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High house dust mite serum-specific immunoglobulin E indicates a high 5-year rhinitis-asthma conversion rate: a cross-sectional study

Rui Tang[1], Xiaohong Lyu[2], Yuelun Zhang[3], Shi Chen[4], Hong Li[1]

[1]Department of Allergy, Peking Union Medical College Hospital (PUMCH), Chinese Academy of Medical Sciences (CAMS) and Peking Union Medical College (PUMC), Key Laboratory of Precision Medicine for Diagnosis and Treatment on Allergic Diseases, National Clinical Research Center for Immunologic Diseases, Beijing 100730, China;
[2]Eight-Year Program of Clinical Medicine, Peking Union Medical College Hospital (PUMCH), Chinese Academy of Medical Sciences (CAMS) and Peking Union Medical College (PUMC), Beijing 100730, China;
[3]Central Research Laboratory, Peking Union Medical College Hospital (PUMCH), Chinese Academy of Medical Sciences (CAMS) and Peking Union Medical College (PUMC), Beijing 100730, China;
[4]Department of Endocrinology, Key Laboratory of Endocrinology of National Health Commission, Peking Union Medical College Hospital (PUMCH), Chinese Academy of Medical Sciences (CAMS) and Peking Union Medical College (PUMC), Beijing 100730, China.

Allergic rhinitis (AR) is a costly and highly prevalent chronic disease now.[1] More seriously, many patients with AR also have allergic asthma (AA). The presence of AR is a risk factor for the development of AA.[2] Moreover, AA is still a significant cause of mortality for all ages.[3] Therefore, predicting and preventing AA can reduce accidental death, severe health hazards, and the society's enormous economic burden.

House dust mite allergy is an unsurpassed cause of atopic sensitization and allergic illness worldwide, including AR and AA. Li *et al*[4] found that house dust mites were the most prevalent allergens in AA and/or AR patients in China. The purpose of this study was to investigate the association of house dust mite serum-specific immunoglobulin E (sIgE) levels with the onset of asthma in AR patients.

The Institutional Review Board of Peking Union Medical College Hospital approved the study. Written informed consent was obtained from each patient and the parents of all participating children.

This was a cross-sectional study of 393 patients with allergies. The participants were children and adults (6–76 years old) from North China and had AR with/without AA. Senior allergists took a thorough medical history. All participants underwent intradermal skin tests (IDT) to inhaled allergens and house dust mite sIgE tests. Allergists made AR and/or AA's diagnosis based on characteristic symptoms, clinical history, physical, and accessory examination findings. The individuals involved in the analysis met the following criteria: all suffered from AR; having recurrent nasal itching, sneezing, rhinorrhea, and hyperemia; having definite living environment (basement, bungalow, or apartment); clearly diagnosed as AA or not; all sIgE tests of house dust mites were conducted; all kinds of inhaled allergens are tested for the skin.

sIgE was measured using ImmunoCAP (Phadia1000, Thermofisher Scientific, Uppsala, Sweden). sIgE with a value of 0.35 kU/L or more (0.35–100 kU/L) was considered sIgE-positive. sIgE was divided into six degrees: level 1, values ≥0.35 and <0.7 kU/L; level 2, values ≥0.7 and <3.5 kU/L; level 3, values ≥3.5 and <17.5 kU/L; level 4, values ≥17.5 and <50 kU/L; level 5, values ≥50 and <100 kU/L; and level 6, values ≥100 kU/L. IDT was performed with commercial allergen extracts (Xinhualian®, Beijing, China) according to a standard protocol.

The baseline data of the two groups (AR with asthma group and AR alone group) were compared by Chi-squared test or Student's *t* test. Univariate analysis was performed to estimate the crude odds ratio (ORs), and a significance value of 0.05 was used to generate a 95% confidence interval (95% CI). Multivariate logistic regression analysis of four models (factors incorporated in model 1: sIgE; model 2: sIgE, age at visiting clinics, and gender; model 3: sIgE, age at visiting clinics, gender, food

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Rui Tang and Xiaohong Lyu contributed equally to the work.

Correspondence to: Dr. Hong Li, Department of Allergy, Peking Union Medical College Hospital (PUMCH), Chinese Academy of Medical Sciences (CAMS) and Peking Union Medical College (PUMC), Beijing 100730, China
E-Mail: lihong1228sec@163.com

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allergy and living environment; model 4: sIgE, age at visiting clinics, gender, food allergy, living environment, drug allergy, AR duration, family allergy history, and having pets in the family) was used to analyze the adjusted OR of different parameters and to analyze whether other allergens were the confounding factors in this study. The correlation between clinical parameters and sIgE was analyzed by the Pearson correlation test. The Kaplan–Meier survival function model was used to estimate the cumulative rhinitis-asthma conversion rate (RACR) which was defined as the incidence of asthma after the patients suffer from allergic rhinitis. The analysis was performed using SPSS version 25 for MAC (SPSS Inc., Chicago, IL, USA).

Based on the AA status of 321 participants, 213 (66.4%) had AR and AA, and 108 (33.6%) had AR alone. For the asthmatic group and non-asthmatic group, the percentage of levels 5 and 6 of sIgE to house dust mite was 21.6% (46/213) *vs*. 9.3% (10/108) ($\chi^2 = 8.051$, $P < 0.01$), and the crude OR was 3.163 (95% CI: 1.400–7.144); the percentage of AR duration >15 years was 14.6% (31/213) *vs*. 6.5% (7/108) ($\chi^2 = 7.928$, $P < 0.01$), and the crude OR was 3.452 (95% CI: 1.410–8.450); the percentage of bungalows as their living environment was 30.0% (63/210) *vs*. 14.2% (15/106) ($\chi^2 = 9.518$, $P < 0.01$), and the crude OR was 2.600 (95% CI: 1.398–4.837).

In all the four models, which included different parameters, house dust mite sIgE was significantly associated with AA's onset in AR patients. In model 1, only house dust mite sIgE was involved (adjusted OR = 1.390, 95% CI: 1.108–1.744, $P = 0.004$). Based on sIgE, age at visiting clinics and gender were added in model 2 (sIgE, adjusted OR = 1.466, 95% CI: 1.160–1.852, $P = 0.001$). Based on model 2, food allergy and living environment, whose P values with sIgE were <0.05 in the Pearson correlation test, were added in model 3 (sIgE, adjusted OR = 1.425, 95% CI: 1.119–1.815, $P = 0.004$). Based on model 3, new parameters considered by clinical allergists, including drug allergy, AR duration, family allergy history, and having pets in the family were added into model 4 (sIgE, adjusted OR = 1.427, 95% CI: 1.109–1.838, $P = 0.006$). Besides, living environment, drug allergy, and AR duration were also risk factors for AA attacks in model 4 (all $P < 0.05$).

The Kaplan–Meier model was applied to analyze the relationship between AA's onset and the house dust mite sIgE levels of AR patients [Figure 1]. In the first 10 years, the higher the house dust mite sIgE level, the earlier the AA's onset for AR patients ($P = 0.006$). Because of the influence of AR duration and sample size of long duration with AR, cumulative RACR curve crosses appeared after 10 years. The RACR of 0 to 5 years showed that RACR rose along with house dust mite sIgE level every year. For house dust mite sIgE levels 5 and 6, 5-year RACR had reached 70%.

Logistic regression analysis excluded the possibility of other allergens as confounding factors or interaction factors.

Allergy to house dust mite is a high-risk factor for AR and AA. Our study further proposed that high house dust mite sIgE level indicated AA's onset in AR patients earlier.

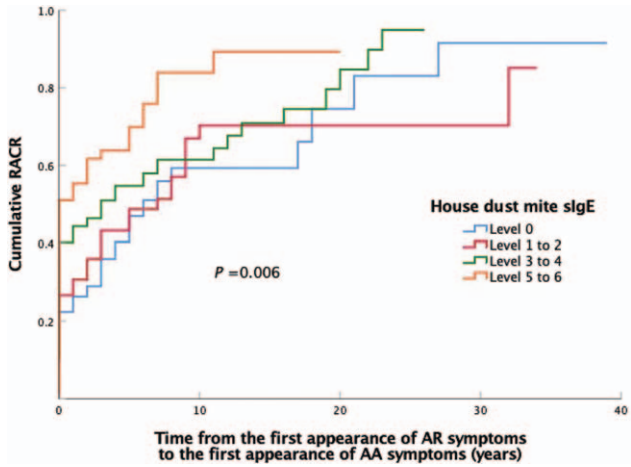

Figure 1: Kaplan-Meier survival analysis of house dust mite sIgE levels and cumulative RACR. AA: Allergic asthma; AR: Allergic rhinitis; RACR: Rhinitis-asthma conversion rate; sIgE: Serum-specific immunoglobulin E.

Moreover, the higher the house dust mite sIgE level, the higher the cumulative incidence of AR patients converted to AA within 5 years.

A possible explanation of high sIgE as an indicator is the systemic propagation of inflammation from the nasal to the bronchial mucosa.[5] As the duration of AR increases, the cumulative damage to the upper and lower respiratory tract might be a high-risk factor for inducing AA.[6] It was broadly proved that immunoglobulin E (IgE) was associated with allergic inflammation.[7] Some drugs were already targeting IgE for AA in the research and development stage.[8] More studies are still needed to clarify the possible mechanism.

High house dust mite sIgE value may become a biomarker for allergists to assess the possibility of AA onset for AR patients. This assessment and intervention should be performed at the early stage of AR. Detecting house dust mite sIgE level does not bring the extra cost to the patient, nor bring redundancy to the doctor's diagnostic steps.

To conclude, our study proved that high-level house dust mite sIgE indicates high 5-year RACR, which means a high risk for AR patients suffering from AA. It provides a theoretical basis for early intervention in AR patients with high sIgE levels to prevent AA. Furthermore, the AA prediction is independent of other allergens. The study also strengthened the relationship between AR and AA, which might be explained by subsequent allergen exposure and systemic propagation.

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Conflicts of interest

None.

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