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Association Between Food Allergy Status and Atopic Dermatitis Control and Persistence: A Longitudinal Analysis of the Pediatric Eczema Elective Registry

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ABSTRACT

Atopic dermatitis (AD) and food allergies (FA) are closely linked manifestations of atopic disease, sharing immunological pathways that contribute to their chronicity and mutual exacerbation. However, the long-term impact of FA on AD remains incompletely understood. To address this knowledge gap, we analyzed 8015 children from the Pediatric Eczema Elective Registry (PEER), exploring the relationship between FA status as an exposure and AD control as an outcome at enrollment, as well as AD persistence as another outcome over 10 years. Our results indicate that at enrollment, children with any FA had significantly higher odds of having uncontrolled AD, and over the course of 10 years, they were more likely to experience persistent AD compared to those without any FA. These associations were particularly pronounced in subgroup analyses of milk, egg, and peanut allergies, highlighting the importance of recognizing FA as a significant prognostic factor in managing long-term AD outcomes in comorbid cases.

1 | Introduction

Atopic dermatitis (AD) and food allergies (FA) are manifestations of atopic disease that share key immunological features, driving inflammation, and hypersensitivity reactions observed in both conditions [1]. These mechanisms may facilitate mutual exacerbation in comorbid cases [2]. Despite these similarities, the influence of FA on long-term AD outcomes remains incompletely understood. Therefore, we analyzed 8015 children from a pediatric eczema registry to investigate the impact of FA status on AD control and persistence.

2 | Methods

The Pediatric Eczema Elective Registry (PEER) is a U.S.-based prospective cohort study evaluating the long-term safety and efficacy of pimecrolimus cream in children aged 2–17 with AD, tracking subjects biannually for 10 years [3]. At enrollment, parents were asked, "Is your child allergic to any food (that you are aware of)?" Those who answered "yes" specified the allergen from a predefined list. AD control was assessed with the question, "In the past six months, how has your child's skin disease been managed: complete, good, limited, or uncontrolled?" Persistent AD was defined as the absence of complete control and/or the use of AD medications. Informed consent was obtained from all participants. This protocol was approved by the University of Pennsylvania Institutional Review Board.

In the cross-sectional analysis at enrollment, AD control was the outcome, categorized as "controlled" (complete and good control) or "uncontrolled" (limited and poor control). Logistic regression estimated adjusted odds ratios (aORs) with 95% confidence intervals (CIs) to assess the association between FA status

TABLE 1 | Baseline characteristics of children with and without food allergies in the Pediatric Eczema Elective Registry Cohort.

	Overall, $N = 8015$	Food allergy, $N = 1822$	No food allergy, $N = 6193$
Enrollment age	7.5 (4.2)	7.0 (4.0)	7.6 (4.2)
Smoking	1264 (16%)	250 (14%)	1014 (17%)
Unknown	107	10	97
Income			
< $24,000	3388 (58%)	550 (43%)	2838 (62%)
$25,000–$49,999	1156 (20%)	309 (24%)	847 (19%)
$50,000–$74,999	562 (9.6%)	185 (14%)	377 (8.3%)
> $75,000	737 (13%)	249 (19%)	488 (11%)
Unknown	2172	529	1643
AD Control			
Controlled	4203 (53%)	853 (47%)	3350 (54%)
Uncontrolled	3798 (47%)	964 (53%)	2834 (46%)
Unknown	14	5	9
Family history of AD	6251 (78%)	1309 (72%)	4942 (80%)
Use of prescription AD cream in the past 6 months	7477 (100%)	1711 (100%)	5766 (100%)
Unknown	527	110	417
Use of pimecrolimus in past 6 months	8013 (100%)	1822 (100%)	6191 (100%)
Use of tacrolimus in past 6 months	914 (12%)	290 (17%)	624 (11%)
Unknown	459	76	383
Use of topical steroids in past 6 months	4835 (60%)	1343 (74%)	3492 (57%)
Unknown	17	2	15
Use of other AD medication in past 6 months	3067 (39%)	944 (52%)	2123 (35%)
Unknown	80	17	63
Asthma	3671 (46%)	1130 (62%)	2541 (41%)
Unknown	9	2	7
Animal allergies	1681 (21%)	863 (47%)	818 (13%)
Unknown	11	2	9
Seasonal allergies	4934 (62%)	1412 (78%)	3522 (57%)
Unknown	22	9	13
Number of other atopic comorbidities			
0	2260 (28%)	210 (12%)	2050 (33%)
1	2250 (28%)	381 (21%)	1869 (30%)
2	2400 (30%)	644 (36%)	1756 (28%)
3	1069 (13%)	574 (32%)	495 (8.0%)
Unknown	36	13	23

Note: Characteristics are reported as mean (standard deviation) for continuous variables and as number (percentage) for categorical variables.

as the exposure and AD control as the outcome, adjusting for animal and seasonal allergies, asthma, race/ethnicity, family history of AD, sex, family income, age at enrollment, and the number of other atopic conditions. In the longitudinal analysis over the course of 10 years, generalized estimating equations with a logit link regression estimated aORs with 95% CIs for persistent AD based on FA status at enrollment. This analysis adjusted for the same covariates while addressing attrition using stabilized inverse probability weights and managing missing data through multiple imputation. Sub-analyses explored the associations between the top three specified FA and AD, and our sensitivity analysis applied a stricter definition of FA status (Table S1).

3 | Results

This study analyzed 8015 children with an average enrollment age of 7.5 ± 4.2 years. 22.73% had FA, with peanuts (9.72%), egg (7.16%), and milk (5.86%) being the most common. Children with FA were less likely to have a family history of AD and lower family incomes (< $50,000/year), but more likely to have uncontrolled AD, use additional AD medications beyond pimecrolimus, and have atopic comorbidities (Table 1).

At enrollment, children with any FA were significantly more likely to have uncontrolled AD compared to those without FA (aOR 1.29; 95% CI 1.15–1.45) (Table 2). Over the 10-year study period, children with FA had a significantly higher likelihood of persistent AD (1.36; 1.17–1.58). Specific allergens were associated with stronger effects: at enrollment, the aORs for having uncontrolled AD for those with milk, egg, and peanut allergies compared to those without were 1.46 (1.20–1.78), 1.49 (1.26–1.75), and 1.50 (1.28–1.77), respectively. Long-term AD persistence was highest among those with egg (1.83; 1.41–2.38), peanut (1.78; 1.43–2.22), and milk allergies (1.73; 1.29–2.33).

TABLE 2 | Cross-sectional and longitudinal analyses of food allergy status and atopic dermatitis outcomes.

Exposure	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Cross-sectional analysis		
Milk	1.59 (1.32, 1.92)	1.46 (1.20, 1.78)
Eggs	1.63 (1.37, 1.94)	1.49 (1.26, 1.75)
Peanuts	1.63 (1.41, 1.90)	1.50 (1.28, 1.77)
Any FA	1.34 (1.20, 1.48)	1.29 (1.15, 1.45)
Longitudinal analysis		
Milk	1.74 (1.29, 2.34)	1.73 (1.29, 2.33)
Eggs	1.76 (1.38, 2.26)	1.83 (1.41, 2.38)
Peanuts	1.71 (1.39, 2.12)	1.78 (1.43, 2.22)
Any FA	1.34 (1.16, 1.54)	1.36 (1.17, 1.58)

Note: This table presents unadjusted and adjusted odds ratios (OR) with 95% confidence intervals (CI) for the association between specific food allergies (milk, eggs, peanuts), any food allergy (FA), with uncontrolled atopic dermatitis (AD) at enrollment (cross-sectional analyses) and with persistent AD over the 10-year study period (longitudinal analyses).

4 | Discussion

Our findings show that FA status is associated with uncontrolled AD at enrollment and long-term AD persistence over 10 years. Our results align with previous research identifying cow's milk and egg sensitization as risk factors for persistent infantile AD [4–8] and extend this understanding through a decade-long longitudinal design. Importantly, to be eligible for PEER, all children had to have mild-to-moderate AD at enrollment, allowing us to examine the natural history of disease progression in this population subset. All analyses adjusted for recent medication use to account for differences in disease course related to FA comorbidity. A key strength of our study was the detailed characterization and granularity of FA status and the specific food types involved, which enabled us to identify distinct associations between specific FA and AD outcomes. However, limitations include the exclusion of severe AD cases, making our findings most applicable to mild-to-moderate disease and the reliance on caregiver-reported FA status without confirmatory diagnostic tests. Future research using objective FA measures could deepen our understanding of the FA-AD relationship and uncover further mechanistic insights.

5 | Conclusion

The observed relationship between FA and AD persistence suggests that FA is an important prognostic factor for long-term AD outcomes. This highlights the need for closer monitoring of children with concurrent atopic conditions, as ongoing allergic responses may lead to more persistent manifestations.

Acknowledgments

J.J.W. and D.J.M. designed the study, conducted, or directed all analyses, and wrote the initial manuscript. J.J.W. and D.J.M. reviewed, edited, and approved the final version of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The Pediatric Eczema Elective Registry data are not currently publicly available. The PEER is an ongoing study sponsored by Bausch Health as part of a post-marketing commitment with the Food and Drug Administration.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.