Allergologia et immunopathologia
Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica
www.all-imm.com

SEICAAP

CODON PUBLICATIONS

ORIGINAL ARTICLE

OPEN ACCESS

Correlation patterns among house dust mite allergens in allergic rhinitis: A molecular sensitization study in Mallorca

Sendy Chugo[a,c], Jaime Pons[b], Danilo Escobar[b], Daniel Hervás[a,c]*

[a]*Allergology, Son Espases University Hospital, Palma, (Mallorca) Spain*
[b]*Immunology, Son Espases University Hospital, Palma, (Mallorca) Spain*
[c]*Allergy Research Group, Health Research Institute of Palma (IdISPa), Palma, (Mallorca) Spain*

Received 5 May 2025; Accepted 28 August 2025
Available online 1 November 2025

KEYWORDS
House dust mites/ immunology;
Allergens / analysis;
Immunoglobulin e/ blood;
Rhinitis, allergic/ immunology;
Molecular diagnostic techniques;
Correlation of data

Abstract
Introduction: Molecular characterization of house dust mite (HDM) and storage mite allergens provides valuable insights into sensitization patterns; however, relationships among different mite allergens and their clinical implications remain unclear.
Methods: A total of 100 patients with allergic rhinitis sensitized to *Dermatophagoides pteronyssinus* were analyzed. Specific IgE (sIgE) levels were measured using singleplex and multiplex assays. Correlations among mite allergens and their associations with clinical and demographic variables were evaluated.
Results: The median sIgE level to Der p was 15.8 kU/L (IQR: 50.25); no relevant Dermatophagoides spp. sensitization was found below 2 kU/L. Among patients with Der p >10 kU/L, 59 of 60 had significant sIgE to at least one major HDM allergen. The highest prevalence was for Der p 1 (92%), though its median level was low (3.19 kU/L, IQR: 8.18). Conversely, Der f 2 had the highest median sIgE (23.4 kU/L, IQR: 33.74). Multivariate analysis revealed that most allergen levels were predictable from clusters of other mite allergens (R^2=0.27–0.98). Mite allergen sIgE (Aca s, Blo t 5/10/21, Der f 1/2, Der p 1/2/5/7) correlated positively with sensitization number. sIgE levels negatively correlated with age and positively correlated with atopic dermatitis (Der p 1/2/23, Der f 1/2), asthma (Aca s, Der p 21), food allergy (Aca s, Der f 1, Der p 1), and rural residence (Der p 7).
Conclusion: Der p source allergen reliably excludes clinically relevant sIgE to HDM components. The correlations among mite allergens highlight challenges in clinical relevance assessment, emphasizing the need for component-resolved diagnostics to optimize immunotherapy responses.
© 2025 Codon Publications. Published by Codon Publications.

***Corresponding author**: Daniel Hervás, Allergology, Son Espases University Hospital, Palma, (Mallorca) Spain. *Email address*: daniel.hervas@ssib.es

https://doi.org/10.15586/aei.v53i6.1407

Introduction

Numerous studies have demonstrated significant variations in mite sensitization profiles across different populations and geographic regions.[1] These differences are influenced by environmental conditions, genetic predisposition, and/or exposure levels, leading to heterogeneous clinical presentations among allergic individuals.[2–4] One of the major challenges in the diagnosis and management of mite allergy is the high prevalence of polysensitization, where patients exhibit IgE reactivity to multiple mite species.[5] This phenomenon is further complicated by the extensive cross-reactivity among mite allergens, making it difficult to determine which specific allergens are clinically relevant.

The introduction of molecular component-resolved diagnosis (CRD) has revolutionized the field of allergy diagnostics, offering a more detailed characterization of sensitization patterns.[6,7] However, this increased resolution has also highlighted the complexity of mite sensitization. The current challenge is no longer limited to determining the clinical relevance of different mite species but has expanded to understanding a growing number of individual allergens, many of which remain poorly characterized. Furthermore, the interactions between these allergens and their potential impact on disease severity and treatment outcomes remain largely unknown.

In this study, we analyze the associations between sIgE responses to mites and their molecular components based on the sensitization profiles of patients with allergic rhinitis. By identifying patterns of sIgE reactivity, we aim to contribute to a better understanding of mite allergen interactions and provide insights into optimizing diagnostic approaches and personalized immunotherapy strategies.

Methods

Study design, population, and clinical assessment

This study was conducted in a cohort of patients diagnosed with allergic rhinitis and confirmed sensitization to *Dermatophagoides pteronyssinus*. Participants were recruited from the Allergy Unit of Son Espases University Hospital in the Island of Mallorca. Inclusion criteria encompassed individuals aged 18–60 years with a clinical history of allergic rhinitis and a positive allergy test to *D. pteronyssinus* determined by skin prick testing (SPT) and/or sIgE. Patients undergoing immunotherapy for aeroallergens, receiving systemic immunomodulatory treatments, or with cognitive impairments that hindered informed consent were excluded. A total of 102 patients were recruited; 2 did not undergo blood sampling, resulting in a final study population of 100 patients.

Clinical assessment included a standardized evaluation of allergic rhinitis severity following ARIA guidelines.[8] Patients were also assessed for comorbidities such as asthma, atopic dermatitis, IgE-mediated food allergy, and chronic urticaria based on assessment by an allergist. The duration of allergic rhinitis symptoms was recorded based on patient-reported history. Geographic data regarding urban or rural residence were collected to explore environmental influences.

Sample collection and IgE analysis

SPT was performed using standardized extracts (LETI Pharma laboratories) for the most common environmental allergens in our area. Blood samples were collected from all participants for the quantification of sIgE levels against a comprehensive panel of house dust mite (HDM) and storage mite allergens. sIgE measurements were performed using both a singleplex (ImmunoCAP) and a multiplex assay (ALEX2). The allergens analyzed using the multiplex assay included Der p 1, Der p 2, Der p 5, Der p 7, Der p 10, Der p 11, Der p 20, Der p 21, Der p 23, Der f 1, Der f 2, Blo t 5, Blo t 10, Blo t 21, Lep d 2, Gly d 2, Tyr p 2, and Aca s, among others. Singleplex assay included Der p and Lep d source allergens. Standardized procedures were followed for serum processing and IgE quantification as described elsewhere.[9,10] Positivity cut points were defined as follows: for ImmunoCAP, positivity to source allergens (Der p and Lep d) was considered at ≥0.35 kU/L; for ALEX2, positivity was defined as ≥0.10 kU/L.

Statistical analyses

Data were analyzed using STATA v.18 (StataCorp, College Station, TX, USA). Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR), depending on distribution. Categorical variables were summarized as frequencies and percentages. Comparisons between groups were performed using Student's *t*-test or Mann–Whitney U test for continuous variables and x^2 test for categorical variables. Pairwise correlations between sIgE levels were evaluated using Pearson's or Spearman's correlation coefficients, as appropriate. Multivariate linear regression models were constructed to assess independent associations between mite allergens and between sIgE levels and clinical or demographic factors. Logistic regression analyses were used to evaluate associations between sIgE levels and the prevalence of comorbidities. Post-estimation analyses were performed after regression, including checks for multicollinearity, heteroscedasticity, and residual diagnostics. A two-sided p-value <0.05 was considered statistically significant.

Results

Clinical and demographic characteristics

A total of 100 patients with allergic rhinitis caused by *D. pteronyssinus* were enrolled. Mean age was 37.8 years (SD: 11.7); 64 were female and 22 lived in rural environments. Regarding comorbidities, 60 patients had asthma, 57 had atopic dermatitis, 10 had chronic urticaria, and 11 had food allergy. Overall, 31% of patients reported experiencing nasal symptoms for more than two decades. Female patients were younger than male patients (median age: 36 vs. 40.9 years; $t = -2.03$; $p = 0.046$). In addition, patients without asthma were younger than those with asthma (median age: 33.7 vs. 40.4 years; $t = -2.91$; $p = 0.004$). No significant differences in age or sex were observed between patients with or without atopic dermatitis, food allergies, or chronic urticaria.

Mite-sIgE serodominance

HDMs

All patients exhibited increased sIgE levels to Der p (ImmunoCAP), with a median of 15.8 kU/L (IQR: 50.25). Sensitization rates and median sIgE levels for the mite allergens assessed are summarized in Table 1. Der p 1 was the most prevalent sIgE allergen (92%), although its median sIgE levels were lower compared to other *Dermatophagoides* allergens, except for Der p 10 and Der p 11 (to which no sensitization was observed). The highest sIgE levels were against group 2 *Dermatophagoides* allergens, followed by Der p 5 and Der p 21.

Der p sIgE showed an adequate prediction (AUC = 0,97) of sIgE levels <5kU/L to major Dermatophagoides allergens (shown in Figure S1). No patient with Der p sIgE <2 kU/L exhibited sIgE >5 kU/L to *D. pteronyssinus* or *farinae* allergens in ALEX2. However, among the 25 of 100 patients with ImmunoCAP sIgE levels between 2 and 10 kU/L, ALEX2 results showed substantial variability. Of the 60 patients with ImmunoCAP Der p sIgE >10 kU/L, all but one had relevant sIgE responses to *D. pteronyssinus* or *farinae* allergens from groups 1, 2, or 23. No sensitizations to additional *Dermatophagoides* allergens were observed without at least one sensitization to group 1 or group 2 allergens.

Only two patients with low sIgE levels to group 1 or group 2 allergens showed possible significant levels to other *Dermatophagoides* allergens: patient 38, with sensitization to Der p 1 (3.15 kU/L) and Der p 7 (7.9 kU/L); and patient 56, with sensitization to Der p 1 (1.7 kU/L), Der p 20 (3.8 kU/L), and Der p 23 (14.2 kU/L).

Storage mites

Among the ALEX2 sIgE responses to mites, Aca s was the most frequently identified storage mite allergen. SIgE levels to all storage mite allergens were generally low (shown in Table 1), although they displayed a wide range. The number of sensitizations to *Lepidoglyphus destructor* (N = 53) detected via ImmunoCAP was significantly higher than that observed with ALEX2. However, the sIgE levels remained low, with a median of 2.5 kU/L (IQR: 10.7).

Association between mite allergens

Simple correlations

Statistically significant correlations among sIgE levels to mite allergens were frequently observed (shown in Table 2), particularly for source allergens Der p, Lep d, and Aca s. Correlations between sIgE to Der p source allergen (ImmunoCAP) and Der p allergens (ALEX2) were observed for all allergens except Der p 10. However, a positive correlation trend emerged when only patients sensitized to Der p 10 were considered ($r = 0.52$; $p = 0.067$). Statistical significance was not achieved for correlation between sIgE to Tyr p source allergen and Tyr p 2 ($r = 0.2$; $p = 0.077$).

Statistically significant correlations were identified within certain allergen groups, including group 2 allergens (Der f 2, Der p 2, Gly d 2, Lep d 2, and Tyr p 2), group 5 allergens (Blo t 5, Der p 5), and group 21 allergens (Blo t 21, Der p 21). Although univariate regressions reached statistical significance, they did not appear relevant for certain allergen groups, as shown in Figure S2.

Multivariate regression

The predictive models for sIgE to mite allergens are summarized in Table 3. Sensitization levels to Aca s and Tyr p were strongly associated ($R^2 = 0.97$; $p < 0.001$). sIgE levels to Blo t 5 were independently associated with sIgE to Blo t 10, Tyr p 2, and Aca s ($R^2 = 0.75$; $p < 0.001$). The predictive model for Blo t 10 sIgE showed an independent association only with the sIgE to Der p 10 ($R^2 = 0.42$; $p < 0.001$). sIgE levels to Blo t 21 were independently associated with sIgE to Blo t 5 and Der p 20 ($R^2 = 0.73$; $p < 0.001$).

A strong relationship was observed between sIgE levels to *Dermatophagoides* group 1 and group 2 allergens, explaining 78% ($p < 0.001$) and 98% ($p < 0.001$) of their respective variances. The variance in sIgE levels to Der p source allergen (ImmunoCAP) was predicted by sIgE to Der p 1, Der p 2, Der p 10, Der p 21, and Der p 23 with 85% accuracy ($p < 0.001$). Independent associations were also observed for Der p 5 sIgE with Der p 2 and Lep d 2 ($R^2 = 0.43$; $p < 0.001$). Der p 7 sIgE levels were independently associated with sIgE to Lep d 2 and Der p 1 ($R^2 = 0.38$; $p < 0.001$). The predictive model for Der p 20 sIgE was relatively weak, showing an independent association only with Blo t 21 ($R^2 = 0.27$; $p < 0.001$). sIgE levels to Der p 21 were explained by sIgE to Blo t 21, Der p 23, and Tyr p 2 ($R^2 = 0.53$; $p < 0.001$).

sIgE levels to the storage mite allergen Gly d 2 were independently associated with sIgE to Lep d 2 and Tyr p 2 ($R^2 = 0.75$; $p < 0.001$). Similarly, the variance in sIgE levels to Lep d source allergen (ImmunoCAP) was explained by sIgE levels to Aca s, Lep d 2, and Tyr p 2 with 65% accuracy ($p < 0.001$). Finally, sIgE to Lep d 2 was independently associated with sIgE to Gly d 2 and Tyr p 2 ($R^2 = 0.77$; $p < 0.001$), while Tyr p 2 sIgE levels were independently associated with sIgE to Gly d 2 and Lep d 2 ($R^2 = 0.65$; $p < 0.001$).

Association between mite allergen sIgE levels and sensitization number

ImmunoCAP sIgE levels for Der p and Lep d were significantly associated with the number of mite allergen sensitizations ($r = 0.65$, $p < 0.001$; and $r = 0.5$, $p < 0.001$, respectively). Except for Der p 10, sIgE levels for all mite allergens measured with the ALEX2 diagnostic platform showed a positive correlation with the number of mite allergen sensitizations (shown in Table S1).

Mite allergens and clinical/demographic variables' interactions

Association between mite sIgE and clinical/ demographic variables

Multivariate regression analyses were conducted to evaluate how sIgE levels to mite allergens relates to clinical and demographic variables (shown in Table 4). sIgE levels to all mite allergens, except Aca s, Blo t 5, Blo t 10, Blo t 21, Der p 10, Der p 20, and Tyr p, were inversely associated with age. Meanwhile, Der f 1, Der f 2, Der p, Der p 1, Der p 2, and Der

Table 1 Comparison of median sIgE levels (kU/L) to mite allergens across clinical and demographic groups.

Variables	Aca s	Blo t 5	Blo t 10	Blo t 21	Der f 1	Der f 2	Der p 1	Der p 2	Der p 5	Der p 7	Der p 10	Der p 20	Der p 21	Der p 23	Gly d 2	Lep d 2	Tyr p	Tyr p 2
Num. sens.	45	16	9	20	79	84	92	85	38	49	12	5	36	88	45	33	27	29
All	0	0	0	0	3.2	23.4	3.2	19.8	0	0	0	0	0	4.6	0	0	0	0
Only sens.	0.6	2	0.1	0.4	7.3	30.1	3.9	28.3	9.7	4.7	0.2	3.8	7.7	5.6	1.6	2.5	0.5	2.7
Sex																		
Female	0.6	1	0.1	0.6	5.6	30.7	2.9	28.6	10.3	5.3	0.2	2.3	8.9	5.7	1.6	4.4	0.7	2.5
Male	0.4	22.4	0.2	0.3	9.3	28.9	4.4	26.3	6.5	4.2	0.2	10.4	6.3	5	3.2	2.1	0.4	3.2
Habitat																		
Urban	0.6	1.9	0.1	0.2	7.6	30.6	3.2	27.6	9.0	2.8	0.2	3.8	7.7	5.3	3.3	2.5	0.5	2.5
Rural	0.3	19.4	0.1	6	5.9	29.5	4.1	29.7	12.0	14.7	0.2	8.9	13.6	6.4	1.3	4.6	0.4	4.8
Severity																		
Mild	0.2	-	-	0.1	4.8	17.8	4	19.6	10.3	6.1	0.1	16.9	4.3	6.3	3.6	2.0	0.4	2
Moderate	0.6	1.6	0.2	0.2	8.7	31.1	4.5	29.9	9.1	4.5	0.2	11.9	8.9	5.1	1.6	4.2	0.9	5.4
Severe	0.6	2.5	0.1	1.0	4.6	30.6	2.3	18.7	15.9	1.7	0.2	2.3	14.9	6.5	1.6	7.1	0.4	2.3
Evolution																		
1-10 years	0.4	23.2	0.1	5.1	5.2	32.1	3.2	29.1	9.1	7.9	0.2	3.8	14.9	6.1	2.5	6.4	0.7	9.5
11-20 years	0.3	1	0.1	0.1	5.1	34.2	3.7	32.1	14.8	5	0.1	-	5.3	5.4	1.6	4.7	0.3	3
21-30 years	0.3	2.6	-	1.1	7.9	27.2	4.5	25.6	6.5	2.4	0.2	16.9	8.3	5.1	3.6	1.5	0.8	1
31-40 years	2.2	0.2	-	0.6	13.6	14.2	4.5	13.1	9.5	3.4	0.2	0.9	13.1	8	2.2	8.1	0.3	5.9
Asthma																		
Yes	0.3	10.8	0.2	0.2	5.0	27.9	3.2	26.3	8.9	5	0.2	10.4	7.7	6.8	3.0	1.7	0.2	2.2
No	0.8	2.0	0.1	1.0	8.1	31.6	4.2	29.9	10.6	3.4	0.2	0.9	19.0	4.9	1.6	6.8	1.1	4.8
Dermatitis																		
Yes	0.6	0.8	0.1	0.4	10	34.2	5	34.3	10.3	5.3	0.1	8.9	5.3	7.2	3.2	2.5	0.5	2.4
No	0.5	21	0.2	8.3	4.6	24.6	2.1	20.7	9.1	4.2	0.2	3.8	19	4.3	1.5	4.2	0.5	4.8
C. urticaria																		
Yes	0.9	16.3	-	0.6	8	30.7	2.1	13.3	12.4	5.9	0.1	0.9	24.5	5.7	2.4	7.1	1.2	5.9
No	0.6	1.6	0.1	0.3	6.7	29.5	4	29.7	9.7	3.5	0.2	10.4	6.6	5.6	1.6	2	0.5	2.7
Food allergy																		
Yes	5.9	8.6	0.2	0.4	16.1	38.1	7.4	34.9	13.7	2.3	0.2	0.9	4	5.6	0.2	3.7	4	0.7
No	0.4	1.9	0.1	0.8	5.6	28.5	3.3	27.6	9.1	5	0.2	10.4	7.7	5.6	3.2	2.5	0.4	3.5
Seasonality																		
Winter	0.6	14.8	0.1	1.5	6.7	35.2	5.1	31.6	9	4.5	0.2	21.4	7.7	8.4	1.5	6.2	0.5	11.3
Primavera	0.3	1.4	0.2	0.8	6.7	30.7	3.3	28.3	12	10	0.2	10.4	8.3	5.8	4.1	6.3	0.6	2.6
Summer	0.2	0.6	0.1	0.2	8.6	12.6	1.7	10.6	6.5	1.2	0.2	-	4.0	3.3	0.2	1.2	1.0	0.4
Autumn	0.6	3.0	0.1	0.4	14.3	24	2.3	24.4	9.1	0.7	0.1	1.6	16.1	3.7	0.5	1.7	0.5	0.9

Table 2 Pairwise correlations between specific IgE levels to mite allergens.

	Der p	Lep d	Aca s	Blo t 5	Blo t 10	Blo t 21	Der f 1	Der f 2	Der p 1	Der p 2	Der p 5	Der p 7	Der p 10	Der p 20	Der p 21	Der p 23	Gly d 2	Lep d 2	Tyr p	Tyr p 2
Der p	1,00																			
Lep d	0,48**	1,00																		
Aca s	0,52**	0,40**	1,00																	
Blo t 5	0,26**	0,51**	0,37**	1,00																
Blo t 10	0,19	−0,02	0,25*	0,16	1,00															
Blo t 21	0,22*	0,35**	0,19	0,79**	0,05	1,00														
Der f 1	0,85**	0,43**	0,53**	0,22*	0,09	0,19	1,00													
Der f 2	0,83**	0,35**	0,42**	0,26**	−0,02	0,23*	0,72**	1,00												
Der p 1	0,84**	0,46**	0,49**	0,19	0,07	0,16	0,88**	0,68**	1,00											
Der p 2	0,84**	0,35**	0,41**	0,20*	−0,02	0,20	0,74**	0,99**	0,70**	1,00										
Der p 5	0,60**	0,42**	0,21*	0,32**	−0,08	0,37**	0,51**	0,53**	0,51**	0,53**	1,00									
Der p 7	0,54**	0,39**	0,29**	0,16	0,08	0,07	0,48**	0,48**	0,58**	0,48**	−0,42**	1,00								
Der p 10	0,04	0,00	0,21*	0,14	−0,65**	0,04	−0,02	−0,12	−0,03	−0,11	−0,09	0,00	1,00							
Der p 20	0,25*	0,22*	0,00	0,26**	−0,05	0,52**	0,25*	0,21*	0,23*	0,21*	0,30**	0,04	−0,06	1,00						
Der p 21	0,56**	0,53**	0,42**	0,56**	0,00	0,52**	0,44**	0,46**	0,51**	0,42**	0,51**	0,40**	−0,03	0,27**	1,00					
Der p 23	0,76**	0,36**	0,43**	0,08	−0,06	0,14	0,69**	0,67**	0,71**	0,68**	0,54**	0,50**	−0,13	0,22*	0,50**	1,00				
Gly d 2	0,40**	0,69**	0,22*	0,60**	−0,11	0,48**	0,32**	0,35**	0,37**	0,31**	0,51**	0,34**	−0,06	0,30**	0,52**	0,39**	1,00			
Lep d 2	0,39**	0,73**	0,24*	0,51**	−0,11	0,55**	0,30**	0,33**	0,37**	0,29**	0,52**	0,42**	−0,06	0,27**	0,55**	0,42**	0,85**	1,00		
Tyr p	0,45**	0,34**	0,99**	0,34**	0,25*	0,18	0,47**	0,36**	0,41**	0,35**	0,14	0,21*	0,21*	−0,02	0,38**	0,38**	0,17	0,19	1,00	
Tyr p 2	0,31**	0,74**	0,22*	0,62**	−0,04	0,43**	0,21*	0,25*	0,25*	0,21*	0,34**	0,24*	0,01	0,20*	0,54**	0,23*	0,78**	0,80**	0,18	1,00

*p<0.05; **p<0.01.

Table 3 Multivariate regression models assessing associations among mite allergen-specific IgE levels.

Model	Variable	Coefficient	SE	t	P>t	95%CI	
Aca s	Tyr p	1.26	0.02	58.84	<0.001	1.22	1.30
Blo t 5	Blo t 21	0.61	0.06	11.03	<0.001	0.50	0.72
	Tyr p 2	0.26	0.05	5.51	<0.001	0.17	0.36
	Aca s	0.56	0.18	3.32	0.001	0.24	0.95
Blo t 10	Der p 10	0.37	0.04	8.51	<0.001	0.29	0.46
Blo t 21	Blo t 5	0.71	0.06	12.97	<0.001	0.60	0.82
	Der p 20	0.69	0.11	6.29	<0.001	0.48	0.91
Der f 1	Der p 1	1.12	0.06	18.80	<0.001	1	1.24
Der f 2	Der p 2	1.0	0.01	74.6	0.000	0.98	1.03
Der p[†]	Der p 1	1.21	0.21	5.78	<0.001	0.80	1.63
	Der p 2	0.82	0.11	7.53	<0.001	0.60	1.04
	Der p 10	59.25	18.50	3.20	0.002	22.53	95.98
	Der p 21	0.29	0.13	2.28	0.025	0.04	0.55
	Der p 23	0.56	0.19	2.96	0.004	0.18	0.93
Der p 1	Der f 1	0.70	0.04	18.80	<0.001	0.62	0.77
Der p 2	Der f 2	0.97	0.013	74.59	0.000	0.95	0.99
Der p 5	Lep d 2	0.54	0.11	4.91	<0.001	0.32	0.76
	Der p 2	0.25	0.04	5.19	<0.001	0.15	0.34
Der p 7	Lep d 2	0.27	0.1	2.76	0.007	0.08	0.47
	Der p 1	0.43	0.076	5.68	<0.001	0.28	0.58
Der p 10	Blo t 10	1.13	0.13	8.51	<0.001	0.87	1.4
Der p 20	Blo t 21	0.26	0.04	6.07	<0.001	0.17	0.34
Der p 21	Der p 23	0.43	0.08	5.32	<0.001	0.27	0.59
	Blo t 21	0.71	0.17	4.27	<0.001	0.38	1.04
	Tyr p 2	0.56	0.14	3.87	<0.001	0.27	0.84
Der p 23	Der p 1	0.45	0.1	4.43	<0.001	0.25	0.65
	Der p 2	0.21	0.1	3.73	<0.001	0.2	0.31
	Lep d 2	0.24	0.1	2.42	0.017	0.04	0.43
Gly d 2	Lep d 2	0.63	0.08	7.54	<0.001	0.46	0.79
	Tyr p 2	0.31	0.10	3.27	0.001	0.12	0.51
Lep d[†]	Tyr p 2	0.78	0.2	3.96	<0.001	0.39	1.18
	Lep d 2	0.61	0.17	3.56	0.001	0.27	0.96
	Aca s	1.83	0.50	3.64	<0.001	0.83	2.83
Lep d 2	Gly d 2	0.59	0.08	7.54	<0.001	0.43	0.74
	Tyr p 2	0.40	0.09	4.42	<0.001	0.22	0.57
Tyr p	Aca s	0.77	0.01	58.84	<0.001	0.75	0.80
Tyr p 2	Lep d 2	0.42	0.10	4.42	<0.001	0.23	0.62
	Gly d 2	0.32	0.10	3.27	0.001	0.12	0.51

[†]ImmunoCAP.

p 23 were independently associated with atopic dermatitis. Independent associations were also found between Aca s and Der p 21 and asthma, and between Aca s, Der f 1, and Der p 1 and food allergy. In addition, Der p 7 independently correlated with living in rural environments and Tyr p with rhinitis duration. No significant relationships emerged for Blo t 5, Blo t 10, Blo t 21, Der p 10, or Der p 20 with any clinical or demographic variable.

Association between comorbidities' prevalence and mite sIgE levels

To determine whether clinical comorbidities could be predicted by sIgE to levels of mite allergens, logistic regression analyses were performed. The prevalence of atopic dermatitis was only associated with Der p 23 (OR 1.07; 95%CI: 1.02–1.12; $p = 0.008$). Although the prevalence of asthma approached significance with Aca s ($p = 0.07$), it did not reach the statistical threshold. The prevalence of food allergy was independently associated only with Der p 1 sIgE (OR: 1.05; 95%CI: 1.0–1.11; $p = 0.038$). No significant associations were found between the prevalence of urticaria and any mite allergen sIgE.

Discussion

In this study, we analyzed the sIgE profile and the associations between allergens in mite-allergic patients with allergic rhinitis using a recently introduced allergen multiplex array. Our findings revealed that, while sIgE to Der p 1 was the most prevalent, sIgE to group 2 allergens (Der p 2 and Der f 2) exhibited the highest levels. Notably, Der p 1 levels

Table 4 Multivariate regression models between mite allergen-specific IgE levels and clinical or demographic factors.

Allergen	Variables	Coeff.	SE	t	P>t	95%CI	
Aca s	Asthma	0.60	0.28	2.16	0.033	0.049	1.15
	Food Allergy	0.87	0.43	2.02	0.046	0.016	1.73
Der f 1	Age	−0.34	0.10	−3.36	<0.001	−0.53	−0.14
	Dermatitis	7.10	2.34	3.04	0.003	2.46	11.74
	Food Allergy	8.12	3.70	2.19	0.031	0.763	15.48
Der f 2	Age	−0.49	0.145	−3.37	<0.001	−0.77	−0.20
	Dermatitis	8.95	3.42	2.62	0.010	2.20	15.74
Der p†	Age	−0.92	0.26	−3.52	<0.001	−1.44	−0.42
	Dermatitis	23.07	6.19	3.73	<0.001	10.79	35.35
Der p 1	Age	−0.27	0.08	−3.40	<0.001	−0.43	−0.11
	Food Allergy	8.15	2.96	2.75	0.007	2.27	14.03
	Dermatitis	4.44	1.87	2.38	0.019	0.74	8.15
Der p 2	Age	−0.49	0.14	−3.47	<0.001	−0.77	−0.21
	Dermatitis	9.45	3.33	2.84	0.006	2.84	16.06
Der p 5	Age	−0.32	0.085	−3.72	<0.001	−0.48	−0.15
Der p 7	Age	−0.19	0.07	−2.60	0.011	−0.33	−0.05
	Rural home	6.09	2.02	3.02	0.003	2.09	10.09
Der p 21	Age	−0.30	0.10	−2.91	0.004	−0.51	−0.10
	Asthma	5.32	2.47	2.15	0.034	0.42	10.21
Der p 23	Age	−0.35	0.08	−4.21	<0.001	−0.51	−0.18
	Dermatitis	6.56	1.96	3.36	<0.001	2.68	10.45
Gly d 2	Age	−0.17	0.06	−2.65	0.009	−0.29	−0.04
Lep d†	Age	−0.30	0.11	−2.80	0.006	−0.52	−0.09
Lep d 2	Age	−0.20	0.06	−3.10	0.003	−0.32	−0.07
Tyr p	Age	−0.20	0.06	−3.10	0.003	−0.32	−0.07
Tyr p	Age	−0.13	0.06	−2.31	0.023	−0.24	−0.018

†ImmunoCAP.

were lower than those of most other *Dermatophagoides* allergens, except for Der p 10 and Der p 11. This result contrasts slightly with the study by Rodinkova et al.[11] in an atopic population, where sIgE to Der p 2 and Der f 2 were the most prevalent, and Der p 1 sIgE levels were comparable to other allergens.[11] Interestingly, the prevalence of sIgE to minor allergens such as Der p 5, Der p 7, and Der p 21 was significantly higher than previously reported.[12] The clinical relevance of this increased prevalence remains unclear, but it suggests that these allergens may play a more substantial role in allergic sensitization than previously assumed.

In addition, the apparent absence of sensitization to Der p 11 should be interpreted with caution. Reports using the ALEX2 platform have indicated a decreasing prevalence of this allergen compared to others, which may reflect technical limitations rather than a true absence of sensitization.[11-15] Beyond differences in diagnostic platforms, these discrepancies may also be influenced by variations in study populations, allergen isoforms, or environmental exposures, underscoring the importance of considering regional differences in allergen sensitization patterns.

The molecular profile of storage mites was also evaluated, revealing a high prevalence of sensitization with a wide range of sIgE levels among these patients. Previous studies have highlighted significant geographical variability in the molecular sensitization profile of storage mites, suggesting that climatic factors are key drivers of this variability.[16] Environmental variables such as humidity, temperature, and solar radiation have been shown to modulate the expression of specific mite allergens and their corresponding IgE seasonal responses.[17] Consequently, the seasonal pattern of specific mite allergens may vary depending on their origin (e.g., cuticle- or feces-derived proteins) or function (e.g., digestive enzymes) in response to annual meteorological fluctuations. In this study, we assessed the seasonality of each allergen, and although statistical significance was not reached because of sample size limitations, a consistent seasonal pattern was observed across all allergens, existing differences between allergens of the same mite specie. Overall, these findings further support the hypothesis that climate and environmental conditions play a fundamental role in influencing allergen exposure and sensitization patterns.

The clinical significance of our findings may extend to the evaluation of allergen-specific immunotherapy (AIT). sIgE to Der p 1, Der p 2, and Der p 23 appear to be reliable markers for identifying clinically relevant sensitizations in our population. However, whether these allergens can improve patient stratification or treatment outcomes requires confirmation in prospective studies with clinical follow-up. Notably, patients with *Der p* source allergen levels <2 kU/L were unlikely to exhibit substantial sensitization to any HDM components, while those with levels >10 kU/L were highly likely to have elevated sIgE to at least one major allergen. These findings align with previous studies in Spain, where Der p source allergen below 2kU/L was an adequate cut point to reliably rule out major allergens and potentially optimize treatment efficacy.[18] However, further research is required to determine whether minor HDM components contribute to the overall immunogenic response and whether their exclusion affects the efficacy of AIT. In this context, multipanel allergen arrays have an important advantage in allergic rhinitis diagnosis and treatment planning because of their ability to comprehensively evaluate sensitization profiles. This approach allows for the identification of both major and minor allergenic components, providing a more precise assessment of a patient's molecular sensitization pattern.[19] This, in turn, facilitates a more targeted selection of allergens for AIT, potentially improving therapeutic outcomes and reducing unnecessary exposure to allergens with limited clinical relevance.[20] Future studies should explore the long-term impact of CRD on the efficacy and personalization of AIT strategies.

Our correlation analyses revealed significant associations within specific allergen groups, including group 2 (Der f 2, Der p 2, Gly d 2, Lep d 2, and Tyr p 2), group 5 (Blo t 5, Der p 5), and group 21 (Blo t 21, Der p 21). However, we also observed significant associations between allergens with scarce similarities in molecular structure. This suggests that associations not only depend on molecular cross-reactivity but also parallel exposure and/or sensitization to different allergens. In this context, the discrepancy observed between Lep d (ImmunoCAP) and Lep d 2 (ALEX2) deserves attention. No systematic pattern emerged from the residuals of the regression models (*data not shown*), suggesting that technical differences between platforms are unlikely to account for the observed results. A more plausible explanation is the existence of additional, clinically relevant *L. destructor* allergens beyond Lep d 2, which may distort the correlation between source and molecular allergen measurements.

One of the primary objectives of this study was to evaluate the associations between mite allergens to identify those most relevant for clinical decision-making. The significant interspecies correlations observed highlight the inherent challenges of using serological methods for this purpose. A representative case is patient 70, who, like others in the cohort, exhibited multiple strong sensitizations: *Der p 2* (17.25 kU/L), *Gly d 2* (34.25 kU/L), *Lep d 2* (20.25 kU/L), and *Tyr p 2* (32.35 kU/L). Determining the most appropriate AIT in such patients is particularly complex in regions like Mallorca, where *Dermatophagoides* and *Lepidoglyphus* are predominant in household dust. These findings suggest that while multipanel allergen arrays provide valuable insights, they may not always be sufficient for guiding AIT decisions in patients with extensive polysensitization. Nevertheless, our data provide some guidance on allergen selection in this setting. In Dermatophagoides spp.-sensitized patients, the probability of clinically relevant sensitization to other minor allergens is very low in the absence of Der p 1, Der p 2, or Der p 23. Therefore, these molecules—particularly Der p 2 and Der p 23—emerge as the most relevant candidates for identifying patients suitable for AIT. Regarding storage mites, the high prevalence of sensitization observed in our cohort indicates that, in Mallorca and in regions with similar climatic and environmental conditions, at least one representative of the Acaridae family and one of the Glycyphagidae family should be considered when designing AIT strategies.

Regarding the association with clinical factors, we observed that Aca s and *Der p 21* sIgE levels were statistically higher among patients with asthma, which aligns with previous studies suggesting a role for *Der p 21* in respiratory conditions.[21] However, this association did not translate into a higher incidence of asthma in our cohort, underscoring the complexity of allergen sensitization in disease expression. The role of mite allergens in other atopic diseases remains an area of active investigation. Our study found that atopic dermatitis was associated with increased sIgE levels to *Dermatophagoides* group 1, 2, and 23 allergens, yet only *Der p 23* was independently linked to the prevalence of atopic dermatitis. These findings add to the existing discrepancies in the literature, including the association observed in our cohort between Der p 23 and atopic dermatitis, as some studies have found no clear association between specific HDM components and atopic dermatitis,[22] while others have linked *Der p 11* sensitization to this condition.[13]

Future studies will likely continue to report different sensitization profiles associated with atopic diseases, reflecting the multifactorial nature of these conditions. As Walsemann et al. propose, variations in molecular profiles and their association with atopic diseases, may be driven by differences in sensitization routes, which involve both allergen characteristics (concentration, enzymatic activity, and stability) and individual predispositions (genetics, microbiota, and immune variability).[21] Consequently, molecular diagnostics should be primarily used to guide immunotherapy rather than to predict atopic disease outcomes.

This study has some limitations. Although the sample size was adequate according to the pre-study power calculation, it was still relatively limited and restricted to a single center, which may reduce the generalizability of the findings. Moreover, the insular characteristics of Mallorca could influence allergen exposure patterns and sensitization profiles, and results may differ from those observed in other regions with different geographic and environmental conditions.

Conclusion

Our findings highlight the importance of analyzing regional mite sensitization profiles because of variability in environmental factors and their differential impact on storage and minor HDM allergens. While molecular diagnostics provide valuable insights into allergen-specific sensitization patterns, their application in clinical practice should be tailored to optimize allergen-specific immunotherapy strategies. Further longitudinal studies are needed to clarify the long-term clinical implications of these sensitization patterns and their potential to enhance personalized allergy management.

Ethics Committee Approval

The study was conducted in accordance with the Declaration of Helsinki. The study protocol was reviewed and approved by the Son Espases University Hospital Investigation Board and the Committee for Investigation Ethics of the Balearic Islands, approval number 3801/18. All participants provided written informed consent prior to sample collection and data analysis.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its supplementary material files. Further enquiries can be directed to the corresponding author.

Author's Contributions

All authors meet the ICMJE criteria for authorship. Sendy Chugo, MD, was involved in conceptualization, methodology, data curation, and investigation; Jaime Pons, MD, PhD, looked into methodology and investigation; Danilo Escobar, MD, PhD, was responsible for methodology, investigation, and writing-review and editing; and Daniel Hervás did formal analysis, methodology, validation, and writing-original draft.

Conflict of Interest

The authors have no conflicts of interest to declare.

Funding

This study was supported by an investigation fund by LETI Pharma (Barcelona, Spain). The funder had no role in the design, data collection, data analysis, and reporting of this study.

References

1. Arlian LG, Morgan MS, Neal JS. Dust mite allergens: ecology and distribution. Curr. Allergy Asthma Rep. 2002 Sep;2(5):401-11. https://doi.org/10.1007/s11882-002-0074-2
2. Arlian LG, Platts-Mills TA. The biology of dust mites and the remediation of mite allergens in allergic disease. J. Allergy Clin. Immunol. 2001 Mar;107(3 Suppl):S406-13. https://doi.org/10.1067/mai.2001.113670
3. Acevedo N, Zakzuk J, Caraballo L. House dust mite allergy under changing environments. Allergy Asthma Immunol. Res. 2019 Jul;11(4):450-69. https://doi.org/10.4168/aair.2019.11.4.450
4. Bergmann KC. Biology of house dust mites and storage mites. Allergo. J. Int. 2022 Nov;31(8):272-8. https://doi.org/10.1007/s40629-022-00231-8
5. Ferrándiz R, Casas R, Dreborg S. Cross-reactivity between Dermatophagoides siboney and other domestic mites. II. Analysis of individual cross-reacting allergens after SDS-PAGE and Western blotting inhibition. Int. Arch. Allergy Immunol. 1998 Jul;116(3):206-14. https://doi.org/10.1159/000023946
6. Jakob T, Forstenlechner P, Matricardi P, Kleine-Tebbe J. Molecular allergy diagnostics using multiplex assays: methodological and practical considerations for use in research and clinical routine: Part 21 of the Series Molecular Allergology. Allergo. J. Int. 2015;24:320-32. https://doi.org/10.1007/s40629-015-0087-8
7. Matricardi PM, Kleine-Tebbe J, Hoffmann HJ, Valenta R, Hilger C, Hofmaier S, et al. EAACI molecular allergology user's guide. Pediatr. Allergy Immunol. 2016 May;27 Suppl 23:1-250.
8. Canonica GW, Ansotegui IJ, Pawankar R, Schmid-Grendelmeier P, van Hage M, Baena-Cagnani CE, et al. A WAO - ARIA - GA²LEN consensus document on molecular-based allergy diagnostics. World Allergy Organ. j. 2013;6:17. https://doi.org/10.1186/1939-4551-6-17
9. Bousquet J, Chanez P, Chanal I, Michel FB. Comparison between RAST and Pharmacia CAP system: a new automated specific IgE assay. J. Allergy Clin. Immunol. 1990 Jun;85(6):1039-43. https://doi.org/10.1016/0091-6749(90)90048-9
10. Lis K, Bartuzi Z. Selected technical aspects of molecular allergy diagnostics. Curr. Issues Mol. Biol. 2023 Jun;45(7):5481-93. https://doi.org/10.3390/cimb45070347
11. Rodinkova VV, Yuriev SD, Kryvopustova MV, Mokin VB, Kryzhanovskyi YM, Kurchenko AI. Molecular profile sensitization to house dust mites as an important aspect for predicting the efficiency of allergen immunotherapy. Front. Immunol. 2022;13:848616. https://doi.org/10.3389/fimmu.2022.848616
12. Posa D, Perna S, Resch Y, Lupinek C, Panetta V, Hofmaier S, et al. Evolution and predictive value of IgE responses toward a comprehensive panel of house dust mite allergens during the first 2 decades of life. J. Allergy Clin. Immunol. 2017 Feb;139(2):541-549.e8. https://doi.org/10.1016/j.jaci.2016.08.014
13. Banerjee S, Resch Y, Chen KW, Swoboda I, Focke-Tejkl M, Blatt K, et al. Der p 11 is a major allergen for house dust mite-allergic patients suffering from atopic dermatitis. J. Invest. Dermatol. 2015 Jan;135(1):102-9. https://doi.org/10.1038/jid.2014.271
14. Čelakovská J, Bukač J, Cermákova E, Vaňková R, Skalská H, Krejsek J, et al. Analysis of results of specific IgE in 100 Atopic dermatitis patients with the use of multiplex examination ALEX2—Allergy explorer. Int. J. Mol. Sci. 2021 May;22(10):5286. https://doi.org/10.3390/ijms22105286
15. Lee CS., Tsai LC., Chao PL., Lin CY., Hung MW., Chien AI., et al. Protein sequence analysis of a novel 103-kDa dermatophagoides pteronyssinus mite allergen and prevalence of serum immunoglobulin E reactivity to rDer p 11 in allergic adult patients. Clin. Exp. Allergy. 2004 Mar;34(3):354-62. https://doi.org/10.1111/j.1365-2222.2004.01878.x
16. Boquete M, Carballada F, Armisen M, Nieto A, Martín S, Polo F, et al. Factors influencing the clinical picture and the differential sensitization to house dust mites and storage mites. J. Investig. Allergol Clin. Immunol. 2000;10(4):229-34.
17. Hervás D, Pons J, Milá J, Matamoros N, Hervás JA, García-Marcos L. Specific IgE levels to dermatophagoides pteronyssinus are associated with meteorological factors. Int. Arch. Allergy Immunol. 2013;160(4):383-6. https://doi.org/10.1159/000342444
18. Letrán A, García I, Espinazo-Romeu M, Moreno-Aguilar C, Moreno F. Cut-off value of D. pteronyssinus specific IgE in double negative patients Der p 1 and Der p 2 and its clinical repercussion. Sci. Rep. 2021 Dec;11(1):23585. https://doi.org/10.1038/s41598-021-03005-4
19. Sánchez-Borges M, Fernandez-Caldas E, Thomas WR, Chapman MD, Lee BW, Caraballo L, et al. International

consensus (ICON) on: clinical consequences of mite hypersensitivity, a global problem. World Allergy Organ. J. 2017;10:14. https://doi.org/10.1186/s40413-017-0145-4

20. Valenta R, Lidholm J, Niederberger V, Hayek B, Kraft D, Grönlund H. The recombinant allergen-based concept of component-resolved diagnostics and immunotherapy (CRD and CRIT). Clin. Exp. Allergy. 1999 Jul;29(7):896–904. https://doi.org/10.1046/j.1365-2222.1999.00653.x
21. Walsemann T, Böttger M, Traidl S, Schwager C, Gülsen A, Freimooser S, et al. Specific IgE against the house dust mite allergens Der p 5, 20 and 21 influences the phenotype and severity of atopic diseases. Allergy. 2023 Mar;78(3):731–42. https://doi.org/10.1111/all.15553
22. Kidon MI, Chiang WC, Liew WK, Ong TC, Tiong YS, Wong KN, et al. Mite component-specific IgE repertoire and phenotypes of allergic disease in childhood: the tropical perspective. Pediatr. Allergy Immunol. 2011 Mar;22(2):202–10. https://doi.org/10.1111/j.1399-3038.2010.01094.x

Supplementary

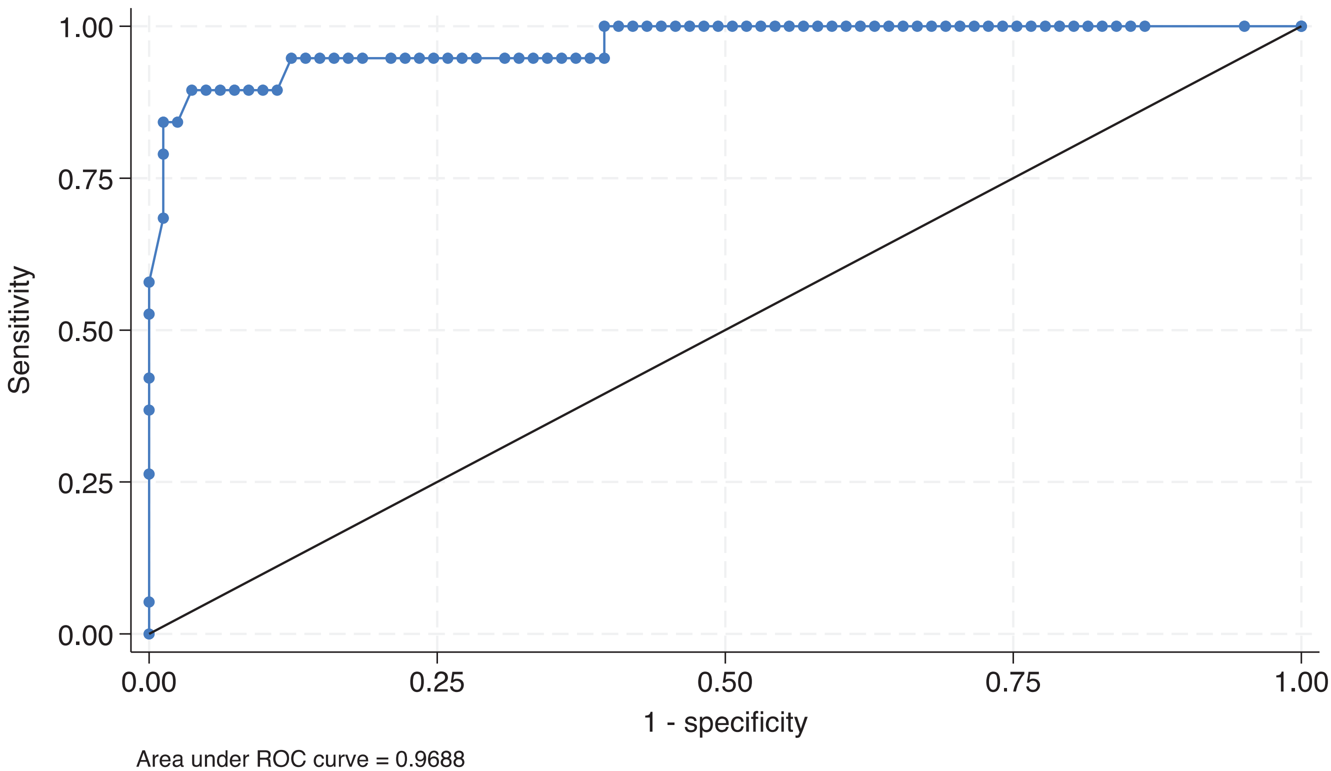

Figure S1 ROC curve for predicting the absence of major allergens (Der p 1, Der p 2, Der p 23) based on the sIgE to Der p source allergen.

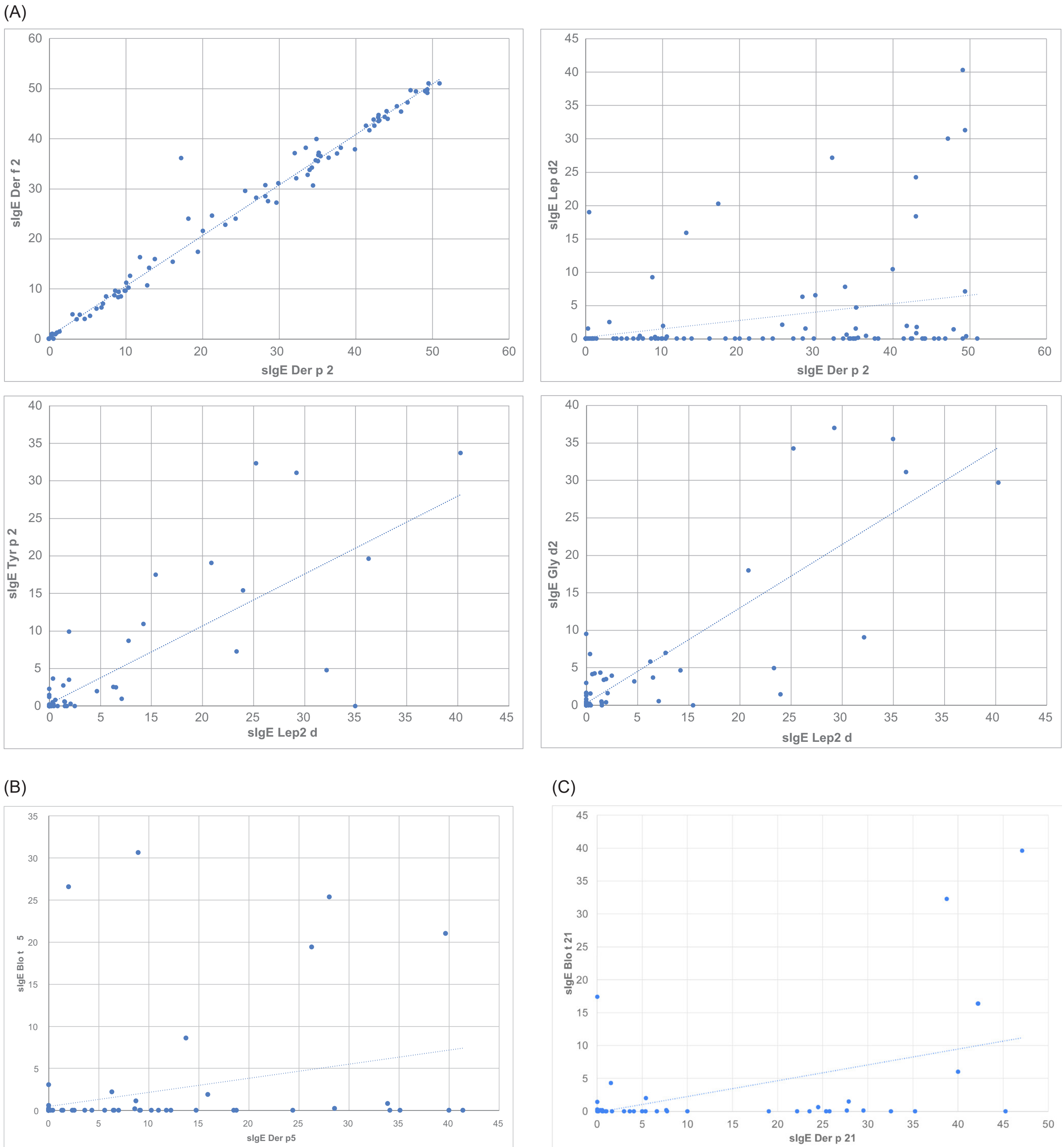

Figure S2 (A) Scatter plots illustrating the univariate regression between group 2 allergens. (B) Scatter plot illustrating the univariate regression between group 5 allergens. (C) Scatter plot illustrating the univariate regression between group 21 allergens.

Table S1 Simple correlation between mite allergen sIgElevels and sensitization number

Allergens	r
Aca s	0,44**
Blo t 10	0,21*
Blo t 21	0,43**
Blo t 5	0,48**
Der f 1	0,49**
Der f 2	0,65**
Der p 1	0,50**
Der p 2	0,64**
Der p 5	0,51**
Der p 7	0,44**
Der p 10	0,19
Der p 20	0,26**
Der p 21	0,56**
Der p 23	0,49**
Gly d 2	0,51**
Lep d 2	0,54**
Tyr p	0,37**
Tyr p 2	0,47**

*p<0.05; **p<0.01