ORIGINAL ARTICLE

Allergen Sensitization of Parents and Children With Respiratory Allergic Diseases

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ABSTRACT

Objective: To study the differences in allergen sensitization of parents and their offspring with respiratory allergic diseases.

Methods: We included parents and their children who were both diagnosed with allergic asthma and/or allergic rhinitis, between January 2018 and December 2022. Parent-child dyads were evaluated for sensitization to six categories of allergens viz, dust mite, fungus, animal dander, weed pollen, tree pollen and food allergen, by measuring the allergen-specific immunoglobulin E levels (sIgE). Data of gender, age, feeding history, serum total IgE (tIgE), and absolute eosinophil counts (AEC) were collected and analyzed for differences in allergen sensitization of parents and children.

Results: Overall, the AEC in children were significantly higher than that of parents. The sensitivity to fungal allergens in children was significantly higher than that in fathers (33.3% vs 6.7%, $P = 0.01$) as well as mothers (29.3% vs 8.3%, P = 0.03). Sensitization to food allergens was also higher in children compared to fathers (25.4% vs 7.9%, $P = 0.01$). Fathers with tree pollen allergen sensitivity, and mothers with weed pollen allergen sensitivity had a significantly increased risk (aOR, 95% CI) of having increased sensitivity to these allergens in their offspring; 24.01 (1.08, 53.99; $P = 0.04$) and 3.27 (1.08, 9.92; $P = 0.04$), respectively.

Conclusion: Children had greater sensitivity for fungal allergens compared to both parents, as well as food allergy compared to fathers. Fathers with tree pollen allergen sensitivity, and mothers with weed pollen allergen sensitivity had an increased risk of having their children sensitive to these types of allergens.

***Keywords*:** Allergy, Asthma, Hypersensitivity, IgE, Rhinitis, Sensitization.

INTRODUCTION

Allergic diseases induced by different allergens differ significantly in epidemiology as well as hypersensitivity response [1,2]. Parental history of atopic disease is a well-established risk factor for developing atopic diseases in offspring [3], given the fact that they share similar genetic make-up and environment. Only a few studies have addressed the differences in allergen sensitization between children and their parents, reporting inconsistent results with respect to different allergic diseases, age, sex, allergens, residence and gender of the parent [4-6].

Allergen sensitization plays an important role in the pathogenesis of allergic diseases [7]. A few allergens lead to long-lasting allergic diseases through persistent allergen sensitization [8]. Preventive interventions towards allergens sensitization can prevent allergy and allergic diseases [9]. With this background, this study, analyzed the differences and association of allergen sensitization between the parent and their offspring diagnosed with respiratory allergic diseases in the eastern coastal areas of China.

METHODS

The study enrolled parents and their children (aged 2-18 years) diagnosed with allergic asthma and/or allergic rhinitis attending the outpatient Department of Allergy, Yantai Yuhuangding Hospital, Shandong, People's Republic of China, between January 2018 and December 2022. Diagnosis of asthma and rhinitis was established according to the Global Initiative for Asthma [9], and/or Allergic Rhinitis and its Impact on Asthma [10] criteria. Patients who received immunotherapy, immunosuppressants, or biologics within three months, or those receiving systemic glucocorticoids within one month, and those with a recent respiratory or parasitic infection, severe dysfunction of the heart, liver, or kidney, known immunodeficiency diseases, autoimmune diseases, or other non-allergic diseases associated with abnormal eosinophils and immunoglobulin E levels were excluded.

The study was approved by the institutional ethics committee. Children were enrolled after obtaining consent from the parent/ guardian. Data regarding the age, gender, household income, types of residence (rural or urban) and dietary history (for children) were collected. Low socioeconomic status was defined with a monthly household income below 5,000 China Yuan.

Blood samples from the participants were collected on the same day after the symptoms due to the acute allergy were relieved. Sera were separated and analyzed for total immunoglobulin E (tIgE) and allergen-specific IgE (sIgE) levels against common inhaled allergens. The detected allergens were divided into six categories for statistical analysis, (i) dust mites: *Dermatophagoides pteronyssinus* (d1) and *Dermatophagoides farinae* (d2); (ii) fungus: *Alternaria alternata, Aspergillus fumigatus* and mixed term mx1 (including *Penicillium chrysogenum, Cladosporium herbarum, Aspergillus fumigatus,* and *Alternaria alternata*); (iii) animal dander: *cat dander, dog dander* and mixed term ex1 (including *cat dander, horse dander, cow dander, dog dander*); (iv) weed pollen: *Humulus, Mugwort* and mixed term wx5 (including *Ambrosia artemisiifolia, Artemisia vulgaris, Chrysanthemum leucanthemum, Taraxacum vulagare,* and *Solidago virgaurea*); (v) tree

pollen: mixed term tx5 (including *Alnus incana, Corylus avellana, Ulmus americana, Salix caprea,* and *Populus deltoides*); (vi) food: *milk, egg white, wheat, shrimp, crab, peanut, soybean*, mixed term fx1 (including *peanut, hazelnut, brazilnut, almond, coconut*) and mixed term fx5 (including *egg white, milk, fish, wheat, peanut*, and *soybean*) [11]. Phadia 250 type automatic fluoroenzyme immunoassay system (ImmunoCAP) was used to detect the tIgE and allergen-specific IgE (sIgE) in the sera of all participants. A positive test for sIgE was defined as ≥ 0.35 kU/L for at least one of the tested allergens. Absolute eosinophil values were determined by an automated outpatient hematology analyzer (Beckman Coulter, USA).

Based on the assumption of 40% incidence of positive allergen testing in the parent group and an odds ratio of 2.5 for parental matched sensitization with their offspring to the allergen [4], a sample size of 254 (127 per group) was calculated at 5% level of significance and 90% power.

Statistical analysis: SPSS 22.0 software was used for statistical analysis. Quantitative data with non-normal distribution were described by median (IQR), and comparison between groups was performed by Wilcoxon signed rank test. Data with normal distribution were expressed as means (SD) and compared using Student's t-test. The categorical variables were expressed as frequency (*n*) and percentage (%), and the comparisons between the parent and their offspring were performed by Chi-square test. A logistic regression model was established to evaluate the factors influencing sensitization to allergens in children. $P < 0.05$ was considered statistically significant.

RESULTS

A total of 147 parent-child pairs (63 father-child pairs and 84 mother-child pairs) were included in this study; 82 children were aged between 2-6 years and 65 were aged 6-18 years. The demographic factors and allergens exposure shown in Table I. 58.7% (*n* = 37) father-child dyads and 69% (*n* = 58) mother-child dyads had urban residence. 30.1% (*n* = 19) father-child dyads and 23.8% (*n* = 20) mother-child dyads had low household income.

The AEC and sensitization to a few allergens were significantly higher in children as shown in Table I. Breastfeeding and low household income reduced the risk (OR (95% CI) of the positive rate of food allergen sensitivity in children; 4.96 (1.09, 22.53), $P = 0.04$; and 0.02 (0.01, 0.19), $P < 0.01$, respectively. With increasing age, the positive rate of mold allergens in children decreased significantly (0.89 (0.73, 0.98); $P = 0.04$). Allergen positivity was not affected by the gender of the child. A binary multifactor logistic regression model to find potential predictors of positive allergen sensitization results in children for six categories of

allergens was established with gender, age, breastfeeding, low household income, types of residence and parent allergen as independent variables (Table II). Fathers with tree pollen allergen sensitivity, and mothers with weed pollen allergen sensitivity had a statistically significant increased risk (aOR, 95% CI) of increased sensitivity to these allergens in children; 24.01 (1.08, 53.99; P = 0.04) and 3.27 (1.08, 9.92; P = 0.04), respectively.

DISCUSSION

This study showed a significant risk of allergy in children with paternal tree pollen and maternal weed pollen allergen positivity. Genetic and environmental factors play an important role in allergen sensitization. Studies have found that specific allergen sensitivity is related to Human Leukocyte Antigen (HLA) class II gene loci [12]. The environmental factors interact with genes related to the development of allergen sensitization through an epigenetic mechanism [13]. It remains unclear whether paternal and maternal genes have different roles in allergen sensitization in their children. Additionally, in countries where most children younger than 18 years live with their parents, they share similar environmental exposures for allergies. This may have been a contributing factor in our study.

The present study found that the sensitivity to fungal allergens in children was higher than that of their parent. Children had higher sensitization to food allergens than their fathers. The study population was from the eastern coastal areas of China, where the climate is warm and humid conducive to propagation of fungi. Younger children spend longer time indoors than their parents that may explain the higher risk of sensitization to fungal antigens in them [14]. Residential environment has been shown to be the most important factor affecting sensitization to allergens in children compared to adults [15]. The survey results from a study in United States also showed that fungus is the most important allergen in children with asthma [16]. Few studies have also reported an inverse relationship between sensitization to *Alternaria alternata* and age [17]. Sensitization to food allergens may be higher in children as the mucosal intestinal barrier is immature in children making them more sensitive to enzymatic allergens and special allergenic proteins [18,19].

The results of this study indirectly suggest that measures to reduce the concentration of fungi and molds in household environment should be taken and younger children should be encouraged to spend longer time outdoors to reduce the chances of respiratory allergic diseases.

The influence of parental allergen sensitization on offspring's allergen sensitization is complex. Maternal allergen exposure can induce an immune response in the fetus during pregnancy, coupled with postpartum lactation factors that could change the susceptibility of children to disease [5,20,21]. Cookson et al sought differences between maternal and paternal patterns of transmission at the 11q13 locus among pairs of siblings in families affected by atopy, and found that transmission of atopy at the chromosome 11q locus was detectable only through the maternal line [22]. However, fathers have been shown to have an equally important role in determining allergen sensitization of children as the mother [4]. Specific allergen sensitivity has been related to certain HLA loci that depend on their parental source, resulting in phenotypic differences between reciprocal heterozygotes [12]. It was believed that identical twins were more likely than fraternal twins to have consistent responses to the skin prick test of house dust mites. However, identical twins showed significant differences in their responses to specific house dust mites and *Alternaria alternata* [23]. Another study concluded that the allergen-specific response was random and independent of the phenotype of first-degree relatives. Our results and these examples illustrate the complexity of the genetics of allergic sensitization that may be affected by different factors including the type of disease, age, race, living environment of the subjects, and the type of allergen.

This study found differences in allergen sensitization measured in terms of sIgE values in the parents and their offspring for different allergens. The development of allergen-specific IgE levels requires environmental exposure and has a dynamic association with age [24]. It is possible that parents outgrew the allergy sensitization after repeated exposures and therefore had a lower proportion of positivity or it may also have been due to immunosenescence [25].

This study had a few limitations. The study enrolled a small sample and, findings are limited to patients diagnosed with respiratory allergic diseases from the eastern coastal areas of China. sIgE values were representative of six types of allergens instead of a broader spectrum of allergens. sIgE $\geq$ 0.35kU/L was considered positive and was evaluated for an association to clinical symptoms.

We conclude that the increased sensitivity to fungi and food allergens in children needs to be explored to understand the reasons for differences from that in parents. Both gene and environment interactions determine the development of childhood allergic diseases.

Ethics clearance: Ethics Committee of Yantai Yuhuangding Hospital. Ref no. 2023-051 dated Mar 17, 2023.

Contributors: LPL, YMS: Study conduct, data collection, drafting the manuscript; XLL: Statistical analysis, study design; GRL: Data acquisition, analysis and interpretation, drafting the manuscript. All authors read and approved the final manuscript.

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Competing interest: None stated.

WHAT THIS STUDY ADDS?

- Sensitivity to fungus and food allergens in children was significantly higher than that in parent.
- Father with tree pollen allergen positivity, and mother with weed pollen allergen positivity, will having their children sensitive to these types of allergens.

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Table I Demographic and Allergen Exposure of Parent and Children

	Father-child (n = 63)			Mother-child (n = 84)		
	Father	Child	P value	Mother	Child	P value
Age[a] (y)	39 (34, 43)	7 (4, 14)	< 0.001	36.5 (33, 40.75)	5 (4,11)	< 0.001
tIgE[a] (kU/L)	152 (56.0, 314.0)	235 (84.4, 637.0)	0.05	109 (26.1, 309.0)	80.1 (46.2, 219.5)	0.82
AEC[a] ($\times 10^9$)	0.20 (0.15, 0.39)	0.32 (0.21, 0.50)	0.01	0.17 (0.10, 0.33)	0.29 (0.16, 0.43)	< 0.001
Breastfeeding	-	48 (76.19)	-	-	62 (73.80)	-
Sensitization to dust mites[b]	33 (52.4)	37 (58.7)	0.47	54 (64.3)	43 (51.2)	0.09
Sensitization to fungus[b]	6 (9.5)	26 (41.3)	< 0.001	7 (8.3)	25 (29.8)	< 0.001
Sensitization to weed pollen[b]	25 (39.7)	15 (23.8)	0.06	31 (36.9)	24 (28.6)	0.25
Sensitization to tree pollen[b]	15 (23.8)	7 (11.1)	0.06	19 (22.6)	13 (15.5)	0.24
Sensitization to animal dander[b]	9 (14.3)	4 (6.3)	0.14	10 (11.9)	12 (14.3)	0.65
Sensitization to food[b]	5 (7.9)	16 (25.4)	0.01	15 (17.9)	22 (26.2)	0.19

Data expressed as n (%) or [a]median (IQR); [b] Expressed as *n* (%) and indicates those who were tested positive; *AEC Absolute eosinophil count, tIgE Total immunoglobulin E levels*

Table II Risk of Allergen Sensitivity in Offspring in Relation to Positivity in Parent

Variables	Father		Mother	
	aOR（95% CI）	P value	aOR（95% CI）	P value
Dust mites	0.47（0.12, 1.82）	0.27	2.429（0.87, 6.81）	0.09
Fungus	3.04（0.44, 20.94）	0.26	0.99（0.66, 4.63）	0.99
Weed pollen	4.97（0.28, 89.16）	0.28	3.27（1.08, 9.92）	0.04
Tree pollen	24.04（1.08, 53.99）	0.04	2.230（0.54, 9.27）	0.27
Animal dander	2.80（0.11, 0.67）	0.99	1.73（0.27, 11.14）	0.57
Food	2.91（0.32, 26.81）	0.34	0.60（0.70, 9.59）	0.15

aOR Adjusted odds ratio; Adjusted for gender, age, breastfeeding, low household income and type of residence (urban or rural)