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LETTER TO THE EDITOR

WILEY

Race is a modifier between parental allergy and food allergy in offspring

To the Editor,

Studies indicate associations between maternal allergy and development of food allergy in their offspring,[1] with higher food allergy risk among those with more than one first-degree relative with allergic disease.[2] However, unnecessary food avoidance among children of allergic parents has important implications since diverse diets in children may decrease the risk for food allergy, and early food introduction with foods such as peanut can be protective for food allergy.[3] We sought to assess the association between parental allergic markers and offspring food sensitization and clinical allergy to milk, egg, or peanut. We also sought to identify the effect modification of maternal race on offspring's food allergic outcomes.

We analyzed data from the racially and socioeconomically diverse population birth cohort, Wayne County Health, Environment, Allergy and Asthma Longitudinal Study (WHEALS) that enrolled pregnant women 21–45 years of age and their offspring following recruitment September 2003–December 2007.[4,5] Institutional Review Board approval was obtained for this study.

Parental factors assessed included questionnaire responses regarding history of allergy or asthma; maternal total IgE and maternal serum allergen-specific IgE (sIgE) levels during pregnancy or 1 month postpartum were evaluated. Atopy was defined as at least one sIgE ≥0.35 IU/mL to eight allergens (dust mite, dog, cat, grass, ragweed, *Alternaria*, egg, and cockroach). Maternal asthma, atopic dermatitis, and food allergy were determined by questionnaire. Due to a paucity of paternal data, only paternal asthma was assessed.

Offspring sensitization to milk, egg, or peanut was determined at 2 years of age by sIgE≥0.35 IU/mL and skin prick testing (SPT; wheal size ≥3 mm larger than the saline control defined a positive test). As sensitization to foods does not always translate to clinical allergy, we formed an algorithm to determine those most likely to have true IgE-mediated food allergy.[6] A consensus panel of allergists determined food allergy status in offspring based on review of the aforementioned data and previously abstracted chart information as previously described.[7] Briefly, infant data were forwarded to the panel only if more than one of the following criteria were met for milk, egg, or peanut allergens: (1) 1 sIgE ≥0.35 IU/mL; (2) a positive SPT; or (3) parental report of infant symptoms potentially related to food allergy plus at least one sIgE >0.10 IU/mL. To standardize classifying infants to the presence of IgE-mediated food allergy (IgE-FA), physicians were asked to combine professional experience with investigator-developed protocols based on the Guidelines for the Diagnosis and Management of Food Allergy in the United States.[8] A third allergist independently reviewed and ruled on discordant decisions.

Logistic regression models of parental variables with each outcome were fit. Interaction terms were added to logistic regression models to assess differences in associations based on race ($p < 0.10$ was considered a significant interaction). Leave-one-out cross-validation was used to obtain predicted probabilities, which were used to construct receiver operating characteristic (ROC) curves and calculate area-under-the-curve (AUC) values.

Of 1258 maternal-child pairs, 761 had sufficient data for analysis (Figure S1). Participant characteristics indicated that families not lost to follow-up had higher household incomes, higher maternal education, married mothers, pet ownership, and breastfeeding (Table S1).

Associations between parental variables and physician panel determination of food allergy are shown in Table 1. After adjusting for child race, seven out of eight parental characteristics were significant or of borderline significance. However, the maximum AUC for ROC curves for any individual variable was 0.54 (maternal total IgE), indicating poor prognostic value (Table S2). Maternal atopy, multi-sensitization, and total IgE significantly interacted with race ($p = .012$, 0.092, 0.068, respectively) indicating strong associations among African American (AA) children only (Table 1). For example, maternal atopy in non-AA children was not associated with food allergy, but was highly associated among AA children (OR [95% CI] = 3.56 [1.55, 9.66], $p = .006$).

Maternal current asthma was also associated with childhood food allergy (OR [95% CI] = 2.27 [1.02, 4.71], $p = .034$), and patterns varied by race with history of maternal asthma associated with food allergy only in non-AA children (OR [95% CI] = 4.92 [1.22, 17.14], $p = .015$), and current asthma among AA children (OR [95% CI] = 2.64 [1.10, 5.92], $p = .022$; Table 1).

Combined, parental variables only modestly impacted food allergy ROC analyses resulting in AUC = 0.66. However, the ROC curves differed by race (non-AA AUC 0.36 vs AA AUC 0.71, $p = .002$) as shown in Figure 1.

Apart from food allergy, parental variables were analyzed for associations with offspring sensitization (positive sIgE or SPT) to peanut, milk, or egg at age 2 years. Maternal atopy, multi-sensitization, and total IgE were associated with offspring positive food sIgE sensitization to at

TABLE 1 Association between individual parental history covariates and physician panel-diagnosed food allergy, overall and by child race

Predictor	N	Comparison	Overall[a]		Interaction	By Race			
						Non-African American (N = 283)		African American (N = 478)	
			OR [95% CI]	p-value	p-value	OR [95% CI]	p-value	OR [95% CI]	p-value
Maternal atopy	572	Yes vs No	1.85 [1.01, 3.57]	0.054	**0.012**	0.62 [0.2, 1.8]	0.39	3.56 [1.55, 9.66]	**0.006**
Maternal Multi-Sensitization	572	Yes vs No	2.92 [1.62, 5.43]	**<0.001**	**0.092**	1.38 [0.44, 4]	0.56	4.25 [2.02, 9.81]	**<0.001**
Maternal Total IgE	576	Per 100IU/mL increase	1.17 [1.05, 1.31]	**0.005**	**0.068**	0.86 [0.38, 1.22]	0.6	1.24 [1.09, 1.44]	**0.003**
Maternal doctor-diagnosed asthma	590	Current vs Never	2.27 [1.02, 4.71]	**0.034**	0.116	1.00 [0.05, 5.75]	1	2.64 [1.10, 5.92]	**0.022**
		Past vs Never	1.94 [0.75, 4.39]	0.135		4.92 [1.22, 17.14]	**0.015**	1.05 [0.24, 3.20]	0.944
Maternal ever have doctor-diagnosed eczema	585	Yes vs No	1.82 [0.92, 3.45]	0.074	0.919	1.72 [0.37, 5.9]	0.427	1.86 [0.84, 3.89]	0.109
Maternal ever have doctor-diagnosed food allergies	590	Yes vs No	3.84 [1.61, 8.47]	**0.001**	0.631	5.66 [0.76, 29.26]	**0.05**	3.47 [1.29, 8.46]	**0.009**
Paternal ever have doctor-diagnosed asthma	520	Yes vs No	2.11 [1, 4.18]	**0.038**	0.241	1 [0.15, 4.01]	1	2.72 [1.17, 6]	**0.015**

[a]Adjusted for race.
Significant p-values listed in bold.

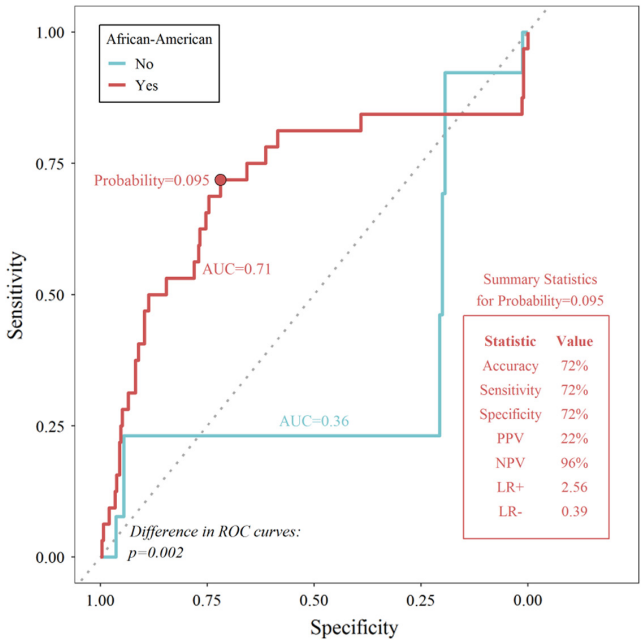

FIGURE 1 Predictive ability of all parental history covariates for physician panel-diagnosed food allergy, by race. The optimal probability threshold determined by Youden's index is indicated by a point on the curve; corresponding summary statistics for that threshold are also provided

least one food. Analysis stratified by race indicated these associations were significant only among AA children. (Table S3). Furthermore, maternal current asthma was associated with food sIgE sensitization only among non-AA children (OR [95% CI] = 4.90 [1.69, 16.20], p = .005). ROC curves were significantly different between AA and non-AA children (p = .036) but predictive ability remained poor in both (AUC 0.55 and 0.44, respectively, as in Figure S2).

Maternal multi-sensitization, total IgE and current asthma, and paternal asthma were statistically significantly associated with any positive food SPTs only among AA children. (Table S4). Additionally, race modified the relationship between maternal atopy and SPTs (p = .039); AA children of atopic mothers had elevated odds of food SPT positivity (OR [95% CI] = 1.96 [1.15, 3.45], p = .016). Despite ROC differences by race (p = .015; Figure S3), parental variables again had minimal predictive ability.

The importance of genetic factors in food allergy is supported by twin studies showing higher concordance of peanut allergy among monozygotic compared with dizygotic twins (64.3% and 6.8%, respectively).[9] In addition, heritability among parents and offspring for overall food sensitization has been reported.[1] However, our report indicates parental variables related to allergy have poor predictive ability for offspring food sensitization. The results from the physician panel demonstrate a moderate degree of risk and capability of predicting food allergy in offspring from parents having clinical allergy.

We previously reported similar food allergy prevalence for milk, egg, and peanut in AA and non-AA children.[7] We report here that the inherited risk as measured by parental allergic variables and predictive ability of parental allergic variables on food allergy

development in offspring varies by race and is more strongly associated with clinical food allergy versus sensitization, among AA children. The potential mechanisms behind this racial discrepancy are require further studies.

Potential study limitations include the physician panel to determine clinical food allergy status as opposed to performing oral food challenges. These challenges are time-consuming and impractical to implement in large epidemiological studies.[10] Another limitation is that non-AA children included multiple ethnicities, which was done to preserve sample size. These groups may have different incidences of disease, and the risk may vary. Further, these findings should be confirmed in larger studies, as we also chose to examine interactions at level 0.10 and were unable to adjust for potential confounders due to sample size. Finally, included and excluded WHEALS participants differed by demographic variables, so findings may not be generalizable to the target population.

Parental allergy and atopy, although associated with offspring food allergy, is only a weak predictor and depends upon race. Further studies of familial factors contributing to food allergy and these disparities are needed to precisely identify children at risk for food allergy.

KEYWORDS

allergen sensitization, food allergy, parental allergy, race

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CONFLICTS OF INTEREST

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.