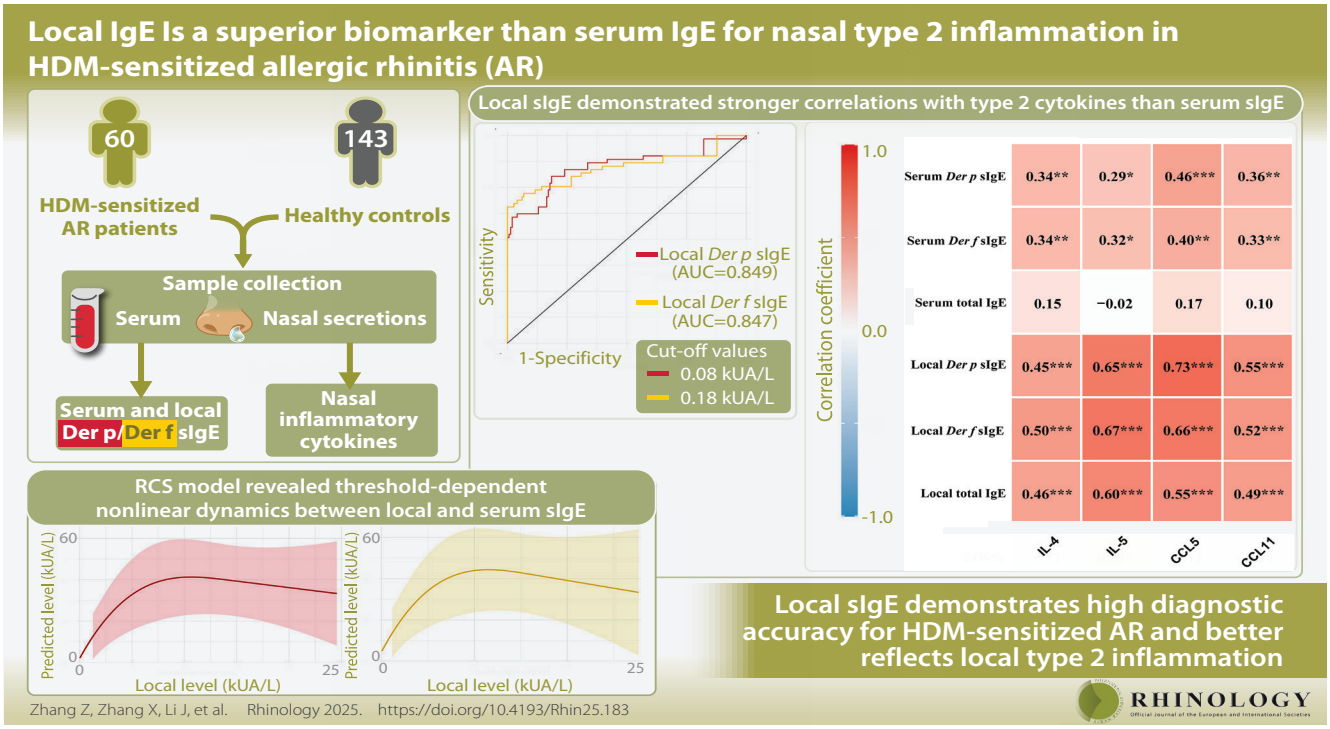
Local IgE is a superior biomarker than serum IgE for nasal type 2 inflammation in house dust mites sensitized allergic rhinitis

Zengxiao Zhang[1,2,3,4], Xu Zhang[1,2,4], Jingyun Li[2,4], Yu Song[1,2,4], Lin Xi[1,2,4], Chengshuo Wang[1,2,3,4], Luo Zhang[1,2,3,4], Yuan Zhang[1,2,3,4]

Rhinology 64: 1, 0 - 0, 2026

https://doi.org/10.4193/Rhin25.381



Abstract

Background: Allergic rhinitis (AR), an immunoglobulin E (IgE)-mediated inflammatory disease, is frequently associated with house dust mites (HDMs), particularly *Dermatophagoides pteronyssinus* (*Der p*) and *Dermatophagoides farinae* (*Der f*). While serum allergen-specific IgE (sIgE) is widely used, the diagnostic value of local sIgE and its interplay with systemic IgE and nasal cytokines remains unclear. This study evaluated local sIgE performance, nasal cytokine profiles, and nonlinear local-serum sIgE dynamics for AR patients. **Methodology**: This prospective study enrolled 60 HDM-sensitized AR patients and 143 healthy controls from February 2023 to September 2024. Serum and local *Der p*/*Der f* sIgE and total IgE were quantified; and nasal cytokines were analyzed by Luminex. Logistic regression, ROC analysis, and Spearman correlation assessed diagnostic performance and associations. Restricted cubic spline (RCS) modeling explored nonlinear local-serum sIgE relationships. **Results**: AR patients exhibited elevated local *Der p* and *Der f* sIgE logistic regression confirmed their associations with AR, supported by strong diagnostic accuracy. Local sIgE demonstrated stronger correlations with type 2 cytokines (IL-4, IL-5, CCL5, CCL11) than serum sIgE. RCS analysis identified inflection points for *Der p* and *Der f*, revealing threshold-dependent nonlinear dynamics between local and serum sIgE. **Conclusions**: Local sIgE demonstrates high diagnostic accuracy for HDM-sensitized AR and better reflects local Th2-driven inflammation. The nonlinear local-serum sIgE relationship advocates dual-compartment profiling, advancing precision diagnostics in AR.

Key words: allergic rhinitis, house dust mite, local specific immunoglobulin E, nasal immunopathology, nonlinear biomarker dynamics

Introduction

Allergic rhinitis (AR), a chronic inflammatory disease of the nasal mucosa driven by immunoglobulin E (IgE)-mediated hypersensitivity, affects 10–50% of the global population, with rising prevalence and substantial socioeconomic burdens due to its impact on quality of life, productivity, and healthcare costs [1-4].

Allergen testing, particularly serum allergen-specific immunoglobulin E (sIgE), serves as the cornerstone of AR diagnosis, enabling differentiation of AR from other rhinitis subtypes [5, 6]. Recent studies have demonstrated that allergen-sIgE can be detected in the nasal secretions of patients with AR, underscoring the potential of local molecular allergen diagnostics for precise diagnosis and treatment guidance [7-12]. However, its diagnostic value and relationship with systemic IgE levels remain insufficiently explored.

House dust mites (HDMs), particularly *Dermatophagoides pteronyssinus* (*Der p*) and *Dermatophagoides farinae* (*Der f*), are the most common allergens triggering AR [13, 14]. They stimulate IgE production and disrupt the balance between type 2 and type 1 inflammatory responses, leading to persistent type I hypersensitivity reactions in the nasal mucosa [15-17]. While serum sIgE is widely used to diagnose HDM-sensitized AR, the role of local sIgE in diagnosis is unclear. Additionally, the relationship between local IgE, nasal inflammatory cytokines, and systemic IgE levels has not been fully explored. Addressing these gaps could enhance diagnostic precision and inform targeted therapies.

Therefore, we conducted this study to evaluate the diagnostic performance of local sIgE for HDM-sensitized AR, characterize nasal cytokine profiles and their associations with IgE metrics, and explore the nonlinear dynamics between local and serum sIgE. By integrating clinical, immunological, and advanced statistical analyses, this study aimed to provide novel insights into the mucosal immunopathology of AR, with implications for biomarker discovery and therapeutic optimization.

Materials and methods

Study design and endpoints

This prospective, single-center study was approved by the Ethics Committee of Beijing Tongren Hospital, Capital Medical University (ID: TREC2023-KY046) and conducted in accordance with the STROBE guidelines.

The study was designed with a hierarchical structure of endpoints. The primary endpoint was to evaluate the diagnostic performance of local *Der p* and *Der f* sIgE for HDM-sensitized AR, including the determination of optimal cut-off values. Upon establishing its diagnostic utility, two layered secondary endpoints were investigated to provide a comprehensive characterization of local sIgE as a biomarker: 1) to compare the correlation strength of local sIgE versus serum sIgE with nasal inflammatory cytokines, thereby assessing its superiority in reflecting local inflammation; and 2) to characterize the dose-response dynamics between local and serum sIgE, in order to better understand the complex interplay between the mucosal and systemic compartments.

Study participants

Participants were recruited between February 2023 and September 2024, including patients with HDM-sensitized AR and healthy controls.

The inclusion criteria were as follows: 1) Age between 14 and 70 years; 2) A clinical diagnosis of HDM-sensitized AR, confirmed by a clinician according to criteria of ARIA guidelines [18], with typical AR symptoms and signs, and a positive serological allergy test (serum *Der p* sIgE and/or *Der f* sIgE > 0.35 kUA/L); 3) Healthy controls with no nasal symptoms or signs, no history of allergic diseases, negative serological allergy test (all allergen-sIgE < 0.35 kUA/L), and total IgE < 60 kUA/L; 4) Written informed consent provided and voluntary participation in the study.

The exclusion criteria were as follows: 1) Coexisting other sinonasal diseases such as chronic rhinosinusitis; fungal sinusitis, cystic fibrosis, primary ciliary dyskinesia, or sinonasal tumors; 2) Severe nasal septal deviation; 3) Treatment with medications that could interfere with immune or nasal mucosal status, including systemic corticosteroids within the past 3 months, intranasal corticosteroids within the past 4 weeks, antihistamines within the past 2 weeks, or topical nasal decongestants within the past 1 week. 4) Treatment with monoclonal antibodies within the past six months; 5) Participation in another clinical trial within the past six months; 6) History of nasal surgery; 7) Pregnancy or breastfeeding; 8) Diagnosed autoimmune disorders; 9) History of malignancy.

Sample collection

Peripheral venous blood was drawn from each participant using standard aseptic techniques. The blood samples were allowed to clot at room temperature for 30 minutes and then centrifuged at 3,000 rpm for 15 minutes. The supernatant serum was carefully separated, and stored at −80°C until further testing.

Nasal secretions were collected using the cotton piece method, as previously described [19]. Briefly, a sterile cotton piece (Purnote, Jiangsu, China; dimensions: 3 × 0.8 × 0.1 cm) were gently placed in the middle nasal meatus of each nasal cavity and left in place for 5 minutes. After removal, the cotton piece was placed on a flat slotted tray and dried in a 25°C oven for 2 hours. The cotton piece was then immersed in 150 µL of 0.9% saline within a 0.5 mL Eppendorf tube and incubated at room temperature for 10 minutes. A small hole was made at the bottom of the 0.5 mL tube, which was placed into a 1.5 mL Eppendorf tube and centrifuged at 12,000 rpm for 5 minutes. The nasal secretions were collected and stored at −80°C until further analysis.

Laboratory assays

Total IgE (tIgE) (Cat. No. R00112) and the sIgE levels of *Der p* (Cat. No. R00312), and *Der f* (Cat. No. R00912), in serum and nasal secretions were quantified using the ALLEOS 2000 system (HYCOR Biomedical) according to the manufacturer's protocol. The ALLEOS 2000 software generated a calibration curve from known standards, enabling calculation of tIgE and sIgE concentrations. Inflammatory cytokines IL-4, IL-5, CCL5, CCL11, IFN-γ, CXCL9, GM-CSF, and IL-17A in nasal secretions were measured using the Luminex Discovery Assay Human Premixed Multi-Analyte Kit (LXSAHM, R&D Systems) following the manufacturer's protocol. Briefly, 50 µL of each sample was added to a magnetic 96-well plate with 50 µL of diluted antibody-coated beads and incubated at room temperature for 2 hours on a shaker. After three washes, 50 µL of biotinylated detection antibodies was added and incubated for 1 hour, followed by three washes and addition of 50 µL Streptavidin-PE for 30 minutes. Following a final set of three washes, beads were resuspended in 100 µL buffer, and data were acquired using a Bio-Rad Bio-Plex 200 analyzer within 90 minutes. Cytokine concentrations were calculated against the kit's standards using a five-parameter logistic curve fit.

Statistical analyses

Normality tests were performed for quantitative data. Normally distributed data were demonstrated using mean ± standard deviation (± SD), and comparisons between groups were performed using the Student's t-test. Non-normally distributed data were presented as median ± interquartile range (M±QR), and compared using the Mann–Whitney U test. Frequencies and proportions were used to summarize qualitative data; the χ^2 test was used for comparisons between groups. Logistic regression was applied to assess the association between local sIgE and the diagnosis of AR, with odds ratios (ORs) and 95% confidence intervals (CIs) reported. The diagnostic performance of local sIgE was evaluated by receiver operating characteristic (ROC) curve analysis. Spearman's rank correlation analysis was used to assess the relationship between local and serum IgE levels and inflammatory cytokines in nasal secretions.

Restricted cubic spline (RCS) modeling was used to explore the nonlinear relationship between local and serum sIgE. The optimal number of knots was determined based on the lowest Akaike information criterion (AIC). Model assumptions were assessed using the Shapiro–Wilk test for normality and the Breusch–Pagan test for homoscedasticity. Nonlinearity was tested by comparing the RCS model with a linear model via ANOVA. Predicted values and 95% confidence intervals were plotted across the range of local sIgE, with knot positions indicated. First-order derivatives of the fitted curve were used to identify critical inflection points, such as slope change and zero-slope positions.

All statistical analyses were performed using Statistical Package for the Social Sciences version 27.0 (IBM Corp., Armonk, NY, USA) and R version 4.3.3 (R Foundation for Statistical Computing, Vienna, Austria). All tests were two-sided, and $P < 0.05$ was considered statistically significant.

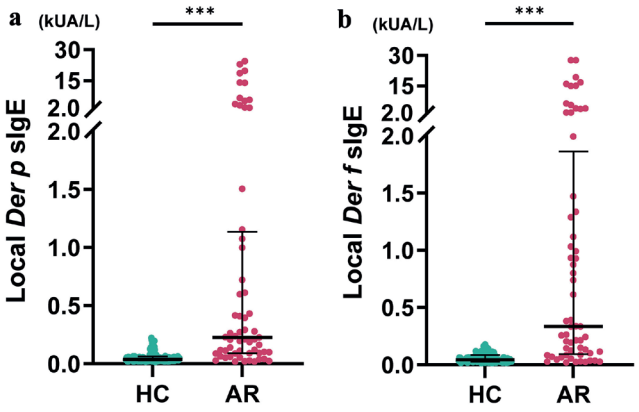


Figure 1. Distribution of local allergen-specific IgE levels in HDM-sensitized AR patients and healthy controls. A) Der p sIgE levels in local nasal secretions. B) Der f sIgE levels in local nasal secretions. AR, allergic rhinitis; Der f, Dermatophagoides farina; Der p, Dermatophagoides pteronyssinus; HC, healthy controls; HDM, house dust mite; sIgE, specific immunoglobulin E. *** $P < 0.001$.

Results

Baseline features and distribution of local and serum IgE

A total of 203 participants were included in this study, comprising 60 patients with HDM-sensitized AR and 143 healthy controls. Demographic and IgE-related characteristics of both groups are summarized in Table S1. The mean age of AR patients was 34.00 ± 14.00 years, with 35 males (58.33%) and 25 (41.67%) females. The healthy control group had a mean age of 48.00 ± 27.00 years, including 47 males (32.87%) and 96 females (67.13%). Compared to healthy controls, patients with HDM-sensitized AR showed significantly higher levels of serum *Der p*-sIgE, serum *Der f*-sIgE, serum tIgE, local *Der p*-sIgE, local *Der f*-sIgE, and local tIgE. The distributions of local sIgE levels of *Der p* and *Der f* in both groups are illustrated in Figure 1.

Diagnostic value of local sIgE for AR

Logistic regression analyses were performed to assess the association between local sIgE levels and the diagnosis of AR. As shown in Table 1, higher concentrations of local *Der p* sIgE and *Der f* sIgE were significantly associated with increased odds of AR (*Der p*, OR=1.016, 95% CI: 1.010–1.022, P<0.001; *Der f*, OR=1.017, 95% CI: 1.010–1.024, P<0.001). This association remained robust after adjusting for age and gender (Model 2: *Der p*, OR=1.014, 95% CI: 1.009–1.020, P<0.001; *Der f*, OR=1.016, 95% CI: 1.009–1.023, P<0.001) and further adjusting for asthma and atopic dermatitis (Model 3: *Der p*, OR=1.014, 95% CI: 1.008–

Table 1. Logistic regression of local *Der p* and *Der f* sIgE as diagnostic indicators of AR.

							95% CI for OR	
		β	se	Wald	P	OR	Lower	Upper
Local *Der p* sIgE, UA/L	Model 1[a]	0.016	0.003	29.280	<0.001	1.016	1.010	1.022
	Model 2[b]	0.014	0.003	24.458	<0.001	1.014	1.009	1.020
	Model 3[c]	0.014	0.003	21.445	<0.001	1.014	1.008	1.020
Local *Der f* sIgE, UA/L	Model 1[a]	0.017	0.004	23.417	<0.001	1.017	1.010	1.024
	Model 2[b]	0.016	0.004	21.060	<0.001	1.016	1.009	1.023
	Model 3[c]	0.017	0.004	20.877	<0.001	1.018	1.010	1.025

[a] No adjustment variable; [b] adjusted for gender and age; [c] adjusted for gender, age, asthma, and atopic dermatitis. AR, allergic rhinitis; β, slope parameter; CI, confidence interval; *Der f, Dermatophagoides farina; Der p, Dermatophagoides pteronyssinus*; OR, odds ratio; sIgE, specific immunoglobulin E.

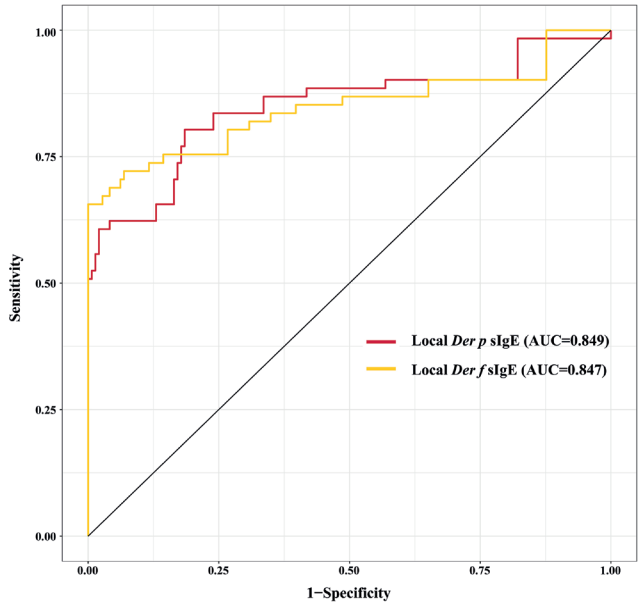


Figure 2. Receiver operating characteristic curves demonstrate the diagnostic performance of local Der p and Der f sIgE for HDM-sensitized AR. AR, allergic rhinitis; Der f, Dermatophagoides farina; Der p, Dermatophagoides pteronyssinus; HDM, house dust mite; sIgE, specific immunoglobulin E.

1.020, P<0.001; *Der f*, OR=1.018, 95% CI: 1.010–1.025, P<0.001). These findings indicate that both local *Der p* and *Der f* sIgE are positively associated with the risk of AR, even after controlling for potential confounding factors.

Figure 2 displays the ROC curves for local *Der p* sIgE and *Der f* sIgE in diagnosing AR. The area under the curve (AUC) for local *Der p* sIgE was 0.849 (95% CI: 0.781–0.917), with a diagnostic cut-off value of 0.08 kUA/L, and the AUC for local *Der f* sIgE was 0.847 (95% CI: 0.774–0.919), with a diagnostic cut-off value of 0.18 kUA/L. These results suggest that both local sIgE markers demonstrated good diagnostic performance for HDM-sensitized AR.

Nasal inflammatory cytokine patterns and their relationship with IgE

Table S2 and Figure 3 illustrate the distribution of inflammatory cytokines in nasal secretions of AR patients and healthy controls. Compared with healthy controls, AR patients exhibited significantly higher levels of IL-4 (P<0.001), IL-5 (P<0.001), CCL5 (P=0.004), CCL11 (P<0.001), and CXCL9 (P=0.033), as well as a significantly lower level of IFN-γ (P=0.021). No statistically significant differences were observed for GM-CSF (P=0.592) or IL-17A (P=0.288).

Spearman correlation analyses (Figure 4) revealed that serum *Der p* sIgE was correlated with IL-4 (r_s=0.34, P=0.008), IL-5 (r_s=0.29, P=0.024), CCL5 (r_s=0.46, P<0.001), and CCL11 (r_s=0.36, P=0.005). Similarly, serum *Der f* sIgE correlated with IL-4 (r_s=0.34, P=0.008), IL-5 (r_s=0.32, P=0.012), CCL5 (r_s=0.40, P=0.001), and CCL11 (r_s=0.33, P=0.009). In contrast, local *Der p* sIgE displayed stronger associations with IL-4 (r_s=0.45, P<0.001), IL-5 (r_s=0.65, P<0.001), CCL5 (r_s=0.73, P<0.001), CCL11 (r_s=0.55, P<0.001), and CXCL9 (r_s=0.29, P=0.025). Local *Der f* sIgE showed similarly high correlations with IL-4 (r_s=0.50, P<0.001), IL-5 (r_s=0.67, P<0.001), CCL5 (r_s=0.66, P<0.001), CCL11 (r_s=0.52, P<0.001), and CXCL9 (r_s=0.28, P=0.029). Local tIgE also correlated positively with IL-4 (r_s=0.46, P<0.001), IL-5 (r_s=0.60, P<0.001), CCL5 (r_s=0.55, P<0.001), CCL11 (r_s=0.49, P<0.001), and CXCL9 (r_s=0.39, P=0.002). By contrast, peripheral blood eosinophil (EOS) percentage correlated only with IL-5 (r_s=0.28, P=0.035), and EOS count correlated weakly with IL-4 (r_s=0.30, P=0.026), IL-5 (r_s=0.36, P=0.007), CCL11 (r_s=0.27, P=0.047), and CXCL9 (r_s=0.36, P=0.006). These findings indicate that local IgE levels have substantially stronger associations with nasal inflammatory cytokines than serum IgE or peripheral EOS metrics.

Nonlinear association between local and serum sIgE

RCS analyses revealed significant nonlinear dynamics between local and serum sIgE levels for both *Der p* and *Der f* allergens

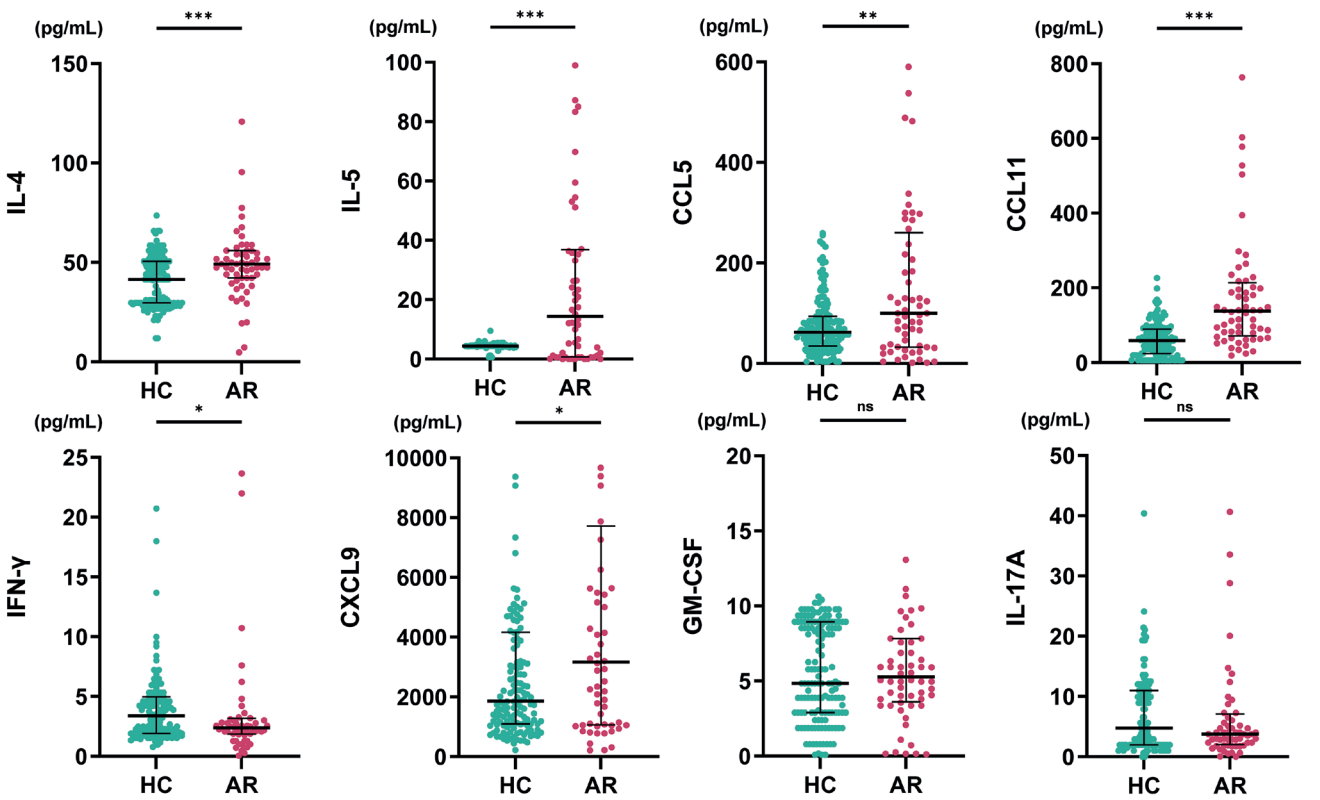


Figure 3. Nasal cytokine profiles in HDM-sensitized AR patients and healthy controls. AR, allergic rhinitis; CCL5, chemokine (C-C motif) ligand 5; CCL11, Chemokine (C-C motif) ligand 11; CXCL9, chemokine (C-X-C motif) ligand 9; GM-CSF, granulocyte-macrophage colony-stimulating factor; HC, healthy controls; HDM, house dust mite; IFN-γ, interferon-gamma; IL-4, interleukin-4; IL-5, interleukin-5; IL-17A, interleukin-17A; ns, not significant. * $P < 0.05$, **$P < 0.01$, *** $P < 0.001$.

in AR patients (Figure 5). As shown in Table S3, both the linear and nonlinear terms for *Der p* and *Der f* sIgE were statistically significant, indicating that while local sIgE and serum sIgE were overall positively correlated, their relationship was characterized by a significant nonlinear component.

For *Der p* sIgE, the model identified two critical inflection points at 0.39 kUA/L and 10.8 kUA/L in nasal secretions. Below the first threshold (0.39 kUA/L), each unit increase in local *Der p* sIgE was associated with a marked 8.99-unit elevation in serum levels. However, this association progressively attenuated beyond the initial threshold, culminating in a complete directional reversal above 10.8 kUA/L.

A parallel pattern emerged for *Der f* sIgE, with transition thresholds at 0.45 kUA/L and 11.62 kUA/L. The linear phase below 0.45 kUA/L demonstrated robust serum escalation, while the nonlinear component exhibited accelerated attenuation beyond the second threshold. Notably, serum sIgE plateaued when nasal *Der f* sIgE exceeded 11.62 kUA/L, despite continued mucosal sIgE accumulation.

Discussion

In this study, we systematically established local *Der p* and *Der f* sIgE as a superior biomarker for HDM-sensitized AR. Our primary finding confirms that local *Der p* and *Der f* sIgE levels exhibit high diagnostic accuracy, with optimal clinical cut-off values for identifying AR patients. Building upon its clinical utility, our first secondary analysis revealed the biological rationale for this superiority: local sIgE correlates more strongly with nasal type 2 inflammatory cytokines compared to systemic biomarkers. Finally, we identified a nonlinear, threshold-dependent relationship between local and serum sIgE levels, suggesting compartmentalized regulation of IgE production in mucosal versus systemic compartments.

Several studies [7-12] have reported elevated sIgE levels in the nasal secretions or lavage fluid of AR patients, underscoring the promise of local allergen testing and aligning with our findings. In this study, we demonstrated that local *Der p* and *Der f* sIgE accurately diagnose HDM-sensitized AR, with strong diagnostic performance (AUC: 0.849 for *Der p* and 0.847 for *Der f*). Furthermore, we identified optimal cut-off values for both assays, enabling clinicians to translate these measurements into actionable diagnostic decisions and substantially improving diagnostic accuracy and clinical utility.

Kim et al. [8] reported correlations between IgE levels in nasal secretions and eosinophil cationic protein (ECP), IL-8, and vascular endothelial growth factor (VEGF) in AR patients. Our study

Figure 4. Correlations between IgE metrics, peripheral blood eosinophil parameters, and nasal inflammatory cytokines in HDM-sensitized AR patients. AR, allergic rhinitis; CCL5, chemokine (C-C motif) ligand 5; CCL11, Chemokine (C-C motif) ligand 11; CXCL9, chemokine (C-X-C motif) ligand 9; *Der f, Dermatophagoides farina; Der p, Dermatophagoides pteronyssinus*; EOS, eosinophil; GM-CSF, granulocyte-macrophage colony-stimulating factor; HDM, house dust mite; IFN-γ, interferon-gamma; IL-4, interleukin-4; IL-5, interleukin-5; IL-17A, interleukin-17A; sIgE, specific immunoglobulin E. * $P < 0.05$, **$P < 0.01$, *** $P < 0.001$.

expanded upon this foundation by comprehensively profiling inflammatory cytokines, including type 2 (IL-4, IL-5, CCL5, CCL11) (20, 21), type 1 (IFN-γ) (22), and type 3 (IL-17A) [23] inflammatory mediators, and pioneering a direct comparison between local sIgE and systemic biomarkers (serum IgE, peripheral blood EOS count and percentage) in reflecting nasal mucosal inflammation. We demonstrated that local sIgE exhibited robust correlations with type 2 inflammatory markers—including IL-4, IL-5, CCL5, and CCL11—outperforming serum sIgE and peripheral EOS parameters. These results not only establish local sIgE as a sensitive biomarker of mucosal Th2 inflammation but also highlight the necessity of dual-tissue IgE profiling to distinguish localized immune activation from systemic sensitization, thereby informing personalized therapeutic strategies in AR management.

While studies by Gökkaya et al. [12] and Bliss et al. [24] reported a linear positive correlation between local and serum sIgE, our findings revealed a threshold-dependent nonlinear dynamic relationship. RCS analyses identified two critical inflection points: beyond the first threshold (*Der p*: 0.39 kUA/L; *Der f*: 0.45 kUA/L), the rate of serum sIgE increase markedly decelerated, and after surpassing the second threshold (*Der p*: 10.8 kUA/L; *Der f*: 11.62 kUA/L), serum sIgE plateaued despite continued mucosal sIgE accumulation. This nonlinearity likely underlies the weaker correlation between serum sIgE and nasal inflammatory cytokines. Notably, in patients with high local sIgE, serum sIgE failed to mirror mucosal inflammation intensity, resulting in potential underestimation of disease severity through serum testing alone. Thus, dual-tissue IgE profiling is essential for accurate diagnosis and tailored therapeutic stratification.

Conventional paradigms posit IgE production by B cells in secondary lymphoid organs and bone marrow [25]; however, emerging evidence highlights IgE synthesis within mucosal tissues, including the nasal mucosa [26, 27]. This localized IgE production has been validated in patients with local AR and animal models [28-30]. The nonlinear serum-local sIgE relationship observed here reinforces a "dual-compartment IgE paradigm", wherein mucosal

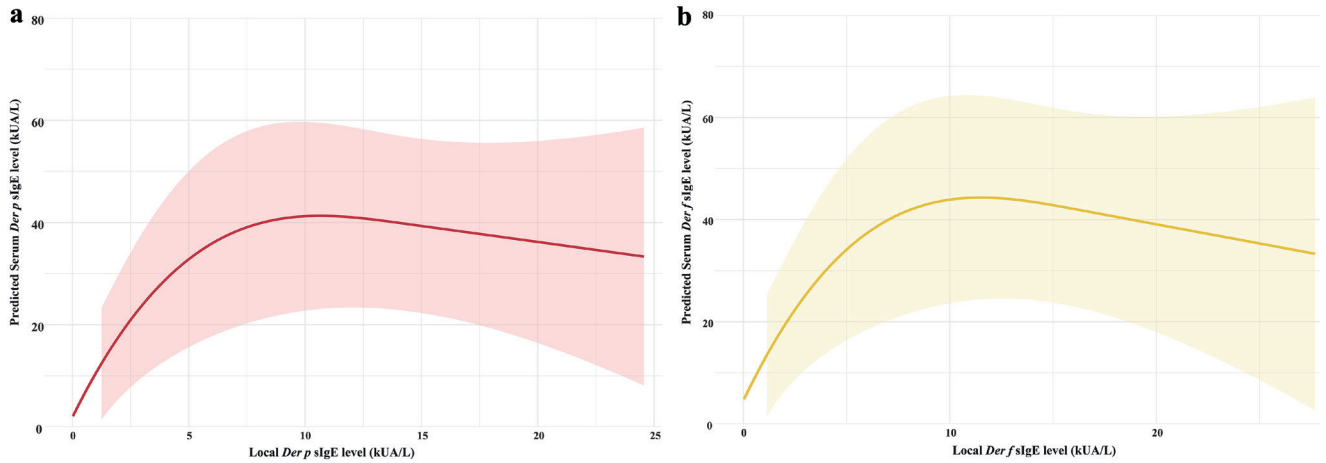


Figure 5. Nonlinear dynamics between local and serum sIgE levels in HDM-sensitized AR patients. A) RCS analysis curve between local and serum *Der p* sIgE after adjustment for age, sex, asthma, and atopic dermatitis; B) RCS analysis curve between local and serum *Der f* sIgE after adjustment for age, sex, asthma, and atopic dermatitis. AR, allergic rhinitis; *Der f, Dermatophagoides farina; Der p, Dermatophagoides pteronyssinus*; HDM, house dust mite; RCS, Restricted cubic spline; sIgE, specific immunoglobulin E.

and systemic IgE pools are interconnected yet functionally distinct. Intriguingly, while Eckl-Dorna et al. [31] proposed serum sIgE as a spillover from local tissues, our data suggest that elevated mucosal sIgE may trigger regulatory pathways to attenuate systemic dissemination. These findings offer novel insights into mucosal-systemic IgE dysregulation, though the precise molecular mechanisms warrant further investigation.

Our study highlights the translational potential of local allergen-sIgE quantification in AR management. Non-invasive nasal secretion sampling enables site-specific biomarker profiling, overcoming the limitations of conventional serum testing. The robust correlations between local sIgE and nasal type 2 related inflammatory cytokines—IL-4, IL-5, CCL5, and CCL11—provide a direct biological rationale for its utility in precision diagnosis, longitudinal monitoring, and therapeutic evaluation. This is particularly relevant given recent clinical trials demonstrating that anti-IL-4Rα monoclonal antibodies are effective only in seasonal AR patients with a high-EOS phenotype [32, 33]. This stratified efficacy reflects the heterogeneity of AR, where high local IL-4 levels are not uniformly present across all patients. Aligning with these trial findings, our data confirmed a positive correlation between peripheral EOS counts and local IL-4. Crucially, however, we found that local sIgE exhibited superior associations with nasal Type 2 biomarkers, including IL-4. This suggests that local sIgE could be a more direct and sensitive stratification marker than systemic biomarkers for identifying patients most likely to benefit from Th2-targeted biologics, thereby enhancing personalized AR therapy.

Local sIgE testing shows considerable promise for clinical translation. Our study applied and validated a standardized protocol for non-invasive nasal sampling [19], providing a practical reference for the future development of routine clinical collection guidelines. Moreover, the quantification was performed on an automated immunoassay platform of the type also used for serum sIgE quantification in clinical practice, suggesting that local sIgE testing could be integrated into existing clinical laboratory workflows. While this provides a clear pathway, concerted efforts are still needed to streamline this process and rigorously evaluate its clinical value and utility for widespread adoption.

Several limitations should be acknowledged. First, this single-center, exploratory study requires validation in multicenter, large-scale cohorts—especially those representing diverse geographic regions and ethnicities—to assess potential heterogeneity. Second, we focused on HDM-sensitized AR patients and major allergens (*Der p*/*Der f*), future work should include other allergens, especially seasonal allergens, to confirm the broader diagnostic utility of local sIgE. Third, although our cross- sectional design revealed nonlinear local–serum sIgE dynamics, the underlying causal mechanisms remain unclear; elucidating these mechanisms will require integrated approaches such as in vitro models and longitudinal cohort studies. These limitations also delineate critical pathways for future research. Addressing these limitations will guide critical pathways for future research.

Conclusion

This study establishes local sIgE as a sensitive biomarker for HDM-sensitized AR and elucidates its central role in nasal Type 2 inflammation. The nonlinear serum-local sIgE relationship challenges conventional diagnostic paradigms, advocating for dual-tissue biomarker profiling. These findings advance our understanding of AR immunopathology and pave the way for precision medicine strategies targeting mucosal immune dysregulation.

Conflict of interest

The authors have no conflicts of interest to declare.

Funding

This work was supported by grants from National Key R&D Program of China (2022YFC2504100), the Program for the Changjiang Scholars and Innovative Research Team (IRT13082), Natural Science Foundation of China (82471132 and 82071022) and Beijing Hospitals Authority Clinical Medicine Development of Special Funding (ZLRK202303).

Authors contributions

Concept and design: LZ and YZ. Acquisition, analysis, or interpretation of data: ZZ, XZ, JL, YS, and LX. Drafting of the manuscript: ZZ, CW, LZ, and YZ. Critical review of the manuscript for important intellectual content: CW, LZ, and YZ. Statistical analysis: ZZ, XZ, and JL. Obtained funding: LZ and YZ. Administrative, technical, or material support: CW. Supervision: LZ and YZ.

Acknowledgement

None.

Ethics approval

This study was approved by the Ethics Committee of Beijing Tongren Hospital, Capital Medical University (ID: TREC2023-KY046). Written informed consent was obtained from all participants before their enrollment in the study

References

1. Bernstein JA, Bernstein JS, Makol R, Ward S. Allergic rhinitis: a review. JAMA. 2024;331(10):866-877.
2. Brozek J, Borowiack E, Sadowska E, et al. Patients' values and preferences for health states in allergic rhinitis-An artificial intelligence supported systematic review. Allergy. 2024;79(7):1812-1830.
3. Vandenplas O, Vinnikov D, Blanc PD, et al. Impact of rhinitis on work productivity: a systematic review. J Allergy Clin Immunol Pract. 2018;6(4):1274-1286.e1279.
4. Bousquet J, Anto JM, Bachert C, et al. Allergic rhinitis. Nat Rev Dis Primers. 2020;6(1):95.
5. Bousquet J, Shamji MH, Anto JM, et al. Patient-centered digital biomarkers for allergic respiratory diseases and asthma: the ARIA-EAACI approach - ARIA-EAACI Task Force Report. Allergy. 2023;78(7):1758-1776.
6. Wise SK, Damask C, Roland LT, et al. International consensus statement on allergy and rhinology: Allergic rhinitis - 2023. Int Forum Allergy Rhinol. 2023;13(4):293-859.
7. Meng Y, Lou H, Wang Y, Wang C, Zhang L. The use of specific immunoglobulin E in nasal secretions for the diagnosis of allergic rhinitis. Laryngoscope. 2018;128(9):E311-e315.
8. Kim JH, Yoon MG, Seo DH, et al. Detection of allergen specific antibodies from nasal secretion of allergic rhinitis patients. Allergy, Asthma Immunol Res. 2016;8(4):329-337.
9. Eckrich J, Hinkel J, Fischl A, et al. Nasal IgE in subjects with allergic and non-allergic rhinitis. World Allergy Organ J. 2020;13(6):100129.
10. Krzych-Fałta E, Lishchuk-Yakymovych K, Majsiak E, Borkowska W, Białek S, Wojas O. Nasal lavage fluid sIgE levels in differential diagnostics of allergic rhinitis. Postepy Dermatol Alergol. 2022;39(6):1008-1014.
11. Castelli S, Arasi S, Tripodi S, et al. IgE antibody repertoire in nasal secretions of children and adults with seasonal allergic rhinitis: a molecular analysis. Pediat Allergy Immunol. 2020;31(3):273-280.
12. Gökkaya M, Schwierzeck V, Thölken K, et al. Nasal specific IgE correlates to serum specific IgE: first steps towards nasal molecular allergy diagnostic. Allergy. 2020;75(7):1802-1805.
13. Calderón 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.
14. Valero A, Quirce S, Dávila I, Delgado J, Domínguez-Ortega J. Allergic respiratory disease: different allergens, different symptoms. Allergy. 2017;72(9):1306-1316.
15. Ciprandi G, Tosca MA. House dust mites-driven allergic rhinitis: could its natural history be modified? Exp Rev Clin Immunol. 2021;17(2):109-114.
16. Ogulur I, Mitamura Y, Yazici D, et al. Type 2 immunity in allergic diseases. Cell Mol Immunol. 2025;22(3):211-242.
17. Zhang Y, Lan F, Zhang L. Update on pathomechanisms and treatments in allergic rhinitis. Allergy. 2022;77(11):3309-3319.
18. Brożek 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.
19. Xu X, Zhang X, Liu D, et al. Development of a method of nasal secretions sampling for local nasal inflammation studies. Exp Rev Clin Immunol. 2023;19(8):1013-1021.
20. Maspero J, Adir Y, Al-Ahmad M, et al. Type 2 inflammation in asthma and other airway diseases. ERJ Open Res. 2022;8(3)
21. Li Z, Yu S, Jiang Y, Fu Y. Chemokines and chemokine receptors in allergic rhinitis: from mediators to potential therapeutic targets. Eur Arch OtoRhinoLaryngol. 2022;279(11):5089-5095.
22. Annunziato F, Romagnani C, Romagnani S. The 3 major types of innate and adaptive cell-mediated effector immunity. J Allergy Clin Immunol. 2015;135(3):626-635.
23. Zhai Z, Shao L, Lu Z, et al. Characteristics of mucin hypersecretion in different inflammatory patterns based on endotypes of chronic rhinosinusitis. Clin Transl Allergy. 2024;14(1):e12334.
24. Bliss A, Sheehan C, Erwin E, Jatana K, Elmaraghy CA. Local allergen-specific IgE production in turbinate tissue of pediatric patients. Ann Otol Rhinol Laryngol. 2023;132(10):1216-1221.
25. Hoddeson EK, Wise SK. The role of IgE production in the pathophysiology of rhinitis and rhinosinusitis. Curr Allergy Asthma Reports. 2011;11(3):230-235.
26. De Schryver E, Devuyst L, Derycke L, et al. Local immunoglobulin E in the nasal mucosa: clinical implications. Allergy, Asthma Immunol Res. 2015;7(4):321-331.
27. Eguiluz-Gracia I, Layhadi JA, Rondon C, Shamji MH. Mucosal IgE immune responses in respiratory diseases. Curr Opin Pharmacol. 2019;46:100-107.
28. Campo P, Canonica GW. Local allergic rhinitis. J Allergy Clin Immunol Pract. 2024;12(6):1430-1433.
29. Hellings PW, Klimek L, Cingi C, et al. Non-allergic rhinitis: position paper of the european academy of allergy and clinical immunology. Allergy. 2017;72(11):1657-1665.
30. Kato Y, Akasaki S, Muto-Haenuki Y, Fujieda S, Matsushita K, Yoshimoto T. Nasal sensitization with ragweed pollen induces local-allergic-rhinitis-like symptoms in mice. PloS One. 2014;9(8):e103540.
31. Eckl-Dorna J, Pree I, Reisinger J, et al. The majority of allergen-specific IgE in the blood of allergic patients does not originate from blood-derived B cells or plasma cells. Clin Exp Allergy. 2012;42(9):1347-1355.
32. Zhang Y, Yan B, Zhu Z, et al. Efficacy and safety of stapokibart (CM310) in uncontrolled seasonal allergic rhinitis (MERAK): an investigator-initiated, placebo-controlled, randomised, double-blind, phase 2 trial. EClinicalMed. 2024;69:102467.
33. Zhang Y, Li J, Wang M, et al. Stapokibart for moderate-to-severe seasonal allergic rhinitis: a randomized phase 3 trial. Nat Med. 2025;31(7):2213-2221.

Luo Zhang, MD, PhD
President-elect, Chinese Society of Allergy
Department of Otolaryngology Head and Neck Surgery and Department of Allergy
Beijing Tongren Hospital, Capital Medical University
No. 1, DongJiaoMinXiang
Dongcheng District
Beijing 100730
P.R. China

Tel: (+8610) 58265719 or 65264431 (office)
Fax: (+8610) 85115988
E-mail: dr.luozhang@139.com

Yuan Zhang, MD, PhD
Department of Allergy
Beijing TongRen Hospital, Capital Medical University
17, HouGouHuTong
DongCheng District
Beijing 100005
P.R. China

Fax: (+8610) 85115988
E-mail: summer_zhang1211@126.com

Zengxiao Zhang[1,2,3,4], Xu Zhang[1,2,4], Jingyun Li[2,4], Yu Song[1,2,4], Lin Xi[1,2,4], Chengshuo Wang[1,2,3,4], Luo Zhang[1,2,3,4], Yuan Zhang[1,2,3,4]

[1] Department of Allergy, Beijing Tongren Hospital, Capital Medical University, Beijing, China
[2] Department of Otolaryngology Head and Neck Surgery, Beijing Tongren Hospital, Capital Medical University, Beijing, China
[3] Beijing Laboratory of Allergic Diseases and Beijing Key Laboratory of Nasal Diseases, Beijing Institute of Otolaryngology, Beijing, China
[4] Laboratory for Clinical Medicine, Capital Medical University, Beijing, China

Rhinology 64: 1, 0 - 0, 2026
https://doi.org/10.4193/Rhin25.381

Received for publication:
July 12, 2025
Accepted: August 27, 2025

Associate Editor:
Sanna Toppila-Salmi

This manuscript contains online supplementary material

SUPPLEMENTARY MATERIAL

Table S1. Baseline characteristics and IgE levels in AR patients and healthy controls.

	AR patients (n=60)	Healthy controls (n=143)	P
Gender, male	35 (58.33%)	47 (32.87%)	<0.001
Age, years	34.00±14.00	48.00±27.00	<0.001
Serum *Der p* sIgE, kUA/L	1.77±5.77	0.04±0.02	<0.001
Serum *Der f* sIgE, kUA/L	2.44±12.89	0.04±0.02	<0.001
Serum total IgE	146.09±355.24	15.23±27.18	<0.001
Local *Der p* sIgE, kUA/L	0.23±1.02	0.04±0.03	<0.001
Local *Der f* sIgE, kUA/L	0.34±1.64	0.04±0.06	<0.001
Local total IgE, kUA/L	8.18±26.09	0.12±0.19	<0.001

AR, allergic rhinitis; *Der f, Dermatophagoides farina; Der p, Dermatophagoides pteronyssinus*; IgE, immunoglobulin E; sIgE, specific immunoglobulin E.

Table S2. Inflammatory cytokine levels in nasal secretions of AR patients and healthy controls.

	AR patients (n=60)	Healthy controls (n=143)	P
IL-4, pg/mL	49.18±13.67	41.48±20.84	<0.001
IL-5, pg/mL	14.35±36.13	4.41±0.49	<0.001
CCL5, pg/mL	99.78±227.38	62.16±58.82	0.004
CCL11, pg/mL	137.62±142.36	58.86±65.23	<0.001
IFN-γ, pg/mL	2.38±1.32	3.39±3.05	0.021
CXCL9, pg/mL	3163.18±6661.58	1860.80±3064.54	0.033
GM-CSF, pg/mL	5.28±4.21	4.84±6.05	0.592
IL-17A, pg/mL	3.78±5.08	4.75±9.00	0.288

AR, allergic rhinitis; CCL5, chemokine (C-C motif) ligand 5; CCL11, Chemokine (C-C motif) ligand 11; CXCL9, chemokine (C-X-C motif) ligand 9; GM-CSF, granulocyte-macrophage colony-stimulating factor; IFN-γ, interferon-gamma; IL-4, interleukin-4; IL-5, interleukin-5; IL-17A, interleukin-17A.

Table S3. Linear and nonlinear association between local and serum sIgE in AR patients.

	β (Coefficient)	se	t-value	P
Linear term of *Der p* sIgE	8.123	2.505	3.242	0.002
Nonlinear term of *Der p* sIgE	-83.239	31.296	-2.660	0.001
Linear term of *Der f* sIgE	9.060	2.588	3.501	<0.001
Nonlinear term of *Der f* sIgE	-229.240	80.127	-2.861	0.006

AR, allergic rhinitis; β, slope parameter; *Der f, Dermatophagoides farina; Der p, Dermatophagoides pteronyssinus*; sIgE, specific immunoglobulin E.