Journal of Asthma and Allergy

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Association of Mite Molecular Sensitization Profiles with Respiratory Allergies and Asthma Control in Children from East China

Jing He[1,*], Nan Lin[2,*], Ting Jin[2], Ming Lin[1], Zuowei Huang[1], Shuxian Li[1], Jinling Liu[1], Lin Su[1], Xian Ye[2], Lei Wu[1], Zhenghong Song[2], Hongzhen Xu[2], Zhimin Chen[1]

[1]Department of Pulmonology, Children's Hospital, Zhejiang University School of Medicine, National Clinical Research Center for Child Health, Hangzhou, People's Republic of China; [2]Nursing Department, Children's Hospital, Zhejiang University School of Medicine, National Clinical Research Center for Child Health, Hangzhou, People's Republic of China

*These authors contributed equally to this work

Correspondence: Zhimin Chen, Department of Pulmonology, Children's Hospital, Zhejiang University School of Medicine, National Clinical Research Center for Child Health, Hangzhou, Zhejiang, 310052, People's Republic of China, Email zmchen@zju.edu.cn; Hongzhen Xu, Master of nursing, Nursing Department, Children's Hospital, Zhejiang University School of Medicine, National Clinical Research Center for Child Health, Hangzhou, Zhejiang, 310052, People's Republic of China, Email 6184020@zju.edu.cn

Background: Allergic conditions, identified as a significant global health challenge, are profoundly influenced by indoor allergens, especially house dust mites (HDM). Yet the relationship between mite sensitized components and respiratory allergies and asthma control remains poorly understood.

Methods: A cohort of 96 children, either with allergic rhinitis (AR) or rhinitis with asthma syndrome (ARAS), was assessed. Protein microarray technology was deployed to quantify sIgE responses to the allergenic components of Der p and Der f.

Results: The study cohort comprised 18 AR and 78 ARAS patients; with 43 mild and 53 moderate-to-severe AR; with 28 uncontrolled, 21 partially controlled, and 29 well-controlled asthma. Sensitization prevalence for HDM components was highest with Der p (97.9%), Der f 2 (97.9%), Der p 2 (94.8%), Der f 1(94.8%), Der p 1 (93.8%), Der p 23 (57.3%). Notably, sIgE concentrations for Der f and Der f 2 were significantly greater in the ARAS compared to AR ($P < 0.05$). While sIgE levels varied between mild and moderate-to-severe AR, the differences were not statistically significant ($P > 0.05$). However, Der p 23 sIgE levels demonstrated a significant fluctuation across the asthma control strata ($P < 0.05$), with the well-controlled group exhibiting the lowest readings.

Conclusion: The sIgE levels to HDM allergens were higher in ARAS group compared to AR group, especially Der f and Der f 2, indicating an association between sIgE reactivity and the diagnosis of asthma. Reduced Der p 23 sIgE levels were indicative of enhanced asthma control.

Keywords: house dust mite, allergic rhinitis, asthma, molecular sensitization, children

Introduction

Allergic diseases have been designated by the World Health Organization (WHO) as one of the three major diseases for focused research and management in the 21st century, spotlighting them as a global public health concern.[1] Allergic airway diseases, including allergic rhinitis (AR) and asthma, affect 10% to 40% of the global population, with an increasing incidence, particularly among children.[2] In China, the prevalence of AR among children varies significantly by region, ranging from 4.5% to 22.4%, and continues to rise.[3] As children age, AR may progress to allergic asthma, culminating in the so-called allergic rhinitis with asthma syndrome (ARAS).[4]

Allergic asthma is a heterogeneous disorder characterized by chronic airway inflammation induced by allergens, leading to recurrent wheezing, shortness of breath, chest tightness, and/or cough. Epidemiological surveys revealed that

Received: 31 May 2024
Accepted: 23 September 2024
Published: 7 October 2024

approximately 5% to 16% of the global population is afflicted with asthma, and the proportion of children with asthma keeps on rising.[5] Asthma not only influence the quality of daily life and normal growth and development of children but also imposes a considerable burden on families and the entire society. Additionally, children with persistent asthma and reduced pulmonary function were at increased risk of developing fixed airflow obstruction and possibly chronic obstructive pulmonary disease in early adulthood.[6] Therefore, it is of great significance to emphasize the prevention and treatment of asthma in childhood and prevent the acute attack of asthma.

Studies indicate that up to 80% of children are sensitive to one or more allergens, with the majority exhibiting polysensitivities (sensitized to more than one allergen).[7] House dust mites (HDM) are a principal indoor allergen, implicated in the global affliction of 65 to 130 million individuals with allergic rhinitis and asthma through their allergenic molecules.[8] In China, HDM is the major inhaled allergen inducing AR and asthma, with Dermatophagoides pteronyssinus (Der p) and Dermatophagoides farinae (Der f) being the most common.[9] Studies showed that the living, excrement and dead remains of mites can induce allergic diseases.[10] The complexity of mite allergenic protein components and the unclear relationship between different allergenic components and respiratory allergies have been noted. Molecular allergen diagnostics, including component-resolved diagnosis (CRD),[11] offer a new avenue for research by identifying allergenic components at the molecular level. This approach allows researchers to assess specific IgE reactivity using a set of purified allergenic components, rather than crude extracts, to accurately identify the components to which subjects are genuinely allergic.[12,13] To date, more than 30 hDM allergenic components have been identified.[14]

Geographical variations in HDM allergy prevalence and the molecular mechanisms of sensitization differ significantly across regions.[15,16] The temperate and subtropical climate, high humidity, and dense population of East China provide an ideal environment for the proliferation of dust mites. Nevertheless, the distribution of mite allergenic protein components in this region, as well as their correlation with the clinical phenotypes of respiratory allergies and AR severity and asthma control, remains to be elucidated. Therefore, our study involved the detection and comparison of dust mite allergenic protein components in children with AR, with or without asthma, and investigated the correlation between these components and clinical phenotypes, AR severity and asthma control. This work aims to deepen the understanding of the mechanisms underlying allergic diseases and to advance prevention and treatment strategies.

Methods

Study Design and Population

In this cross-sectional analysis, we included pediatric patients aged 5–16 years, who visited the Allergology Outpatient Clinic at Zhejiang Children's Hospital between April and October 2022. Eligibility criteria encompassed: (1) diagnosis of AR with or without asthma, according to Allergic Rhinitis and its Impact on Asthma guidelines[4] and Global Initiative for Asthma guidelines;[17] (2) serum allergen tests suggesting elevated sIgE of monosensitized HDM (defined as serum level of Der p- and/or Der f-sIgE $\geq$ 0.35 kUA/L) or HDM sIgE level elevated in predominant, accompanied by other inhalant allergens sensitized; and/or skin prick test results indicating a positive reaction of moderate or greater intensity to HDM. Exclusion criteria were as follows: (1) previous immunotherapy (including allergen-specific immunotherapy); (2) serum allergen tests indicating sensitization to three or more inhalant allergens; (3) concomitant major underlying diseases of the heart, liver, or kidneys; (4) concurrent infections. The study protocol received approval from the ethics committees of the Children's Hospital, Zhejiang University School of Medicine (2022-IRB-060). Written informed consent was obtained from all participants and their guardians. This study was conducted in accordance with the Declaration of Helsinki.

Data Collection

Upon enrollment, participants underwent a comprehensive collection of their medical histories, which encompassed a wide array of variables including age, height, weight, sex, history of eczema, preterm birth history, feeding methods during the first six months post-birth, exposure to tobacco smoke, pet ownership, and familial history of allergies. Tobacco exposure was defined as the presence of any household member who smoked at home from the child's birth to the present. Pet ownership was considered as having a cat or dog in the home following the child's birth. A family history

of allergies was delineated as the occurrence of allergic diseases within three generations of the child's relatives, including allergic rhinitis, asthma, conjunctivitis, eczema, and urticaria.

The severity of AR was categorized into mild and moderate-severe groups according to established guidelines;[4] asthma control status was determined based on scores from the Asthma Control Test (ACT)[18] or the Childhood Asthma Control Test (C-ACT).[19] The ACT, with a total score of 25, and the C-ACT, with a total score of 27, serve as tools to assess the level of asthma control. The ACT is intended for children aged 12 and above as well as adults, and comprises five questions rated on a 5-point scale (1–5 points), with higher scores indicating better control. The C-ACT is tailored for children aged 4 to 11, consisting of seven questions where the first four are answered by the child using a 4-point scale (0–3 points) and the last three by parents using a 6-point scale (0–5 points), again with higher scores denoting better asthma control. The criteria for ACT/C-ACT scores are as follows: a score of ≥24 indicates well-controlled asthma, 20–23 suggests partial control, and ≤19 indicates uncontrolled asthma.

Serum sIgE Levels to Der p and Der f Detection

Patient blood samples were collected and subjected to centrifugation at rest. Subsequent analysis was conducted using the Phadia 250 ImmunoCAP fully automated in vitro allergen detection system (manufactured by Thermo Fisher, Sweden), which boasts an intra-assay variability of less than 8% and a detection limit below 0.1 kUA/L. The sIgE results were stratified into seven categories: levels < 0.35 kUA/L were classified as class 0; 0.35–0.7 kUA/L as class 1; >0.7–3.5 kUA/L as class 2; >3.5–17.5 kUA/L as class 3; >17.5–50 kUA/L as class 4; >50 −100 kUA/L as class 5; and >100 kUA/L as class 6. A serum sIgE level of ≥0.35 kUA/L was considered positive, indicating sensitization to Der p and Der f.

HDM Component sIgE Detection

The detection of serum sIgE levels to HDM components was performed using a protein chip assay, in accordance with the instructions (Hangzhou Zheda Dixun Biological Gene Engineering Co., Ltd). This assay facilitated the measurement of sIgE against a comprehensive panel of HDM allergens, including Der p1, Der f1, Der p2, Der f2, Der p5, Der p7, Der p10, Der p21, and Der p23. These allergenic components were immobilized on nitrocellulose strips. Subsequently, sera from the study participants were applied to these membranes, followed by the addition of anti-human IgE antibodies, enzyme conjugates, and the appropriate substrates. The procedure entailed a total of four incubation and wash steps. After drying, the chips were scanned using an EPSON Perfection U370 Photo scanner. Automated immunoblotting software was employed for result interpretation. A test result was deemed positive for sIgE levels of 0.35 IU/mL or above. The serum sIgE findings for HDM components were classified using the previously mentioned scale (levels 0–6).

Statistical Analysis

Statistical analyses and graphical representations of the data were conducted using SPSS 26.0 and GraphPad Prism 8.0. Skewed distributions were represented by median (M) and interquartile range (IQR). The sensitization rates to Der p, Der f, and their components between groups (AR vs ARAS, mild AR vs moderate-severe AR) were analyzed using the Chi-square test (Pearson's Chi-square or Fisher's exact test). Comparisons of Der p and Der f specific IgE levels, as well as component-specific IgE levels between two groups, were performed using non-parametric tests for independent samples, while comparisons among multiple groups utilized the Kruskal–Wallis test. Correlation analyses were conducted using Pearson and Spearman rank correlation tests. A two-tailed α of 0.05 was set, with $P < 0.05$ considered statistically significant.

Results

Demographic and Clinical Data of Enrolled AR and ARAS Children

A total of 96 children participated in this study, consisted of 61 males and 35 females, with ages ranging from 5.52 to 14.30 years and a median age of 7.57 (IQR: 6.31–9.47) years. The subjects were divided into two diagnostic groups: 18 children with AR (15 males, 3 females; mean age 7.97 years) and 78 children with ARAS (46 males, 32 females; mean age 7.48 years). According to AR severity, 43 were identified with mild AR, and 53 with moderate-to-severe AR. In the

ARAS group, 28 children were categorized with uncontrolled asthma, 21 with partially controlled asthma, and 29 with well-controlled asthma. Statistical analysis revealed no significant differences between the AR and ARAS groups regarding age distribution, height, weight, gender, family history, and personal medical history (Table 1 and Supplementary Figure 1A–H).

HDM Components sIgE in AR and ARAS Groups

The prevalence of sensitization was highest for Der f (100%), followed by Der p (97.9%), Der f 2 (97.9%), Der p 2 (94.8%), Der f 1(94.8%), Der p 1 (93.8%), Der p 23 (57.3%), Der p 21 (42.7%), Der p 7 (33.3%), and Der p 5 (32.3%). The lowest sensitization rate was observed for Der p10 (6.3%) (Table 2). Among the various HDM components, with the exception of Der p 1, Der f 1, Der p 23, and Der p 7 (where both groups had an equal rate of 33.3%), the remaining components exhibited a trend of higher sensitization rates in the ARAS group compared to the AR group. However, these differences did not reach statistical significance ($P > 0.05$).

sIgE levels to Der p were not significantly different between ARAS and AR patients, with median values of 30.03 kUA/L (IQR: 11.61–52.75) for ARAS and 14.75 kUA/L (IQR: 8.43–42.99) for AR, respectively ($P > 0.05$). Conversely, sIgE to Der f were markedly higher in ARAS compared to AR, with medians of 59.95 kUA/L (IQR: 36.54–95.33) vs 29.74 kUA/L (IQR: 17.92–57.89), respectively ($P < 0.05$) as shown in Table 3.

Within the Der p allergens, sIgE for Der p 1, Der p 2, and Der p 23 showed higher trends in ARAS than in AR, though without statistical significance ($P > 0.05$). sIgE for Der p 10 was significantly higher in AR group ($P < 0.05$), but median levels in both remained below 0.35 kUA/L, indicating minimal clinical impact. No significant differences were found in sIgE for Der p 5, Der p 7, and Der p 21 between ARAS and AR ($P > 0.05$). Among Der f allergens, Der f 2 had the highest median sIgE in each group. ARAS showed significantly elevated sIgE for Der f 2, with a median of 100.00 kUA/L (IQR: 88.28–100.00) versus 92.16 kUA/L (IQR: 36.83–100.00) in AR ($P < 0.05$). sIgE for Der f 1 did not significantly differ between ARAS and AR, with medians of 22.57 kUA/L (IQR: 10.01–47.66) and 14.61 kUA/L (IQR: 9.05–26.38), respectively ($P > 0.05$).

Table 1 Demographic and Clinical Data in AR and ARAS Children

Characteristics		AR+ARAS (n=96), M (IQR)/N (%)	AR (n=18), M (IQR)/N (%)	ARAS (n=78), M (IQR)/N (%)	*P*
Age (year)		7.57(6.31–9.47)	7.97(6.32–9.41)	7.48(6.29–9.54)	0.940[a]
Gender	Male	61(63.5)	15(83.3)	46(59.0)	0.053[b]
	Female	35(36.5)	3(16.7)	32(41.0)	
Height (cm)		122(115.2–135)	124.5(120–136.25)	122(115–135.2)	0.673[a]
Weight (kg)		24(20–29.75)	25(20–29.54)	24(20–30)	0.721[a]
Inhalant allergens	Monosentized	78(81.3)	16(88.9)	62(79.5)	0.510[b]
	Polysensitized	18(18.8)	2(11.1)	16(20.5)	
History of atopic dermatitis	No	43(44.8)	7(38.9)	36(46.2)	0.576[b]
	Yes	53(55.2)	11(61.1)	42(53.8)	
History of prematurity	No	93(96.9)	18(100.0)	75(96.2)	1.000[c]
	Yes	3(3.1)	0(0.0)	3(3.8)	
Feeding style in 6 months	Breast	48(50.0)	11(61.1)	37(47.4)	0.296[b]
	Mix	48(50.0)	7(38.9)	41(52.6)	
History of tobacco exposure	No	45(46.9)	11(61.1)	34(43.6)	0.179[b]
	Yes	51(53.1)	7(38.9)	44(56.4)	
Pet feeding history	No	88(91.7)	17(94.4)	71(91.0)	1.000[b]
	Yes	8(8.3)	1(5.6)	7(9.0)	
Family history of allergy	No	21(21.9)	5(27.8)	16(20.5)	0.533[b]
	Yes	75(78.1)	13(72.2)	62(79.5)	

Notes: [a]Mann–Whitney test, [b]Chi-square test, [c]Fisher's exact test.
Abbreviations: AR, allergic rhinitis; ARAS, allergic rhinitis with asthma syndrome.

Table 2 Sensitization and Molecular Profile of HDM in AR and ARAS Groups (%)

HDM Components	AR+ARAS (n=96)	AR (n=18)	ARAS (n=78)	*P*
Der p	97.9	100.0	97.4	1.000[b]
Der f	100.0	100.0	100.0	–
Der p 1	93.8	100.0	92.3	0.590[b]
Der f 1	94.8	100.0	93.6	0.580[b]
Der p 2	94.8	94.4	94.9	1.000[b]
Der f 2	97.9	94.4	98.7	0.341[b]
Der p 5	32.3	27.8	33.3	0.650[a]
Der p 7	33.3	33.3	33.3	1.000[b]
Der p 10	6.3	5.6	6.4	1.000[c]
Der p 21	42.7	33.3	44.9	0.372[a]
Der p 23	57.3	61.1	56.4	0.716[a]

Note: [a]Chi-square test, [b]Fisher's exact test.
Abbreviations: HDM, house dust mites; AR, allergic rhinitis; ARAS, allergic rhinitis with asthma syndrome; Der p, Dermatophagoides pteronyssinus; Der f, Dermatophagoides farinae.

Table 3 Serum sIgE Levels to HDM Components in the AR and ARAS Groups

HDM Components	AR group (n=18), kUA/L	ARAS group (n=78), kUA/L	*Z*	*P*
Der p	14.75 (8.43–42.99)	30.03 (11.61–52.75)	−0.911	0.363
Der f	29.74 (17.92–57.89)	59.95 (36.54–95.33)	−2.205	0.027*
Der p 1	51.60 (9.52–82.48)	55.34 (12.22–99.9)	−0.415	0.678
Der f 1	14.61 (9.05–26.38)	22.57 (10.01–47.66)	−1.380	0.168
Der p 2	11.47 (1.78–55.36)	18.27 (6.09–44.74)	−0.455	0.649
Der f 2	92.16 (36.83–100.00)	100 (88.28–100)	−2.250	0.024*
Der p 5	0.05 (0–0.98)	0.03 (0.00–4.65)	−0.010	0.992
Der p 7	0.11 (0.05–28.61)	0.08 (0.04–24.3)	−0.085	0.933
Der p 10	0.07 (0.01–0.12)	0.02 (0.00–0.06)	−2.279	0.023*
Der p 21	0.09 (0.04–3.03)	0.17 (0.02–11.87)	−0.404	0.686
Der p 23	8.21 (0.04–35.1)	10.11 (0.03–63.23)	−0.339	0.735

Note: *P < 0.05.
Abbreviations: HDM, house dust mites; AR, allergic rhinitis; ARAS, allergic rhinitis with asthma syndrome; Der p, Dermatophagoides pteronyssinus; Der f, Dermatophagoides farinae.

All subjects showed positive to a variety of HDM components, with 100% sensitized to ≥2 components. A higher proportion of ARAS subjects were sensitized to >5 hDM components compared to AR, though this was not statistically significant ($P > 0.05$). Median counts of sensitized HDM components were similar between groups: 6 (IQR: 4–7) in ARAS and 5.5 (IQR: 4–6.25) in AR ($Z = -0.173$, $P = 0.863$), as depicted in Figure 1.

Correlation Analysis of Serum sIgE Levels of HDM Components

The correlation analysis demonstrated a significant positive correlation between Der p and Der f sIgE levels (Figure 2). Specifically, the analysis revealed a strong positive correlation in the magnitude of sIgE responses to Der p and Der f, with a Spearman's rho (ρ) of 0.732 ($P < 0.01$) and a Pearson's correlation coefficient (r) of 0.834 ($P < 0.01$), indicating a highly consistent sensitization pattern to these allergens. Further examination of sIgE levels to HDM components illustrated that the primary (Der p 1, Der f 1) and secondary (Der p 2, Der f 2) allergen components exhibit strong positive correlations both among themselves and with the overall Der p and Der f responses ($P < 0.01$). Additionally, Der p 10 sIgE levels did not show significant correlation with the general responses to Der p, Der f, or other components ($P > 0.05$), except for a moderate correlation with Der p 2, Der p 7, and Der p 21 ($P < 0.05$), suggesting a more specific reactivity pattern for this component.

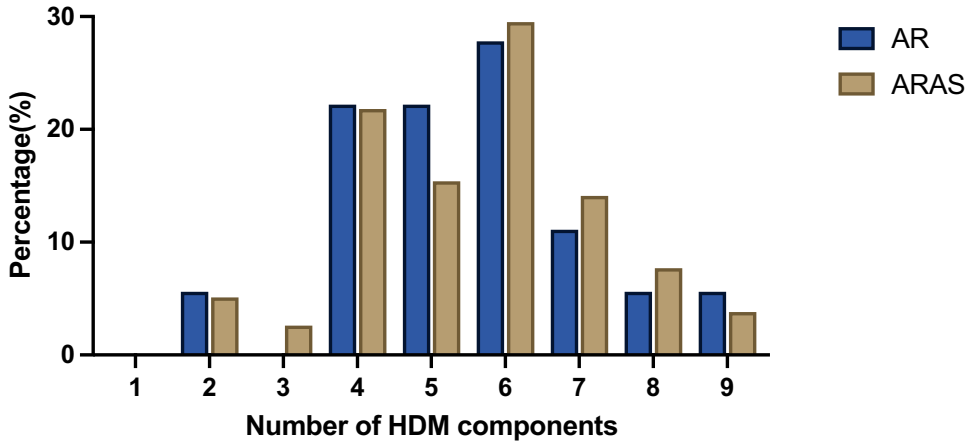

Figure 1 The numbers of sensitized components to HDM between AR and ARAS groups.

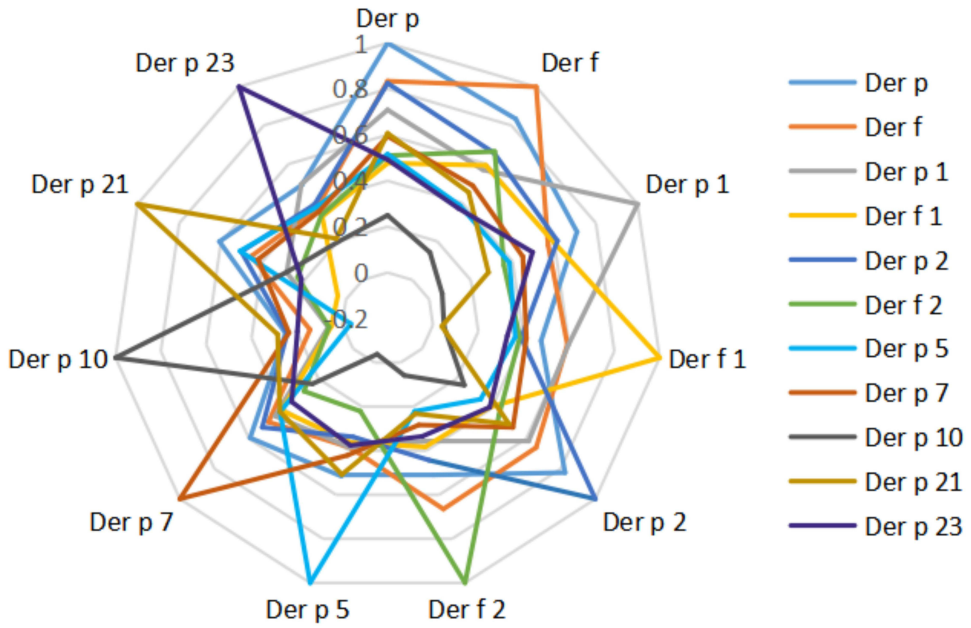

Figure 2 Correlation analysis of serum sIgE levels of HDM components.

Association Between HDM Components and AR Severity

Analysis revealed no significant difference in HDM sensitization prevalence between mild and moderate-severe AR groups ($P > 0.05$, Table 4). Prevalence for Der p and components (Der p 1, Der f 1, Der p 2, Der f 2, Der p 5, Der p 7, Der p 23) trended higher in moderate-severe AR compared to mild AR, while Der p 10 and Der p 21 showed lower prevalence in the former. Median sIgE levels for Der p, Der f, and select components (Der p 1, Der f 1, Der p 2, Der p 23) were higher in moderate-severe versus mild AR (31.86 vs 23.77, 60.40 vs 48.15, 65.23 vs 39.64, 22.54 vs 14.22, 20.23 vs 12.20, 16.88 vs 5.35 kUA/L, respectively), yet without significant differences ($P > 0.05$, Table 4). Der f 2 exhibited the highest median sIgE level at 100 kUA/L in both groups. Multiple sensitization analysis showed similar counts of sensitized proteins in both groups ($Z = -0.968$, $P = 0.333$).

Association Between HDM Components and Asthma Control

The study found significant differences in the prevalence of sensitization to Der p 7 and Der p 23 across three asthma control groups ($P < 0.05$), with lower sensitization prevalence correlating with better asthma control (Table 5). However,

Table 4 Prevalence and Serum sIgE Levels of HDM Components in Mild and Moderate-Severe AR Groups

HDM Components	Mild AR group (n=43)	Moderate-Severe AR group (n=53)	χ^2	P	Mild AR group (n=43), kUA/L	Moderate-Severe AR group (n=53), kUA/L	Z	P
Der p	97.7	98.1	–	1.000[a]	23.77(7.23–41.97)	31.86(14.20–58.05)	−1.757	0.079
Der f	100.0	100.0	–	–	48.15(24.78–80.73)	60.40(29.74–100.00)	−1.616	0.106
Der p 1	88.4	98.1	–	0.086[a]	39.64(8.41–96.73)	65.23(12.19–96.50)	−0.937	0.349
Der f 1	90.7	91.0	–	0.170[a]	14.22(7.53–40.88)	22.54(12.88–49.07)	−1.606	0.108
Der p 2	93.0	96.2	–	0.654[a]	12.20(3.30–36.63)	20.23(7.20–50.03)	−1.257	0.209
Der f 2	97.7	98.1	–	1.000[a]	100.00(72.04–100.00)	100.00(92.155–100.00)	−0.874	0.382
Der p 5	27.9	35.8	0.685	0.408	0.02(0.00–1.44)	0.06(0.00–6.65)	−1.316	0.188
Der p 7	25.6	39.6	2.106	0.147	0.07(0.03–0.57)	0.10(0.06–52.30)	−1.686	0.092
Der p 10	9.3	3.8	-	0.403[a]	0.02(0.00–0.07)	0.02(0.00–0.07)	−0.579	0.563
Der p 21	48.8	37.7	1.196	0.274	0.34(0.01–5.42)	0.08(0.03–18.775)	−0.535	0.592
Der p 23	53.5	60.4	0.460	0.497	5.35(0.03–57.61)	16.88(0.04–60.50)	−0.701	0.483

Note: [a]Fisher's exact test.
Abbreviations: HDM, house dust mites; AR, allergic rhinitis; ARAS, allergic rhinitis with asthma syndrome; Der p, Dermatophagoides pteronyssinus; Der f, Dermatophagoides farinae.

no significant differences were observed in the prevalence of other HDM components among the groups ($P > 0.05$). Specifically, sIgE levels for Der p 23 differed significantly ($P < 0.05$), being lower in the well-controlled asthma group compared to others. While sIgE levels for Der p, Der f, Der p 1, Der f 1, and Der p 2 also trended lower in association with better asthma control, these differences did not reach statistical significance ($P > 0.05$). Among the tested allergens, Der f 2 sIgE levels were the highest, maintaining a median of 100 kUA/L across all groups. Multiple sensitization analysis revealed that the number of sensitized proteins was significantly lower in children with well-controlled asthma compared to those in partially controlled or uncontrolled groups ($H = 6.864$, $P = 0.032$).

Discussion

HDM emerge as the foremost inhalant allergens precipitating respiratory allergic manifestations, predominantly AR and asthma.[20] Our study not only reaffirms the predominant sensitization towards Der p and Der f as the chief contributors to HDM allergy in China, echoing the findings of prior research,[21–23] but it also, for the initial occasion, elucidates the molecular sensitization profiles to these allergens within the pediatric Chinese cohort and examines their association with clinical outcomes.

Our study outlined the molecular sensitization to prevalent HDM allergens, revealing Der f 2 as the most common, followed by Der f 1 and Der p 2 at 94.8%, and then Der p 1 and Der p 23, all with over 50% sensitization. This aligns with the global recognition of these allergens as major.[24,25] Our findings closely align with a study from East China, demonstrating similar sensitization rates for Der p 1 (93.8%) and Der p 2 (94.8%),[26] which are higher than those reported in Central China (71.5%, 64.6%).[27] Der f 1 and Der f 2 sensitization in our cohort (94.8% and 97.9%) also exceeded Northern rates (66.7% and 64.3%).[28] Additionally, Der p 23 prevalence in our study was higher compared to the North[24] but lower than in the South and Central China,[27,29] reflecting HDM epidemiological trends with higher Der f than Der p prevalence, and greater in the South than the North. Compared to international studies[30,31] with Der p1 sensitization between 82.5%-90%, Der p 2 between 63.0%-90%, our study noted one of the highest sensitization levels to Der f and Der f 2, similar to a report of 100% Der f in Korean children,[32] underscoring significant geographical differences in HDM sensitization.

While sensitization rates to HDM components did not significantly differ between the AR and ARAS groups, sIgE levels for Der f and Der f 2 were notably higher in the ARAS group, contrasting with mixed findings from previous research. Wang et al[28] observed elevated sIgE levels for Der p 1, Der p 2, and Der p 23 in ARAS patients. Conversely, Zeng et al[29] found increased serum Der p and Der p 1 sIgE levels in individuals with either asthma or ARAS. Additionally, Resch et al[33] identified a higher sensitization rates and significantly raised serum levels of Der p 1, Der p 2, Der p 5, and Der p 23 in asthmatic children, pointing to a heightened risk of asthma development in those sensitized to Der p 2.

Table 5 Prevalence and Serum sIgE Levels of HDM Components in Asthma with Different Control Levels

HDM Components	Uncontrolled Asthma (n=28)	Partial-Controlled Asthma (n=21)	Well-Controlled Asthma (n=29)	χ^2	*P*	Uncontrolled Asthma (n=28), kUA/L	Partial-Controlled Asthma (n=21), kUA/L	Well-Controlled Asthma (n=29), kUA/L	Z	*P*
Der p	27 (96.4)	21 (100.0)	28 (96.6)	-	1.000[a]	35.37 (8.97–57.12)	29.42 (14.75–3.06)	27.29 (8.3–42.77)	2.074	0.355
Der f	28 (100.0)	21 (100.0)	29 (100.0)	-	-	67.28 (42.11–6.01)	60.14 (43.2–98.03)	48.15 (26.92–2.61)	2.383	0.304
Der p 1	25 (89.3)	21 (100.0)	26 (89.7)	-	0.273[a]	65.46 (13.06–100)	58.44 (22.38–100)	34.66 (5.41–88.8)	2.008	0.366
Der f 1	26 (92.9)	21 (100.0)	26 (89.7)	-	0.429[a]	37.10 (13.43–3.43)	22.54 (12.61–6.61)	13 (7.60–36.87)	4.247	0.120
Der p 2	27 (96.4)	21 (100.0)	26 (89.7)	-	0.444[a]	21.38 (5.5–47.78)	17.31 (7.82–65.33)	17.41 (4.46–28.76)	1.267	0.531
Der f 2	28 (100.0)	21 (100.0)	28 (96.6)	-	1.000[a]	100 (100–100)	100 (90.39–100)	100 (78.99–100)	1.274	0.529
Der p 5	10 (35.7)	8 (38.1)	8 (27.6)	0.717	0.699	0.04 (0.01–3.70)	0.02 (0–4.82)	0.02 (0–9.37)	1.149	0.563
Der p 7	14 (50.0)	7 (33.3)	5 (17.2)	6.879	0.032*	0.4 (0.04–65.45)	0.08 (0.05–52.38)	0.07 (0.03–0.15)	4.421	0.110
Der p 10	3 (10.7)	1 (4.8)	1 (3.4)	–	0.523[a]	0.03 (0–0.10)	0.01 (0–0.08)	0.01 (0–0.04)	3.160	0.206
Der p 21	14 (50.0)	11 (52.4)	10 (34.5)	2.042	0.360	0.58 (0.02–20.08)	0.4 (0.03–5.3)	0.05 (0–12.95)	2.138	0.343
Der p 23	18 (64.3)	15 (71.4)	11 (37.9)	6.660	0.036*	31.62 (0.05–86.76)	46.99 (0.17–80.02)	0.06 (0.03–34.90)	6.278	0.043*

Note: [a]Fisher's exact test, *P < 0.05.

Abbreviations: sIgE, specific IgE; HDM, house dust mites; AR, allergic rhinitis; ARAS, allergic rhinitis with asthma syndrome; Der p, Dermatophagoides pteronyssinus; Der f, Dermatophagoides farinae.

https://doi.org/10.2147/JAA.S480676 DovePress

The data indicate a possible link between sensitization to specific HDM components and the clinical manifestations of respiratory allergic diseases, highlighting that patients with comorbid allergic asthma tend to exhibit higher sIgE levels to these molecular components. Elevated sIgE levels to major HDM allergens in AR patients could signal a progression towards asthma, warranting preventive measures such as allergen immunotherapy (AIT). Conversely, Bronnert et al[31] reported no correlation between Der p 1/2 sensitization and allergic disease phenotypes, like AR and asthma, in terms of both prevalence and sIgE levels. A similar conclusion was drawn from a recent Portuguese study,[34] which found no significant differences in sIgE levels to HDM allergens between ARAS and AR groups, noting only geographic variations in Der p 2 sIgE levels (South > North, $P < 0.05$). This suggests that variations in serum sIgE levels to HDM components might be more closely associated with geographic factors.

Research on the prevalence of IgE recognition and component sIgE levels indicates that HDM components are not only relevant to the allergic phenotype but also correlate with higher sIgE levels and the severity of allergic respiratory diseases.[35] Although sIgE levels to Der p and Der f components were generally higher in children with moderate-to-severe rhinitis than in those with mild rhinitis, this trend did not reach statistical significance, aligning with findings from a Portuguese study that suggested a weak correlation between the severity of AR and HDM allergens.[34]

Significantly, the prevalence of sensitization to Der p 7 and Der p 23 was notably different in relation to asthma control status. Children with well-controlled asthma had lower sIgE levels to major HDM components compared to those in the partially controlled and uncontrolled groups, with a marked difference observed for Der p 23 sIgE levels. Supporting this, Jiménez-Feijoo et al[36] discovered that patients with persistent moderate-to-severe asthma had higher prevalence of sensitization to Der p 23 compared to those with intermittent and mild persistent asthma (90% vs 75.8%, $P = 0.008$), suggesting a link between Der p 23 and moderate-to-severe asthma phenotypes in HDM-sensitized children. Furthermore, our findings revealed a significantly lower sensitization rate to Der p 23 in the well-controlled asthma group (37.9%) compared to the uncontrolled (64.3%) and partially controlled (71.4%) groups ($P < 0.05$). Thus, including Der p 23 testing in the diagnosis and management of HDM-sensitized asthma, particularly for patients with moderate-to-severe symptoms, could be crucial for identifying and addressing a potentially worsening clinical phenotype of asthma.

Our study faced several limitations that warrant consideration. Firstly, the relatively small sample size of the AR group with heavily male biased (15/18), comprising only 18 cases, could potentially influence the statistical analysis outcomes between the groups. Secondly, the cross-sectional design of our investigation limits our capacity to establish causal relationships between the phenotypes of allergic diseases and sensitization to HDM components. Lastly, the assessment of asthma control was conducted using the ACT or C-ACT questionnaire, focusing solely on the control status over the preceding month. This approach did not comprehensively account for the duration of asthma or rhinitis nor the medication regimens of the children, which might have impacted our ability to accurately gauge disease severity.

In conclusion, our research underscores the significance of molecular components in mite allergy, highlighting the critical role of major allergens in children with respiratory allergies to mites. Notably, we point out the clinical relevance of Der p 23, an allergen that is predominantly found in children experiencing a recent deterioration in asthma control. This finding emphasizes the importance of mite molecular components including Der p 23 in the diagnostic and management strategies for mite-related respiratory allergies, particularly in the context of assessing and improving asthma control.

Abbreviations

AA, Allergic Asthma; ACT, Asthma Control Test; AR, Allergic Rhinitis; ARAS, Allergic Rhinitis with Asthma Syndrome; C-ACT, Childhood Asthma Control Test; CRD, Component-Resolved Diagnosis; Der f, Dermatophagoides farinae; Der p, Dermatophagoides pteronyssinus; HDM, house dust mites.

An Author's Summary

By comparing the molecular profiles of HDM in children with AR and those with ARAS, they found the sIgE levels to HDM allergens were higher in ARAS group compared to AR group, especially Der f and Der f 2, indicating an association between sIgE reactivity and the diagnosis of asthma. Reduced Der p 23 sIgE levels were indicative of enhanced asthma control. So far, there are few studies focusing on the relationship between allergenic components of

HDM and clinical manifestation. This study provides meaningful message of the variations of allergic sensitization and their correlation with respiratory allergies and asthma control.

Acknowledgments

The authors are grateful of the technical support and assistance from professor Yongming Tang and his team. Thanks to the doctors and nurses of desensitization clinic in the hospital for their help in data collection.

Author Contributions

Jing He and Nan Lin have contributed equally to this work and share first authorship. Hongzhen Xu and Zhimin Chen are corresponding authors.

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This work was supported by the grant from Key R & D Program of Zhejiang Province (No.2024C03177).

Disclosure

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

References

1. Bousquet J, Anto JM, Bachert C, et al. Allergic rhinitis. *Nat Rev Dis Primers*. 2020;6(1):95. doi:10.1038/s41572-020-00227-0
2. Meng Y, Wang C, Zhang L. Advances and novel developments in allergic rhinitis. *Allergy*. 2020;75(12):3069–3076. doi:10.1111/all.14586
3. Zhang Y, Zhang L. Increasing Prevalence of Allergic Rhinitis in China. *Allergy Asthma Immunol Res*. 2019;11(2):156–169. doi:10.4168/aair.2019.11.2.156
4. Brozek JL, Bousquet J, Agache I, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines-2016 revision. *J Allergy Clin Immunol*. 2017;140(4):950–958. doi:10.1016/j.jaci.2017.03.050
5. Sood S, Castro M. Asthma in 2016: reassured about the old, excited about the new[J]. *Lancet Respir Med*. 2016;4(12):937–939. doi:10.1016/S2213-2600(16)30380-0
6. J MM, P YK, Zhou X, et al. Patterns of growth and decline in lung function in persistent childhood asthma. *N Engl J Med*. 2016;374(19):1842–1852. doi:10.1056/NEJMoa1513737
7. Keglowich L, Tamm M, Zhong J, et al. Proteolytic activity present in house-dust-mite extracts degrades ENA-78/CXCL5 and reduces neutrophil migration. *J Allergy*. 2014;2014(673673). doi:10.1155/2014/673673
8. Calderon MA, Linneberg A, Kleine-Tebbe J, et al. Respiratory allergy caused by house dust mites: what do we really know? *J Allergy Clin Immunol*. 2015;136(1):38–48. doi:10.1016/j.jaci.2014.10.012
9. Lou H, Ma S, Zhao Y, et al. Sensitization patterns and minimum screening panels for aeroallergens in self-reported allergic rhinitis in China[J]. *Sci Rep*. 2017;7(1):9286. doi:10.1038/s41598-017-10111-9
10. Thomas WR, Smith WA, Hales BJ, et al. Characterization and immunobiology of house dust mite allergens[J]. *Int Arch Allergy Immunol*. 2002;129(1):1–18. doi:10.1159/000065179
11. Thomas WR. Hierarchy and molecular properties of house dust mite allergens. *Allergol Int*. 2015;64(4):304–311. doi:10.1016/j.alit.2015.05.004
12. Choopong J, Reamtong O, Sookrung N, et al. Proteome, allergenome, and novel allergens of house dust mite, Dermatophagoides *farinae*. *J Proteome Res*. 2016;15(2):422–430. doi:10.1021/acs.jproteome.5b00663
13. Cao H, Liu Z. Clinical significance of dust mite allergens. *Mol Biol Rep*. 2020;47(8):6239–6246. doi:10.1007/s11033-020-05613-1
14. Sanchez-Borges M, Fernandez-Caldas E, Thomas WR, et al. International consensus (ICON) on: clinical consequences of mite hypersensitivity, a global problem. *World Allergy Organ J*. 2017;10(1):14. doi:10.1186/s40413-017-0145-4
15. Park SC, Hwang CS, Chung HJ, et al. Geographic and demographic variations of inhalant allergen sensitization in Koreans and non-Koreans. *Allergol Int*. 2019;68(1):68–76. doi:10.1016/j.alit.2018.07.005
16. Todkill D, Loveridge P, Elliot AJ, et al. Socioeconomic and geographical variation in general practitioner consultations for allergic rhinitis in England, 2003-2014: an observational study. *BMJ Open*. 2017;7(8):e017038. doi:10.1136/bmjopen-2017-017038
17. Reddel HK, Bacharier LB, Bateman ED, et al. Global Initiative for Asthma Strategy 2021: executive summary and rationale for key changes. *Eur Respir J*. 2022;59(1). doi:10.1183/13993003.02730-2021
18. Nathan RA, Sorkness CA, Kosinski M, et al. Development of the asthma control test: a survey for assessing asthma control. *J Allergy Clin Immunol*. 2004;113(1):59–65. doi:10.1016/j.jaci.2003.09.008
19. Liu AH, Zeiger R, Sorkness C, et al. Development and cross-sectional validation of the childhood asthma control test. *J Allergy Clin Immunol*. 2007;119(4):817–825. doi:10.1016/j.jaci.2006.12.662

20. Li J, Sun B, Huang Y, et al. A multicentre study assessing the prevalence of sensitizations in patients with asthma and/or rhinitis in China. *Allergy*. 2009;64(7):1083–1092. doi:10.1111/j.1398-9995.2009.01967.x
21. Gan H, Luo W, Huang Z, et al. House dust mite components sensitization profile in China, a multi-centre study. *Clin Exp Allergy*. 2023;53 (2):226–229. doi:10.1111/cea.14255
22. Zhang C, Li J, Lai X, et al. House dust mite and storage mite IgE reactivity in allergic patients from Guangzhou, China. *Asian Pac J Allergy Immunol*. 2012;30(4):294–300.
23. Yu JM, Luo QH, Sun JL, et al. Diversity of house dust mite species in xishuangbanna dai, a tropical rainforest region in southwest China. *Biomed Res Int*. 2015;2015:421716. doi:10.1155/2015/421716
24. Huang HJ, Sarzsinszky E, Vrtala S. House dust mite allergy: the importance of house dust mite allergens for diagnosis and immunotherapy. *Mol Immunol*. 2023;158:54–67. doi:10.1016/j.molimm.2023.04.008
25. Huang J, Xiang R, Tan L, et al. Dust mite component Analysis: identifying key allergens components for effective immunotherapy in allergic rhinitis. *Int Immunopharmacol*. 2023;125(Pt A):111111. doi:10.1016/j.intimp.2023.111111
26. Wang HY, Gao ZS, Zhou X, et al. Evaluation of the Role of IgE Responses to Der p 1 and der p 2 in Chinese house dust mite-allergic patients. *Int Arch Allergy Immunol*. 2015;167(3):203–210. doi:10.1159/000438724
27. Yang Y, Zhu R, Huang N, et al. The Dermatophagoides pteronyssinus Molecular Sensitization Profile of Allergic Rhinitis Patients in Central China. *Am J Rhinol Allergy*. 2018;32(5):397–403. doi:10.1177/1945892418787116
28. Wang X, Pu X, Chen L, et al. [Profiles of IgE sensitization to dust mite allergen components in patients with allergic rhinitis and asthma]. *Lin Chuang Er Bi Yan Hou Tou Jing Wai Ke Za Zhi = Journal of Clinical Otorhinolaryngology, Head, and Neck Surgery*. 2022;36(8):576–581. doi:10.13201/j.issn.2096-7993.2022.08.002
29. Zeng G, Luo W, Zheng P, et al. Component-resolved diagnostic study of Dermatophagoides pteronyssinus major allergen molecules in a southern Chinese cohort. *J Investig Allergol Clin Immunol*. 2015;25(5):343–351.
30. Pittner G, Vrtala S, Thomas WR, et al. Component-resolved diagnosis of house-dust mite allergy with purified natural and recombinant mite allergens. *Clin Exp Allergy*. 2004;34(4):597–603. doi:10.1111/j.1365-2222.2004.1930.x
31. Bronnert M, Mancini J, Birnbaum J, et al. Component-resolved diagnosis with commercially available D. pteronyssinus Der p 1, Der p 2 and Der p 10: relevant markers for house dust mite allergy. *Clin Exp Allergy*. 2012;42(9):1406–15). doi:10.1111/j.1365-2222.2012.04035.x
32. Kim HS, Kang SH, Won S, et al. Immunoglobulin E to allergen components of house dust mite in Korean children with allergic disease. *Asia Pac Allergy*. 2015;5(3):156–162. doi:10.5415/apallergy.2015.5.3.156
33. Resch Y, Michel S, Kabesch M, et al. Different IgE recognition of mite allergen components in asthmatic and nonasthmatic children. *J Allergy Clin Immunol*. 2015;136(4):1083–1091. doi:10.1016/j.jaci.2015.03.024
34. Limao R, Spinola Santos A, Araujo L, et al. Molecular Profile of Sensitization to Dermatophagoides pteronyssinus Dust Mite in Portugal. *J Investig Allergol Clin Immunol*. 2021;32(1):33–39. doi:10.18176/jiaci.0533
35. Ballmer-Weber BK, Lidholm J, Lange L, et al. Allergen recognition patterns in walnut allergy are age dependent and correlate with the severity of allergic reactions. *J Allergy Clin Immunol Pract*. 2019;7(5):1560–1567e6. doi:10.1016/j.jaip.2019.01.029
36. Jimenez-Feijoo R, Pascal M, Moya R, et al. Molecular diagnosis in house dust mite-allergic patients suggests that der p 23 is clinically relevant in asthmatic children. *J Investig Allergol Clin Immunol*. 2020;30(2):127–132. doi:10.18176/jiaci.0431