotic exposure, route of delivery, gestational age, and birth weight), postnatal factors (i.e., breast feeding frequency, age of complementary food introduction, and food diversity), and sociodemographic factors (i.e., smoking in the household, pet at home, and family income), of overall patients, and compared between AD preschool children with and without FA are shown in **Table 2** (all between-group comparisons $p > 0.05$).

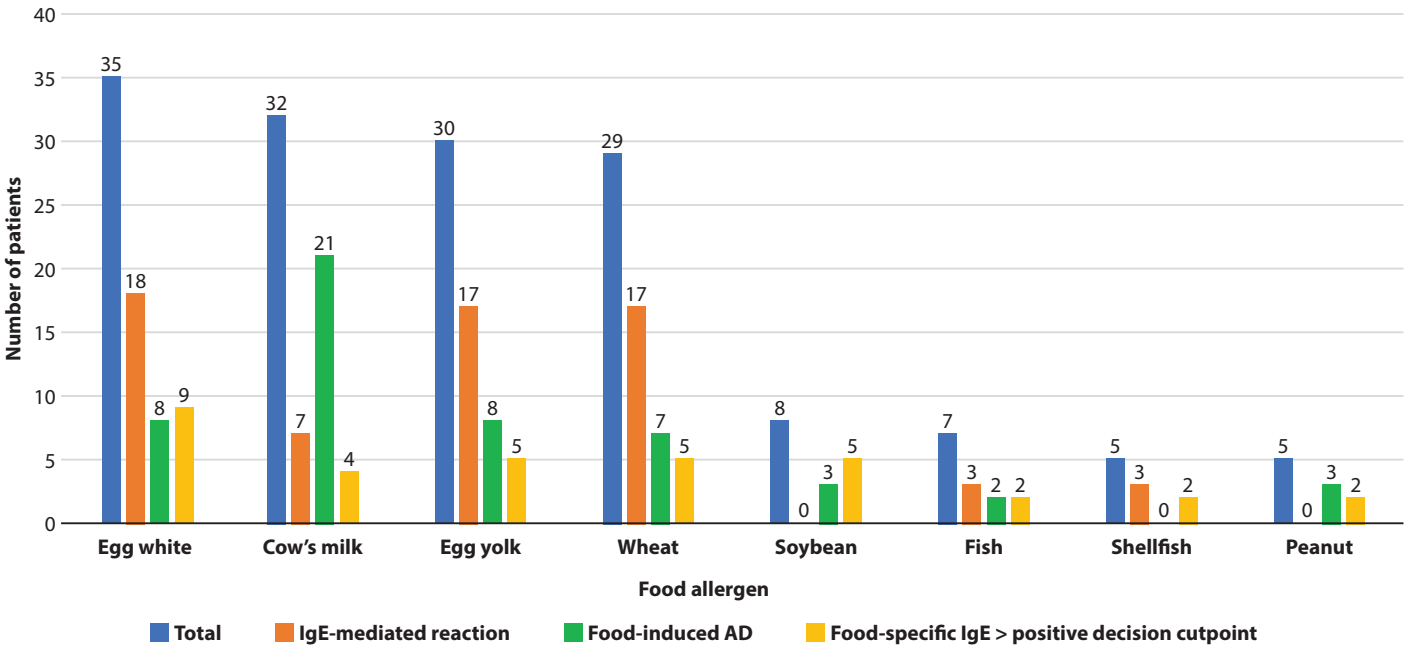

Figure 1. Food allergen and type of food allergy among 53 atopic dermatitis children with food allergy.
Abbreviations: AD, atopic dermatitis; IgE, immunoglobulin E antibody

Table 2. Perinatal, postnatal, and sociodemographic characteristics of overall patients, and compared between AD preschool children without and with food allergy.

Characteristics	Overall patients (N = 110)	AD without food allergy (n = 57)	AD with food allergy (n = 53)	*p*
Perinatal factors				
- Perinatal antibiotic exposure	14 (12.7%)	9 (15.8%)	5 (9.4%)	0.318
- Route of delivery				0.782
- Vaginal delivery	38 (34.5%)	19 (33.3%)	19 (35.8%)	
- Cesarean section	72 (65.5%)	38 (66.7%)	34 (64.2%)	
- Gestational age				0.670
- Preterm (< 37 weeks)	14 (12.7%)	8 (14.0%)	6 (11.3%)	
- Term (≥ 37 weeks)	96 (87.3%)	49 (86.0%)	47 (88.7%)	
- Birth weight				0.877
- < 2,500 grams	21 (19.1%)	11 (19.3%)	10 (18.9%)	
- 2,500-3,500 grams	64 (58.2%)	32 (56.1%)	32 (60.4%)	
- > 3,500 grams	25 (22.7%)	14 (24.6%)	11 (20.8%)	
Postnatal factors				
- Breastfeeding frequency before introduction of complementary food				0.213
- Exclusive	66 (60.0%)	30 (52.6%)	36 (67.9%)	
- Partial	31 (28.2%)	20 (35.1%)	11 (20.8%)	
- Never	13 (11.8%)	7 (12.3%)	6 (11.3%)	
- Age at introduction of complementary food				0.736
- < 6 months	9 (8.2%)	4 (7.0%)	5 (9.4%)	
- ≥ 6 months	101 (91.8%)	53 (93.0%)	48 (90.6%)	
- Food diversity at 6 months of age (types of food)	2.0 (1.0-3.0)	2.0 (1.0-3.0)	2.0 (1.0-3.0)	0.497
- 0-3	98 (89.1%)	48 (84.2%)	50 (94.3%)	0.089
- 4-6	12 (10.9%)	9 (15.8%)	3 (5.7%)	
Sociodemographic factors				
- Pet at home	46 (41.8%)	23 (40.4%)	23 (43.4%)	0.746
- Smoker in the household	37 (33.6%)	19 (33.3%)	18 (34.0%)	0.944
- Family income > 50,000 THB/month	63 (57.3%)	35 (61.4%)	28 (52.8%)	0.364

Data presented as number and percentage or median and interquartile range
A *p*-value < 0.05 indicates statistical significance
Abbreviations: AD, atopic dermatitis; THB, Thai baht

Table 3. Univariable and multivariable logistic regression to identify factors associated with FA in preschool children with AD.

Factors	Univariable			Multivariable		
	OR	95%CI	*p*	aOR	95%CI	*p*
- Male gender	1.12	0.52-2.40	0.779	1.01	0.44-2.30	0.986
- Very early-onset AD (age ≤ 3 months)	0.72	0.33-1.54	0.392	0.60	0.25-1.45	0.259
- Moderate-to-severe AD at onset	2.32	1.04-5.16	**0.040**	2.50	1.06-5.93	**0.037**
- Food diversity at 6 months of age (4-6 types of food)	0.32	0.08-1.25	0.102	0.36	0.09-1.49	0.160
- Preterm delivery	0.78	0.25-2.42	0.670	0.65	0.19-2.26	0.495
- Family history of food allergy	1.79	0.67-4.81	0.246	1.81	0.63-5.26	0.273
- Pet at home	1.13	0.53-2.42	0.746	1.28	0.55-3.00	0.564
- Smoker in the household	1.03	0.47-2.27	0.944	0.88	0.37-2.09	0.766

A *p*-value < 0.05 indicates statistical significance
Abbreviations: AD, atopic dermatitis; aOR, adjusted odds ratio; CI, confidence interval; FA, food allergy; OR, odds ratio

Univariable and multivariable logistic regression analyses to identify factors associated with FA in preschool children with AD are shown in **Table 3**. Moderate-to-severe AD at AD onset was found to be the only significant risk factor associated with FA in univariable analysis (odds ratio [OR]: 2.32, 95% confidence interval [95%CI]: 1.04-5.16; $p = 0.04$). After adjusting for male gender, very early-onset AD (age ≤ 3 months), food diversity at 6 months of age (4-6 types of food), preterm delivery, family history of food allergy, pet at home, and smoker in the household, moderate-to-severe AD at onset of AD revealed significant associated with FA in preschool children with AD (adjusted OR [aOR]: 2.50, 95%CI: 1.06-5.93; $p = 0.037$).

Resolution of AD by 5 years of age was reported in 31 (28.2%) children with a median follow-up time of 17.5 months (IQR: 6-32). Of those, 19 (33.3%) had AD without FA, and 12 (22.6%) had AD with FA ($p = 0.213$). The median age at AD resolution was 18 months (IQR: 12-24) and 22.5 months (IQR: 18-44) in the without and with FA groups, respectively. Among the children who experienced complete resolution of AD, 8.2% resolved by 1 year, 21.8% resolved by 2 years, and 28.2% resolved by 5 years of age (**Figure 2**). AD children with FA showed a strong trend toward a significantly longer duration to achieving AD resolution after adjusting for onset and severity of AD (aHR: 0.46, 95%CI: 0.22-1.00; $p = 0.050$) (**Figure 2** and **Table 4**).

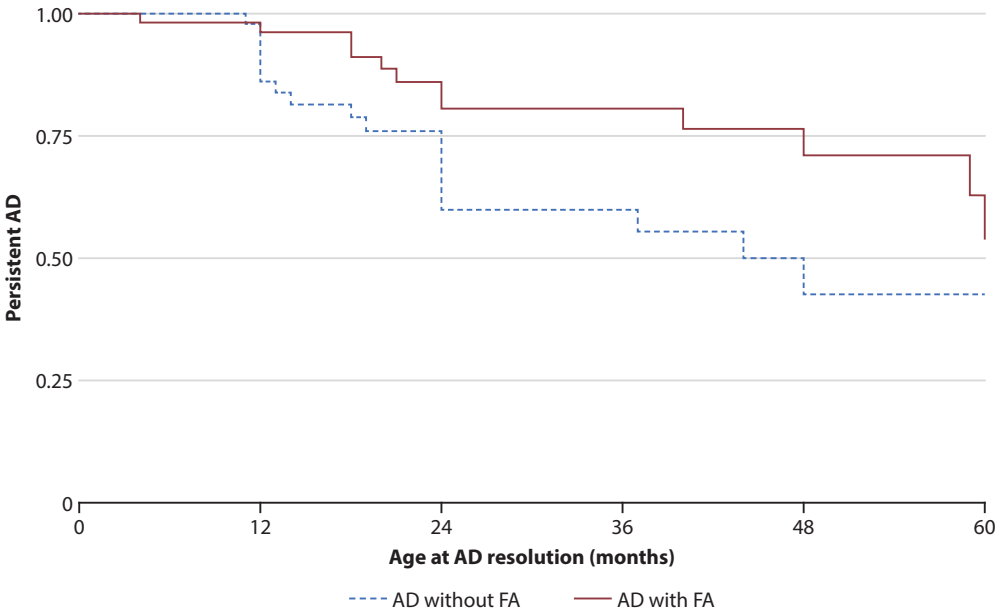

Figure 2. Kaplan-Meier analysis of AD resolution.

Table 4. Cox proportional hazards regression analysis to identify factors associated with AD resolution by 60 months of age among AD preschool children.

Factors	Hazard ratio		
	OR	95%CI	*p*
- Food allergy	0.46	0.22-1.00	0.050
- Very early-onset AD (age ≤ 3 months)	0.74	0.32-1.72	0.489
- Moderate-to-severe AD at AD onset	1.40	0.59-3.31	0.448

A p-value < 0.05 indicates statistical significance
Abbreviations: AD, atopic dermatitis; aHR, adjusted hazard ratio; CI, confidence interval

Discussion

This study set forth to investigate the risk factor that predict FA in AD children aged 6 years or younger, and to compare the rate of AD resolution between children with and without coexisting FA. Our results showed an overall prevalence of FA among AD children of 48.2%, and we found moderate-to-severe AD either at AD onset or at any time during the follow-up period to be the only baseline characteristics that were significantly different between the two groups. Moreover, AD children with FA were very close to having a significantly longer duration to achieving resolution of AD when compared to AD children without FA ($p = 0.05$).

Among children with AD, the rate of food sensitization was reported to range from 30% to 80%, and there is wide variation between and among countries.[33] In addition, discrepancies between food sensitization and confirmed FA highlight the need to establish an accurate diagnosis.[12] Our study found that approximately half of childhood AD had coexisting food allergy. This rate was lower than that from a previous study that was also conducted in Thai population that found a food sensitization rate of 60% among AD children aged 5 years or younger.[34] This result emphasizes the importance of accurately differentiating FA from food sensitization in order to avoid unnecessary food avoidance.

Our study found moderate-to-severe AD at AD onset to be significantly more prevalent in the AD with FA group, and this factor was identified as the only association for FA among AD children. These results are concordant with those from several previous studies that found a higher likelihood of food sensitization or food allergy with increasing AD severity.[17,35-37] Our study emphasize that children who present with moderate-to-severe AD should recognize investigation for food allergy. Interestingly and in contrast to previous studies, our results did not find earlier onset of AD to be significantly associated with FA.[17,37-38] Those studies found AD onset at 2 years of age or younger to be associated with FA. This difference between our results and the results of others may be explained by the fact that 93.6% of our study population experienced AD onset at less than 2 years of age.

Egg, milk, and peanut are the leading causes of food allergy among young AD children in Western countries,[8,17] whereas egg, milk, wheat, and soy are the most commonly reported causes food allergy in Asian countries.[34,39-41] Similarly, we found that egg, milk, and wheat accounted for more than half of all evaluated causative food allergens, and peanut allergy was only found in only 10% of our study population. Interestingly, IgE-mediated FA is not uncommon in these AD children, and more than one type of FA to different food allergens can be found in the same patients.

We found no significant differences between the AD with and without groups for any evaluated perinatal factors, postnatal factors, or sociodemographic factors, and none of these factors was found to significantly associated with FA. AD has a complex etiology that includes both genetic and environmental factors. Therefore, a further larger prospective study may be needed to understand the identified risk factors and their relationship with FA. Several trials have been focusing on skin care and emollient application; however, there is still no standard effective skin care intervention during the first year of life for preventing eczema or FA development.[42]

A previous study by Somanunt, et al. found that 44% of AD children had complete AD resolution by a median age of 6 years.[41] Greater chronicity of AD was reported among AD children with later onset and more disease severity, as well as those with food sensitization and/or food allergy.[6,8,41] Our results showed similar results that one-third of our study children had AD resolution by 5 years, and that AD children with FA demonstrated a strong trend toward a significantly longer duration to achieving AD resolution compared to AD children without FA even after adjusting for very early onset of AD and moderate-to-severe AD at onset.

The main strength of this study is that we only included AD children aged 6 years or younger due to the higher risk of FA compared to other age groups. Furthermore, AD diagnosis and AD severity were done using the standard criteria, and severity of AD were available in all patients.

This study has some mentionable limitations. First, we did not performed OFC in all patients to diagnose FA. However, we carefully diagnosed FA using strict criteria from standard guidelines and recommendations for FA diagnosis,[21-22,26] and all FA diagnoses were made by a pediatric allergist. Second, this single-center study was performed at a university-based national tertiary referral center, which is routinely referred cases thought to insufficiently treatable at other levels of care. However, we captured and enrolled both AD children who presented at our Allergy and Dermatology Clinic, as well as AD children who presented to our hospital via some other route. In addition to this, we deliberately focused on enrolling younger children aged less than or equal to 6 years to better address the higher association with food allergies in this age group. While this age restriction is a deliberate decision intended to enhance the study's relevance to food allergies, it is important to note that it may result in a potentially smaller sample size, which could have implications for the study's statistical power and generalizability. Third, our study's questionnaire-based design rendered it vulnerable to recall bias, to include missing, incomplete, and inaccurate data. To mitigate this weakness, the same physician who conducted the parent interviews (ST) also reviewed the medical records to cross-check and verify as much of the provided information as possible. Fourth and last, our study design did not allow for the collection of information regarding long-term moisturizer usage, and data on skincare practices, which could potentially be confounding factors related to AD resolution.

In conclusion, the results of this study revealed that preschool AD children with FA had significantly greater AD severity at AD onset and a longer duration to AD resolution compared to AD children without FA. These results highlight the importance of identifying the presence of food allergy in AD preschool children to improve patient outcomes and quality of life.

Conflict of interest declaration

All authors declare no personal or professional conflicts of interest relating to any aspect of this study.

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Supplementary Table 1. The diagnostic criteria for 3 different types of food allergy.

Criteria	Type of food allergy	Definition
I	IgE-mediated	**a)** Convincing clinical history of immediate reaction to food allergen with positive skin prick test and/or food-specific IgE **OR** **b)** Positive oral food challenge test with immediate reaction
II	Positive decision cutoff for food-specific IgE	Level of food-specific IgE greater than the positive decision cutoff value for each culprit/suspected culprit food without clinical history of reaction
III	Food-induced atopic dermatitis	**a)** Positive clinical history of food-induced eczema as evaluated by positive diagnostic elimination diet (i.e., improvement and worsening of eczema after withdrawal and reintroduction of the causative food, respectively) **OR** **b)** Positive oral food challenge test with delayed reaction

Abbreviations: IgE, immunoglobulin E antibody

Supplementary Table 2. Reported positive decision cutoff values for food-specific IgE.[1-3]

Food	Level of specific IgE (kU_A/L)	PPV (%)
Cow's milk	15	95%
Cow's milk if younger than 1 year	5	95%
Egg	7	99%
Egg if younger than 2 years	2	95%
Wheat	26	74%
Soy	30	73%
Peanut	14	99%
Fish	20	95%

Abbreviations: IgE, immunoglobulin E antibody; kUA/L, kilounits of allergen-specific IgE per liter; PPV, positive predictive value

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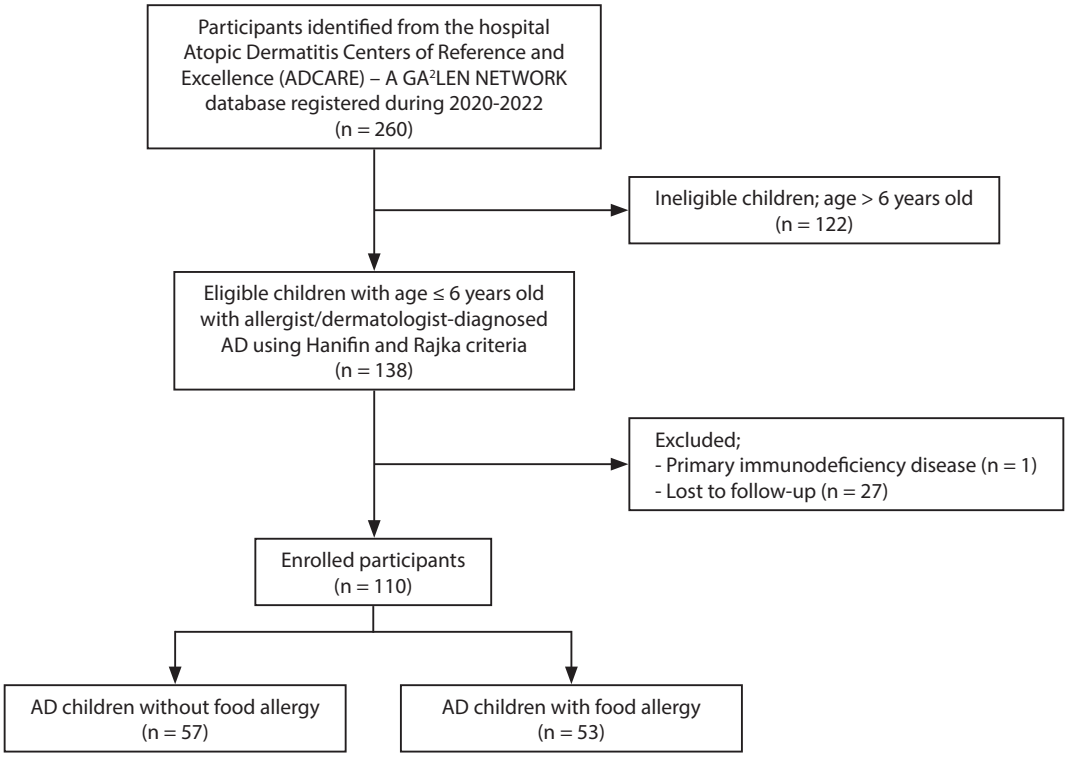
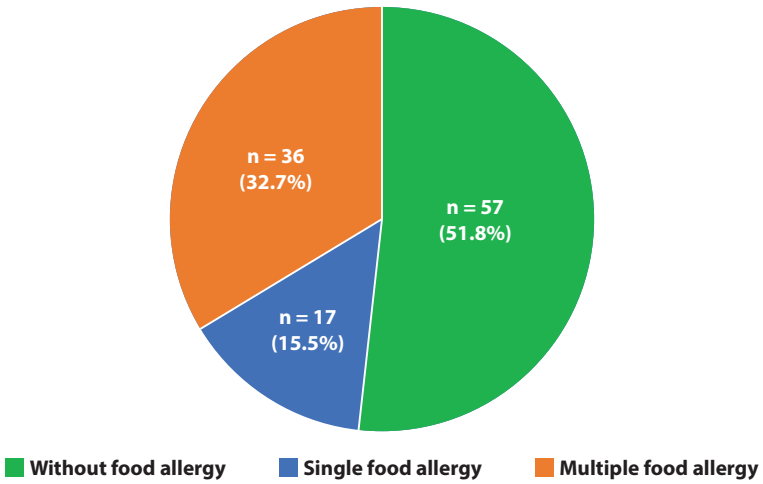


Supplementary Figure 1. Flow diagram of study participants.



Supplementary Figure 2. Food allergy status among preschool children with atopic dermatitis (N = 110).