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Clinical Predictors of Oral Food Challenge Positivity in Skin-Limited, Test-Negative Suspected IgE-Mediated Food Allergy

Ercan YILMAZ, Erdem TOPAL

Department of Pediatric Allergy and Immunology, Inonu University, Faculty of Medicine, Malatya, Türkiye

Corresponding Author: Erdem Topal ✉ erdemtopal44@gmail.com

ABSTRACT

Objective: The oral food challenge (OFC) test is the gold standard for diagnosing IgE-mediated food allergy. However, the clinical decision-making process is difficult in children who present only with skin findings and have negative specific IgE results on skin prick testing (SPT). This study aimed to determine the OFC positivity rate and the clinical factors predicting positivity in children with suspected food allergy and negative specific IgE and skin prick tests who had IgE-mediated allergic reactions limited to skin involvement.

Materials and Methods: The single-center observational study included 111 children with only cutaneous symptoms and negative SPT and specific IgE tests. All patients underwent an open OFC. Demographic characteristics, reaction timing, history of repeated reactions to the same food, atopic comorbidities, family history, total IgE level, and presence of eosinophilia were analyzed.

Results: The OFC test was positive in 14 patients (12.6%). Reaction development within the first hour after food intake (p=0.041) and a history of repeated reactions to the same food (p=0.011) were significantly associated with OFC positivity. Atopic disease in the family (p=0.005), atopic disease in a sibling (p=0.02), a history of food allergy in a sibling (p=0.026) and the presence of eosinophilia (p=0.005) were found to be significant. In the multivariate analysis, a history of previous reaction to the same food (β=1.478, OR: 4.385, 95% CI: 0.062-0.833, p=0.025), sibling history of food allergy (β=2.251, OR: 9.497, 95% CI: 1.298-69.501, p=0.027), and eosinophilia (β=2.043, OR: 7.692, 95% CI: 0.031-0.537, p=0.005) were identified as independent predictors of OFC positivity.

Conclusion: In children with negative tests and only skin findings, clinical history (particularly previous reaction to the same food), sibling history of food allergy, and eosinophilia play a significant role in predicting a positive OFC result. Risk-based clinical assessment may contribute to reducing unnecessary elimination diets.

Keywords: Food allergy, oral food challenge test, skin prick test, specific IgE, eosinophilia, atopy

INTRODUCTION

Food allergy is a significant public health issue due to its increasing prevalence, especially in childhood, and its impact on the quality of life. IgE-mediated food allergies are typically characterized by symptoms such as urticaria, angioedema, vomiting, and rarely anaphylaxis, which occur within the first few minutes to an hour after food intake (1,2). Recent epidemiological studies have shown an increase in the reported prevalence of food allergies in children; however, there is a significant difference between confirmed cases and self-reported allergy rates (1,3). This highlights the importance of diagnostic confirmation.

Although a detailed clinical history is fundamental in the diagnosis of food allergy, skin prick testing (SPT) and specific IgE measurements are commonly used diagnostic tools (2,4). However, the sensitivity and specificity of these tests are limited; positive results do not always indicate clinical allergy, and negative results do not completely rule out IgE-mediated reactions (2,5). Therefore, current guidelines define the oral food challenge (OFC) as the gold

ORCID Ercan Yilmaz / 0000-0002-1188-0918, Erdem Topal / 0000-0002-4439-2689

standard for diagnosis (2,4). Especially in cases where the clinical history is strong but the tests are negative, OFC is critical for confirming or ruling out the diagnosis (5,6).

The clinical decision-making process is more complex in patients with skin findings only, no systemic symptoms, and negative laboratory tests. In this patient group, unnecessary elimination diets may be implemented, which can lead to outcomes such as growth retardation, micronutrient deficiencies, and psychosocial burden (7). The literature emphasizes that initiating an elimination diet based solely on test results may lead to false positive and unnecessary restrictions (2,7). Therefore, predicting which patients with this specific phenotype are more likely to have positive OFC results is clinically important.

Recent studies have shown that factors such as early onset of reaction, recurrent nature, and familial atopic predisposition may increase the likelihood of clinical allergy (5,8). However, clinical and laboratory parameters predicting OFC positivity in suspected IgE-mediated food allergy with negative testing and only skin findings have not been sufficiently defined.

This study aimed to determine the rate of OFC positivity in children with a history of IgE-mediated reactions limited to skin involvement and negative specific IgE and skin prick tests, and to evaluate the clinical and laboratory risk factors predicting positivity. This was intended to contribute to reducing unnecessary elimination diets and developing a risk-based diagnostic approach.

MATERIALS and METHODS

Study Design and Population

Patients who presented to the Inonu University Pediatric Allergy Clinic between January 2015 and December 2024 with suspected food allergy were evaluated. After a detailed history and physical examination, pediatric patients with suspected IgE-mediated food allergy and a history of reactions limited to cutaneous symptoms (such as urticaria, angioedema, pruritus, or flushing) were included. Patients with a history of suspected IgE-mediated food allergy but with normal food-specific IgE levels and negative food skin prick tests were selected. Patients with any positive diagnostic test prior to OFC were excluded from the study.

The patients' demographic characteristics (age, gender), type of IgE-mediated allergic reaction limited to skin involvement, age of symptom onset, suspected food type, time between food intake and reaction, and history of repeated reactions to the same food, food tested in OFC, comorbid atopic diseases; the presence of atopic disease in parents and siblings, and laboratory tests were recorded from patient files.

OFC Protocol

At our clinic, OFC tests are performed in an open OFC format, under the supervision of a physician, after all anaphylaxis precautions have been taken and written consent has been obtained from the patient and/or parent. Patients are examined before starting OFC and before each dose increase. Vital signs, and respiratory and skin examination findings are recorded in the patients' files after each dose. Any reactions that develop after the doses are administered are also recorded in their files. Patients are kept under observation for two hours after the last dose is administered. In open OFC tests, the suspected food is started at a low dose, and dose increases are made at 15-minute intervals until the target dose is reached. In our clinic, the starting doses and dose increments for OFCs for each food are applied in accordance with the American Academy of Allergy, Asthma, and Immunology's "Work Group Report: Oral Food Challenge Testing" guidelines and "Food Challenge Tests: Turkish National Guideline 2020 published by the Turkish National Society of Allergy and Clinical Immunology" (9,10). For cow's milk, the starting dose was 0.1 mL, with stepwise increases to a target cumulative dose of 100 mL. For hen's egg, the challenge started with 1/100 of a whole egg equivalent and was increased to a target cumulative dose of one whole cooked egg. For lentils, the starting dose was 0.2 g (boiled lentil puree equivalent), with escalation up to a target cumulative dose of approximately 91 g of cooked lentils. For peanuts, the initial dose was 1 mg peanut protein equivalent, with incremental increases to a target cumulative dose of 3000 mg peanut protein (approximately 10-12 peanuts). For fish, the oral food challenge was initiated with a starting dose of 1 mg fish protein equivalent, with stepwise increases to a target cumulative dose of 20 gr fish protein. For wheat, the challenge started with 4 mg wheat flour equivalent and was escalated to a target cumulative dose of 64 g of wheat flour. The OFC was considered positive if objective symptoms occurred or if subjective symptoms were reproducible and persistent following repeated dosing. Objective symptoms were defined as reproducible clinical findings such as urticaria, angioedema, vomiting, wheezing, stridor, hypoten-

sion, or oxygen desaturation. Subjective symptoms were defined as patient-reported complaints such as oral pruritus, throat discomfort, abdominal pain, or nausea without accompanying objective signs.

Laboratory Evaluation

Serum total IgE level, eosinophil count, and specific IgE level for the relevant food were measured. Total IgE and sIgE levels were quantified using a fluorescence enzyme immunoassay method (ImmunoCAP system, Thermo Fisher Scientific, Uppsala, Sweden), according to the manufacturer's instructions. The assay has a detection range of 0.1-100 kUA/L, and results were reported quantitatively in kUA/L. A specific IgE level >0.35 kUA/L for any tested food allergen was considered positive. Peripheral blood samples were analyzed using a complete blood count, and an eosinophil percentage greater than 4% was considered eosinophilia

Skin Prick Test

The skin prick test (SPT) was performed with standard commercial extracts or via skin prick to prick technique for non-available extracts on the volar surface of the forearms or on the back of the body with a 1-mm lancet according to EAACI guidelines (2). A positive SPT was defined as a mean wheal diameter 3 mm larger than the negative control. Histamine (10 mg/mL) and saline were used as positive and negative controls, respectively. The commercial food allergen extracts (Abello-ALK, Madrid, Spain) used for the SPT were cow's milk, hen's egg (white and yolk), beef, chicken, fish mix, wheat, rice, soybean, lentil, hazelnut, walnut, peanut, and pistachio.

The research protocol was approved by the Ethics Committee of Non-Invasive Clinical Research of Inonu University (Approval number: 2026/9396). The families of the participants provided written informed consent.

Statement on AI use: No generative artificial intelligence (AI) tools were used in the preparation, writing, or editing of this manuscript.

Statistics Analysis

Statistical analysis was performed with SPSS Statistics (v.21.0; IBM Corp., Armonk, NY). Normality was evaluated by the Kolmogorov-Smirnov and Shapiro-Wilk tests. Descriptive statistics were expressed as the frequency and percentage for categorical variables, whereas the median (min-max) was used for non-normally distributed quantitative data. The categorical variables were compared using Pearson's chi-square test or Fisher's exact test. Continuous variables were analyzed using the Mann-Whitney U test. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to identify factors associated with OFC positivity. A logistic regression model was constructed. In the model, multivariate analysis was used, including statistically significant variables from the univariate analyses to identify independent predictors for OFC positivity. A p-value <0.05 was considered statistically significant.

RESULTS

Demographic and Clinical Characteristics

A total of 111 patients were included in the study. The median age of the patients was 66 (1-264) months, and 61 (55%) were male. When looking at the distribution of suspected foods thought to cause IgE-mediated allergic reactions limited to skin involvement, the most common suspected food was milk, detected in 53 cases (47.7%). This was followed by eggs in 30 cases (27.0%), lentils in 13 cases (11.7%), and peanuts in 7 cases (6.3%). Fish and wheat were detected in 4 cases (3.6%) each, with lower frequency. When cutaneous findings were examined, urticaria developed in 80 cases (72%), itching in 30 cases (27%), angioedema in 24 cases (21.6%), and flushing in 20 cases (18%).

The oral food challenge (OFC) test was positive in 14 patients (12.6%) and negative in 97 patients (87.4%). The gender distribution was similar between the OFC positive and negative groups (male ratio was 50% and 55.7%, respectively; p=0.911). The median age was 27.5 months (range 1-228) in the OFC-positive group and 67 months (range 1-264) in the OFC-negative group; no statistically significant difference was found in terms of age (p=0.115). Similarly, the age of symptom onset did not differ between groups (p=0.646).

The incidence of reactions occurring within the first hour after food intake was significantly higher in the OFC-positive group (85.7% vs. 55.7%; OR: 4.78, 95% CI: 0.98-23.3; p=0.041). Repeated reaction history with the same food was also significantly more common in OFC-positive patients (64.3% vs. 26.8%; OR: 4.91, 95% CI: 1.39-17.3; p=0.011).

No significant differences were found between the groups in terms of concomitant atopic diseases (asthma,

allergic rhinitis, and atopic dermatitis) (p=0.422, p=1.00, and p=0.754, respectively). In contrast, a family history of atopic disease (OR: 5.93, 95% CI: 1.79-19.6; p=0.005) and a sibling history of atopic disease (OR: 4.56, 95% CI: 1.39-14.9; p=0.02) were significantly higher in the OFC-positive group. Furthermore, a history of food allergy in a sibling was strongly associated with OFC positivity (21.4% vs. 3.1%; OR: 8.52, 95% CI: 1.54-47.1; p=0.026) (Table I).

Laboratory Findings

No significant difference was observed between OFC-positive and OFC-negative groups in terms of total IgE levels (p=0.936). However, the presence of eosinophilia was significantly higher in OFC-positive patients (71.4% vs. 29.9%; OR: 5.88, 95% CI: 1.76-19.7; p=0.005) (Table I).

Multivariate Logistic Regression Analysis For Independent Predictors

Binary logistic regression analysis was performed to identify independent predictors for OFC positivity. Variables with p<0.05 in univariate analysis were included in the multivariate model. In multivariate logistic regression analysis, a history of previous reaction to the same food (β=1.478, OR: 4.385, 95% CI: 0.062-0.833, p=0.025), sibling history of food allergy (β=2.251, OR: 9.497, 95% CI: 1.298-69.501, p=0.027), and eosinophilia (β=2.043, OR: 7.692, 95% CI: 0.031-0.537, p=0.005) were identified as independent predictors factors for OFC positivity.

DISCUSSION

In this study, the oral food challenge (OFC) positivity rate was found to be 12.6% in children with suspected IgE-mediated food allergy limited to skin involvement and negative specific IgE and skin prick tests. This rate once again demonstrates the diagnostic value of OFC in cases where clinical suspicion persists, but conventional tests are negative. As emphasized in the guidelines of the European Academy of Allergy and Clinical Immunology and the American Academy of Allergy, Asthma & Immunology, negative IgE and skin tests do not completely rule out clinically significant food allergy and OFC remains the gold standard diagnostic method, especially in cases with a strong history (2, 11).

In our study, the relatively low OFC positivity rate (12.6%) is important in terms of preventing unnecessary elimination diets in patients who test negative and only have skin symptoms. Incorrect diagnosis, especially in foods that form the basis of nutrition in early childhood, such as milk and eggs, can result in growth retardation, micronutrient deficiencies, and deterioration in the quality of life. Therefore, strict elimination approaches based solely on history should be avoided and OFC should be planned in selected patients with clinical risk stratification (1,2,12).

Table I: Risk factors associated with positive oral food challenge outcomes in children with suspected food allergy.

	All patients	OFC positive group (n=14)	OFC negative group (n=97)	OR (95% CI)	p value
Gender, male, n (%)	61 (55)	7 (50)	54 (55.7)		0.911
Age, median, (min-max), months	66 (1-264)	27.5 (1-228)	67 (1-264)		0.115
Symptom onset age, (median, min-max), month	7 (1-180)	5.5 (1-160)	7 (1-180)		0.646
Reaction within the first hour after food ingestion, n (%)	66 (59.5)	12 (85.7)	54 (55.7)	4.78 (0.98 - 23.3)	**0.041**
History of recurrent reaction to the same food, n (%)	35 (31.5)	9 (64.3)	26 (26.8)	4.91 (1.39 - 17.3)	0.011
Atopic diseases in patients					
Asthma, n (%)	16 (14.4)	3 (21.4)	13 (13.4)		0.422
Allergic rhinitis, n (%)	12 (10.8)	1 (7.1)	11 (11.3)		1.00
Atopic eczema, n (%)	31 (27.9)	3 (21.4)	28 (28.9)		0.754
Atopic diseases in parent, n (%)	21 (18.9)	7 (50)	14 (14.4)	5.93 (1.79 - 19.6)	**0.005**
Atopic diseases in sibling, n (%)	30 (27)	8 (57.1)	22 (22.7)	4.56 (1.39 - 14.9)	**0.02**
Food allergy history in sibling, n (%)	6 (5.4)	3 (21.4)	3 (3.1)	8.52 (1.54 - 47.1)	**0.026**
Total IgE level, IU/mL (median, min-max)	34 (1-4054)	25,3 (1-2040)	34 (1-4054)		0.936
Eosinophilia, n (%)	39 (35.1)	10 (71.4)	29 (29.9)	5.88 (1.76 - 19.7)	**0.005**

One of the most significant clinical findings found to be significantly associated with OFC positivity is a history of previous reactions to the same food. This finding was also identified as an independent risk factor in the multivariate analysis. The literature reports that a history of recurrent and consistent symptoms is one of the strongest clinical predictors of true food allergy (11). Therefore, a detailed medical history continues to form the basis of the OFC decision-making process.

Another notable finding in our study is that the history of food allergy in a sibling is strongly associated with OFC positivity. The presence of atopic disease in the family increases the risk of food allergy, particularly through genetic predisposition and shared environmental exposures (13). The emergence of a sibling history of food allergy as an independent predictor in this study demonstrates that the family history is critical not only in terms of general atopy but also specifically in relation to food allergy.

No significant association was found between total IgE levels and OFC positivity. This finding supports the view that total IgE has limited predictive value in food allergy and that more specific clinical and laboratory parameters take precedence (14,15). The presence of eosinophilia also showed a significant association with OFC positivity and was identified as an independent risk factor. Eosinophils are an important component of the Th2-mediated immune response and are considered a biological marker of IgE-mediated allergic inflammation. Although peripheral eosinophilia is not a specific marker, it is valuable as a parameter supporting clinical suspicion (2). This finding suggests that evaluating laboratory markers in conjunction with clinical history may improve diagnostic accuracy.

When the results of the multivariate analysis were evaluated together, a history of previous reactions, the presence of food allergy in a sibling, and eosinophilia were identified as factors independently predictive of a positive OFC result. These three parameters are low-cost and accessible markers that can be easily integrated into clinical practice. They may therefore contribute to risk stratification in the planning of OFC tests.

The study has some limitations. First, its retrospective nature may have led to data loss and bias. Patients with similar clinical features may not have undergone OFC and were therefore not included in the analysis. This retrospective, indication-based inclusion may have introduced selection bias; however, this represents an inherent limitation of the study design. Second, its single-center design and relatively small sample size resulted in wide confidence intervals. Third, the limited number of patients with positive oral food challenge results (n=14) precluded meaningful subgroup analyses by specific food allergens. Considering the heterogeneity in clinical course and predictors among different foods, the pooled evaluation may restrict the interpretability and generalizability of the findings. However, its focus on a unique patient group with a history of negative testing and skin-limited reactions is a strength of the study.

CONCLUSION

In conclusion, this study demonstrates that simple parameters such as clinical history (particularly previous reaction to the same food), sibling history of food allergy, and eosinophilia play a significant role in predicting a positive OFC result. These findings highlight the central role of clinical history in the diagnostic algorithm and support a risk-based approach that could help reduce the need for unnecessary diet elimination. Future prospective, multicenter studies are required to validate these predictors and develop more robust risk models.

Conflict of Interest

The authors declare that they have no conflict of interest.

Author Contributions

Concept: **ET,** Design: **EY, ET,** Data collection or processing: **EY,** Analysis or Interpretation: **EY, ET,** Literature search: **EY, ET,** Writing: **ET,** Approval: **EY, ET.**

REFERENCES

1. Sicherer SH, Sampson HA. Food allergy: Epidemiology, pathogenesis, diagnosis, and treatment. J Allergy Clin Immunol 2014;133:291-307.e5.
2. Muraro A, Werfel T, Hoffmann-Sommergruber K, Roberts G, Beyer K, C Bindslev-Jensen, et al. EAACI food allergy and anaphylaxis guidelines: Diagnosis and management of food allergy. Allergy 2014;69:1008-25.
3. Nwaru BI, Hickstein L, Panesar SS, Muraro A, Werfel T, Cardona V, et al. EAACI Food Allergy and Anaphylaxis Guidelines Group. The epidemiology of food allergy in Europe: A systematic review and meta-analysis. Allergy 2014;69:62-75.
4. Calvani M, Bianchi A, Reginelli C, Peresso M, Testa A. Oral Food Challenge. Medicina (Kaunas) 2019;55:651.
5. Celik-Bilgili S, Mehl A, Verstege A, Staden U, Nocon M, Beyer K, et al. The predictive value of specific immunoglobulin E levels in serum for the outcome of oral food challenges. Clin Exp Allergy 2005;35(3):268-73.

6. Fleischer DM, Bock SA, Spears GC, Wilson CG, Miyazawa NK, Gleason MC, et al. Oral food challenges in children with a diagnosis of food allergy. J Pediatr 2011;158:578-83.e1.
7. Meyer R, De Koker C, Dziubak R, Godwin H, Dominguez-Ortega G, Chebar Lozinsky A, et al. The impact of the elimination diet on growth and nutrient intake in children with food protein induced gastrointestinal allergies. Clin Transl Allergy 2016;6:25.
8. Koplin JJ, Allen KJ, Gurrin LC, Peters RL, Lowe AJ, Tang ML,et al. HealthNuts Study Team. The impact of family history of allergy on risk of food allergy: a population-based study of infants. Int J Environ Res Public Health 2013;10:5364-77.
9. Bird JA, Leonard S, Groetch M, Assa'ad A, Cianferoni A, Clark A, et al. Conducting an Oral Food Challenge: An Update to the 2009 AAAAI Work Group Report. J Allergy Clin Immunol Pract 2020;8:75-90.e17.
10. Saçkesen C, Büyüktiryaki B, editors. Turkish National Society of Allergy and Clinical Immunology Food Challenge Tests: Turkish National Guideline 2020.
11. Boyce JA, Assa'ad A, Burks AW, Jones SM, Sampson HA, Wood RA, et al. NIAID-Sponsored Expert Panel. Guidelines for the Diagnosis and Management of Food Allergy in the United States: Summary of the NIAID-Sponsored Expert Panel Report. J Allergy Clin Immunol 2010;126:1105-18.
12. Şimşek Y, Yilmaz O, Yüksel H. IgE mediated food allergy in children: clinical findings, diagnosis and prognostic features. Asthma Allergy Immunol 2014;12:152-6.
13. Lack G. Epidemiologic risks for food allergy. J Allergy Clin Immunol 2008;121:1331-6.
14. Sicherer SH, Sampson HA. Food allergy: A review and update on epidemiology, pathogenesis, diagnosis, prevention, and management. J Allergy Clin Immunol 2018;141:41-58.
15. Xu X, Liu L, Zhang Y, Zhou P, Wang P, Zhou J, et al. Allergen-specific IgE/total IgE ratio for food allergy diagnosis in children. Front Pediatr 2025;13:1628506.