

Predictors of adverse reactions among children undergoing oral food challenges

E. Montag^{1,2,3}, T. Dribin, M.D.³, P. Catlin¹, D. Schnadower, M.D.³, P. Chundi, M.S.⁴, Amal Assa'ad, M.D.¹

¹Division of Allergy and Immunology, Cincinnati Children's Hospital Medical Center and the Department of Pediatrics, Cincinnati, OH

²Xavier University, Cincinnati, OH

³Division of Emergency Medicine, Cincinnati Children's Hospital Medical Center and the Department of Pediatrics, Cincinnati, OH

⁴James M. Anderson Center, Cincinnati Children's Hospital Medical Center, Cincinnati, OH



Abstract

Rationale: Oral food challenges (OFCs) are the gold standard for diagnosing food allergies yet carry the risk of adverse reactions including severe reactions necessitating emergency department (ED) care or hospitalization. Thus, the objective of the study was to assess the prevalence and predictors of adverse reactions among children undergoing OFCs.

Methods: Retrospective review of a prospectively collected database of children presenting to Cincinnati Children's Hospital allergy clinic for diagnostic OFCs to milk, egg, peanuts, and tree nuts from January 2013 to May 2019. Adverse reactions were defined as allergist documentation of "failed OFC" and severe reactions were defined as ED encounters for adverse reactions within 72 hours of the OFC. Past medical history and OFC data were analyzed using univariate as well as multivariate logistic regression with backward elimination. Candidate predictors included OFC allergen (milk, egg, peanut or tree nuts), prior reactions to the allergen stratified by organ system involvement (respiratory, dermatologic, gastrointestinal, or cardiovascular), and history of allergic rhinitis or asthma.

Results: Among the 876 unique OFCs, 220 children (25.1%) had adverse reactions, of which 17 (1.94%) and 3 (0.34%) resulted in ED visits and hospitalizations respectively. In the multivariate analysis, only prior respiratory reactions to the OFC allergen reached statistical significance (OR 3.32, 95% CI 1.37, 8.06).

Conclusions: Adverse reactions are common among children undergoing OFCs; however, severe reactions requiring ED care or hospitalization are rare. Children with prior respiratory reactions to the allergen may be at increased risk of adverse reactions.

Rationale

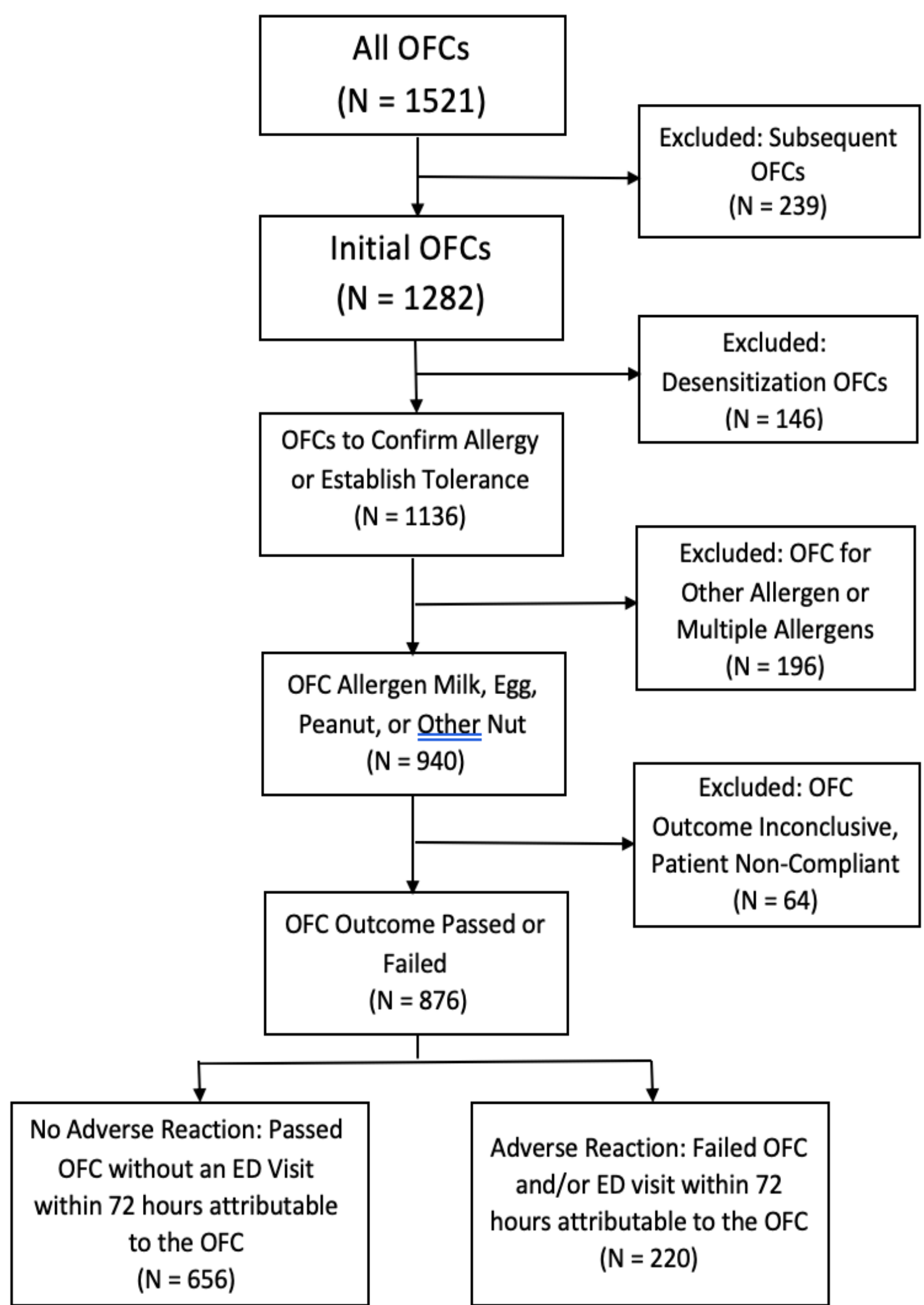
- 5 to 10% of children have diagnosed food allergies, and food allergies produce an annual healthcare cost of \$24.8 billion in the United States alone.^{1,2}
- Oral food challenges (OFCs) are the gold standard for diagnosing food allergies but carry the risk of adverse reactions, including severe reactions necessitating ED care or hospitalization.³
- It is necessary to accurately assess the risk of adverse reactions to OFCs in a large cohort of pediatric patients.

Objective

To assess the prevalence and predictors of adverse reactions among children undergoing OFCs.

Methods

- Retrospective review study of prospectively collected database of children presenting to Cincinnati Children's Hospital allergy clinic for OFCs from January 2013 to May 2019.
- Inclusion Criteria: Initial OFC to milk, egg, peanut, or other nut; OFC for the diagnosis of food allergy or allergen tolerance.
- Exclusion Criteria: Subsequent OFCs; OFCs for other allergens or multiple allergens; desensitization challenges.
- Outcomes:
 - Adverse reaction: based on allergist documentation of "failed OFC" in EMR.
 - Severe adverse reaction: children who had ED encounters for OFC reaction within 72 hrs.
 - Hospitalization: hospitalizations for OFC reactions.



- Past medical history and OFC data were analyzed using univariate and multivariate logistic regression with backward elimination.
- Candidate predictors:
 - OFC allergen: milk, egg, peanut or tree nuts.
 - Prior reactions to the allergen stratified by organ system involvement: respiratory, dermatologic, gastrointestinal, or cardiovascular.
 - Past medical history of allergic rhinitis, atopic dermatitis, or asthma.

Results

Characteristics of children undergoing initial OFCs, stratified by presence of adverse reaction to OFC (N = 876).

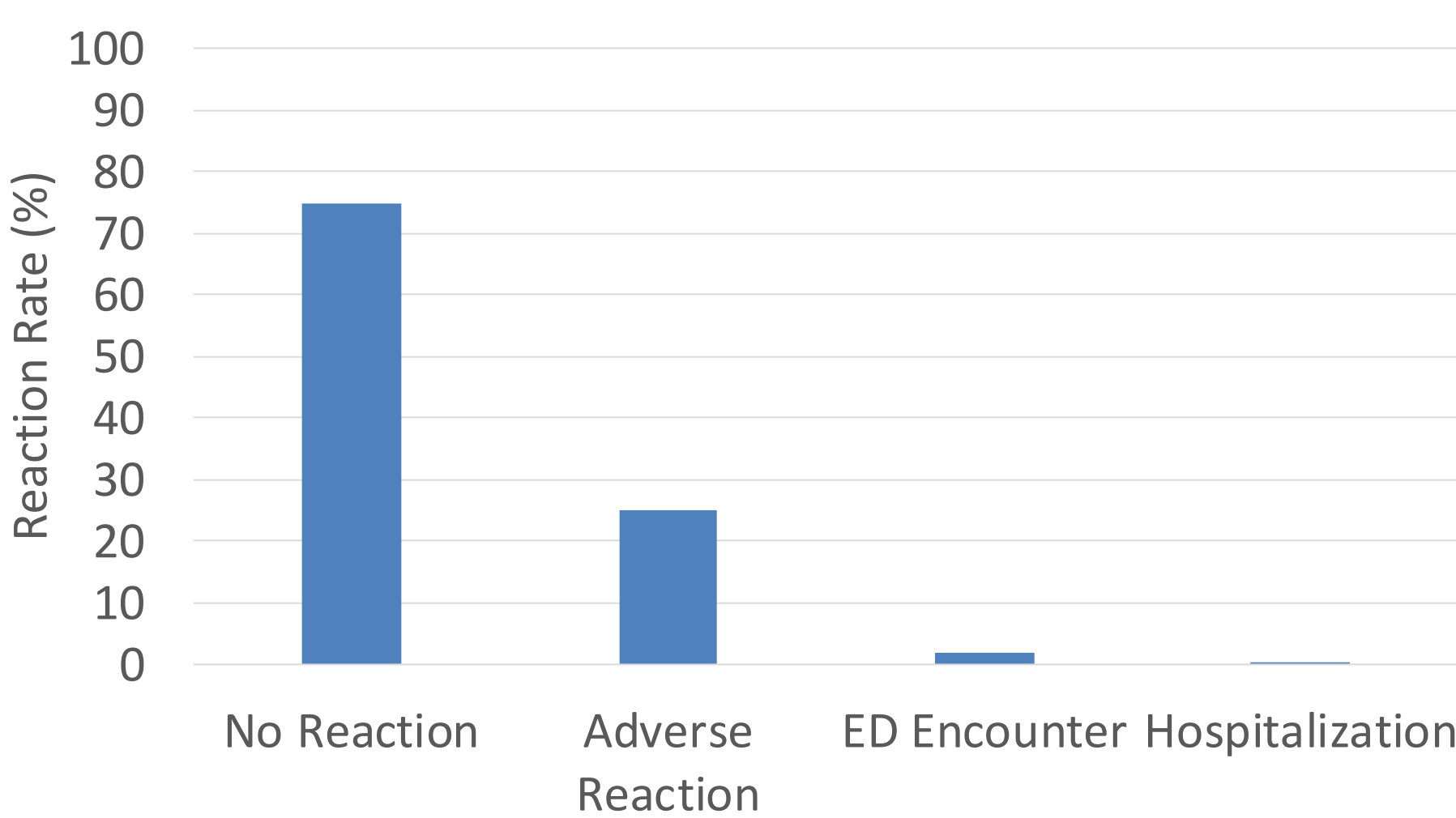
Characteristics	No Adverse Reaction N (%) N = 656	Adverse Reaction N (%) N = 220
Past Medical History		
Asthma	200 (30.5)	58 (26.4)
Allergic Rhinitis	351 (53.5)	125 (56.8)
Atopic Dermatitis	467 (71.2)	174 (79.1)
Multiple Allergic Illnesses	325 (49.5)	111 (50.5)
Allergy History		
Milk	185 (28.2)	67 (30.5)
Prior Allergic Reaction*	154 (23.5)	57 (25.9)
Egg	311 (47.4)	107 (48.6)
Prior Allergic Reaction*	200 (30.5)	65 (29.6)
Peanut	438 (66.8)	158 (71.8)
Prior Allergic Reaction*	222 (33.8)	73 (33.2)
Other Nut	415 (63.3)	144 (65.5)
Prior Allergic Reaction*	109 (16.6)	42 (19.1)
Clinical manifestations of prior allergic reaction		
Dermatologic	480 (73.2)	219 (99.6)
Gastrointestinal	188 (28.7)	65 (29.6)
Respiratory	99 (15.1)**	46 (20.9)**
Cardiovascular	1 (0.15)	1 (0.45)
OFC Allergen		
Milk	90 (13.7)	30 (13.6)
Egg	202 (30.8)	64 (29.1)
Peanut	208 (31.7)	85 (38.6)
Other Nut	156 (23.8)	41 (18.6)
ED Encounters Within 24 Hours		
Hospitalized for Allergic Reaction	0	16 (7.27)
ED Encounters Within 72 Hours		
Hospitalized for Allergic Reaction	0	1 (0.45)

*: Adverse Reaction to Allergen, not including SPT or IgE levels.

** : Proportion is significantly higher for adverse reactions in comparison to no adverse reactions via multivariate analysis (OR 3.32, 95% CI 1.37, 8.06).

Results

Rates of adverse and severe adverse reaction to OFC (N = 876).



Limitations

- Single center.
- Retrospective design.
- Subjective physician perceptions of reaction severity could lead to inconsistent classifications of OFC reactions and decisions to refer patients to the ED or hospitalize.

Conclusions

- Adverse reactions are common among children undergoing OFCs, occurring in approximately one fourth (25.1%) of cases.
- Severe reactions requiring ED care (1.94%) or hospitalization (0.34%) are rare, indicating that OFCs are generally safe procedures.
- Only prior respiratory reactions to the OFC allergen reached statistical significance (OR 3.32, 95% CI 1.37, 8.06).
- Children with history of respiratory reactions to the allergen may be at increased risk of adverse reactions.

References

1. Prescott SL, Pawankar R, Allen KJ, Campbell DE, Sinn JK, Fiocchi A et al. A global survey of changing patterns of food allergy burden in children. *World Allergy Organ J* 2013; 6: 21.
2. Osborne NJ, Koplin JJ, Martin PE, Gurrin LC, Lowe AJ, Matheson MC et al. Prevalence of challenge-proven IgE-mediated food allergy using population-based sampling and predetermined challenge criteria in infants. *J Allergy Clin Immunol* 2011; 127: 668–76.
3. Gupta R, Holdford D, Bilaver L, Dyer A, Holl JL, Meltzer D. The Economic Impact of Childhood Food Allergy in the United States. *JAMA Pediatr* 2013; 167: 1026–1031.