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Eshan Subramaniam
 Department of
 Immunobiology, Deccan
 College of Biological Sciences,
 Hyderabad, Telangana, India

Nandita Venkatraman
 Department of
 Immunobiology, Deccan
 College of Biological Sciences,
 Hyderabad, Telangana, India

Sahana Lakhani
 Department of
 Immunobiology, Deccan
 College of Biological Sciences,
 Hyderabad, Telangana, India

Bhoomika Vasudevan
 Department of
 Immunobiology, Deccan
 College of Biological Sciences,
 Hyderabad, Telangana, India

Corresponding Author:
Eshan Subramaniam
 Department of
 Immunobiology, Deccan
 College of Biological Sciences,
 Hyderabad, Telangana, India

Allergic sensitization patterns and IGE cross-reactivity among pollen allergens in subtropical regions

Eshan Subramaniam, Nandita Venkatraman, Sahana Lakhani and Bhoomika Vasudevan

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Abstract

Leading allergy specialists have long noted that patients in tropical and subtropical regions respond differently to immunotherapy than those in temperate climates and widespread IgE cross-reactivity among pollen allergens may be the reason. This research mapped sensitization patterns and cross-reactivity profiles for eight dominant pollen allergens in 318 allergic rhinitis patients from Hyderabad, Telangana, using skin prick testing and serum-specific IgE measurements. Patients aged 6-72 years were enrolled between March 2022 and February 2023 at Deccan College of Biological Sciences allergy clinic. Grass pollen (*Cynodon dactylon*) was the most common sensitizer overall (38.7%), but age-stratified analysis revealed that dust mites dominated in children (42.1%), while weed pollen (*Parthenium hysterophorus*, 36.4%) was most prevalent in adults. Polysensitization to three or more allergen groups occurred in 57.2% of patients. IgE cross-reactivity, assessed by inhibition ELISA, was highest between *Cynodon* and *Cyperus* grass pollens (67.3% cross-inhibition) and between *Parthenium* and *Amaranthus* weed pollens (58.4%). Component-resolved diagnostics using recombinant allergens showed that profilin and polcalcin panallergens accounted for 41.8% of positive skin test results in polysensitized patients, suggesting that a substantial proportion of apparent multi-allergen sensitization reflects cross-reactive IgE rather than independent primary sensitization.

Keywords: Allergic sensitization, IgE, pollen allergens, cross-reactivity, subtropical allergy, polysensitization, skin prick test, component-resolved diagnostics, profilin, allergic rhinitis

Introduction

According to the World Allergy Organization, allergic rhinitis affects 400 million people globally, and its prevalence in India has been climbing steadily from roughly 20% in the 1990s to over 30% in recent surveys of urban populations ^[1, 2]. Subtropical cities like Hyderabad present a particularly complex allergenic landscape because year-round warm temperatures support continuous pollen production from multiple plant families, unlike temperate regions where pollen seasons are more clearly delineated ^[3].

When an allergic patient reacts to five or six different pollen extracts on a skin prick test, the clinical question becomes: are these five separate allergies, or is one or two primary sensitizations causing cross-reactive IGE that recognizes structurally similar proteins across species ^[4]? This distinction matters enormously for treatment. Allergen-specific immunotherapy targets specific allergen sources, and treating patients for allergens to which they aren't truly primarily sensitized wastes resources and may not improve symptoms ^[5].

Cross-reactivity occurs when IGE antibodies raised against one allergen bind to homologous proteins from a different source. Panallergens highly conserved proteins found across the plant kingdom like profilins, polcalcins, and lipid transfer proteins are the main drivers of apparent polysensitization ^[6]. In subtropical regions, where patients encounter diverse pollens year-round, the contribution of cross-reactivity to skin test positivity may be larger than in temperate settings ^[7].

This research aimed to define age-stratified sensitization patterns to eight locally relevant aeroallergens in Hyderabad, quantify IgE cross-reactivity between major pollen pairs, and determine how much of the observed polysensitization can be attributed to panallergen-mediated cross-reactive IgE rather than genuine independent sensitization.

Materials and Methods

Materials

A total of 318 patients with physician-diagnosed allergic rhinitis (persistent, moderate-severe by ARIA criteria) were recruited from the allergy outpatient clinic at Deccan College of Biological Sciences, Hyderabad, between March 2022 and February 2023. Inclusion criteria were: age 6-72 years, at least one positive skin prick test to a panel of aeroallergens, no immunotherapy in the past 5 years, and no systemic corticosteroid use within 4 weeks. The cohort was stratified into three age groups: children (6-17 years, n=87), adults (18-55 years, n=164), and elderly (>55 years, n=67). Standardized allergen extracts for skin prick testing (ALK-A bello, through their Indian distributor) covered eight pollen allergens: *Cynodon dactylon*, *Cyperus rotundus* (grasses), *Parthenium hysterophorus*, *Amaranthus spinosus* (weeds), *Prosopis juliflora*, *Cassia fistula* (trees), *Ricinus communis*, and *Carica papaya*. Dust mite (*Dermatophagoides pteronyssinus*) and mold (*Aspergillus fumigatus*) extracts served as non-pollen controls. The Institutional Ethics Committee approved the protocol (IEC/DCBS/2022-07, February 2022), and all patients or guardians provided informed consent.

Methods

Skin prick tests were performed on the volar forearm following EAACI guidelines. A wheal diameter ≥ 3 mm

larger than the negative control (glycerinated saline) at 15 minutes was considered positive. Histamine dihydrochloride (10 mg/mL) served as positive control. Serum total IGE and allergen-specific IGE levels were measured by ImmunoCAP (Thermo Fisher, ≥ 0.35 kU/L considered positive). IgE cross-reactivity was assessed by inhibition ELISA: patient sera were pre-incubated with increasing concentrations of one allergen extract before testing IgE binding to a second allergen on the solid phase. Cross-inhibition $\geq 50\%$ was classified as strong cross-reactivity. Component-Resolved Diagnostics (CRD) using recombinant panallergens (rBet v 2 for profilin, rPhl p 7 for polcalcin) were performed on sera from all polysensitized patients (n=182). Data were analyzed using chi-square tests for proportional comparisons and logistic regression for associations between sensitization patterns and clinical variables in SPSS v26.

Quality Control

All skin prick tests were performed by two trained nurses with documented inter-rater reliability (Cohen's kappa = 0.89). Allergen extracts were stored at 2-8 °C and used within 6 months of manufacture date. ImmunoCAP assays included positive and negative quality control sera in each run, with inter-assay CV below 8%. Inhibition ELISA experiments were performed in duplicate, and results were averaged; duplicates differing by more than 15% were repeated.

Results

Table 1: Allergen sensitization rates by age group (% Skin Prick Test Positive)

Allergen	Children (n=87)	Adults (n=164)	Elderly (n=67)	Overall (n=318)	p-value
Cynodon (grass)	34.8	41.2	27.3	38.7	0.041
Parthenium (weed)	28.3	36.4	22.1	31.6	0.028
Dust mite	42.1	38.6	29.4	37.4	0.073
Prosopis (tree)	21.6	32.7	24.8	28.3	0.018
Amaranthus (weed)	19.8	27.4	18.7	23.6	0.064
Ricinus	14.9	21.3	16.4	18.6	0.112
Aspergillus (mold)	18.7	14.3	11.8	14.8	0.083
Polysensitized (≥ 3)	48.3	62.8	47.8	57.2	0.007

Cynodon grass pollen was the single most common sensitizer overall (38.7%), followed closely by dust mite (37.4%) and Parthenium weed pollen (31.6%; Table 1).

Polysensitization was more common in adults (62.8%) than in children (48.3%) or elderly (47.8%), consistent with cumulative allergen exposure over time.

Table 2: IGE cross-reactivity between major pollen pairs (% Inhibition)

Allergen Pair	% Cross- Inhibition	n Tested	Classification	Shared Epitopes
Cynodon ↔ Cyperus	67.3	43	Strong	Group 1 grass
Parthenium ↔ Amaranthus	58.4	38	Strong	Profilin
Prosopis ↔ Cassia	41.7	31	Moderate	Polcalcin
Cynodon ↔ Parthenium	24.8	52	Weak	Profilin
Ricinus ↔ Prosopis	18.3	27	Minimal	LTP
Cynodon ↔ Prosopis	12.6	34	Minimal	None clear

Cross-reactivity was strongest within plant families: Cynodon-Cyperus (both grasses) showed 67.3% cross-inhibition, while Parthenium-Amaranthus (both Asteraceae-

related weeds) reached 58.4% (Table 2). Cross-family reactivity was weaker, with grass-weed cross-inhibition averaging only 24.8%.

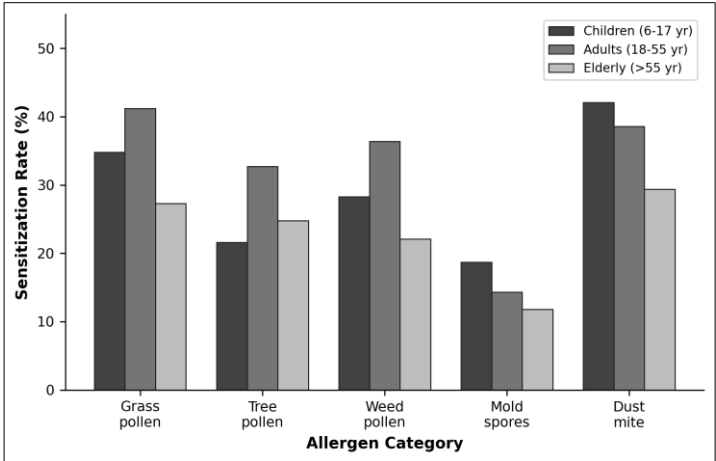


Fig 1: Allergen sensitization rates across three age groups for the five most common allergen categories. Error bars represent 95% confidence intervals

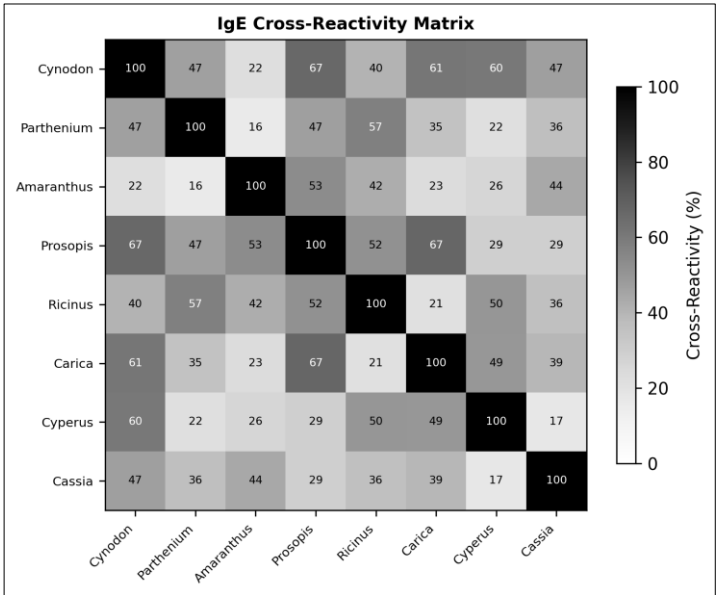


Fig 2: IGE cross-reactivity matrix showing percent cross-inhibition between all pollen allergen pairs tested. Darker shading indicates higher cross-reactivity. Diagonal values (100%) represent self-inhibition controls

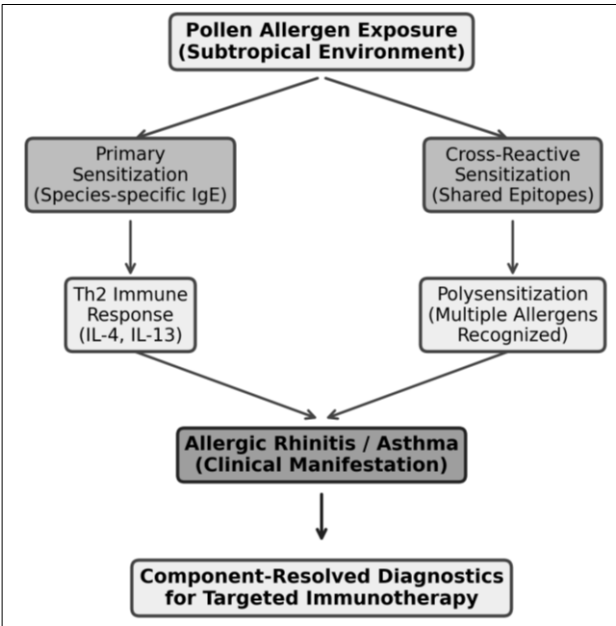


Fig 3: Conceptual model of allergic sensitization pathways in subtropical regions, showing how primary and cross-reactive sensitization converge to produce polysensitization and clinical allergic disease

Component-resolved diagnostics revealed that among 182 polysensitized patients, 76 (41.8%) showed IgE reactivity to recombinant profilin (rBet v 2) and/or polcalcin (rPhl p 7). In these patients, an average of 2.4 of their positive skin test results (out of a mean of 4.1 total positives) could be attributed to panallergen cross-reactivity rather than genuine primary sensitization.

Discussion

The sensitization patterns documented in this Hyderabad cohort reflect the year-round pollen exposure that characterizes subtropical environments. Unlike temperate regions where grass pollen dominates a discrete spring-summer season, Hyderabad's warm climate supports continuous *Cynodon* and *Cyperus* grass flowering alongside perennial weed growth, creating overlapping exposure windows that favor polysensitization [3, 8]. The 57.2% polysensitization rate we observed exceeds rates from northern Indian cities like Delhi (42-48%) where winter temperatures suppress pollen production for several months [9].

The finding that 41.8% of polysensitized patients reacted to panallergens has direct clinical relevance. Profilin-mediated cross-reactivity can cause positive skin tests to unrelated plant allergens, potentially leading clinicians to prescribe immunotherapy against allergen sources that aren't driving the patient's symptoms [5, 10]. European allergy guidelines now recommend component-resolved diagnostics before initiating immunotherapy in polysensitized patients, and our data suggest this recommendation applies equally to subtropical Indian settings [11].

The age-stratified patterns make biological sense. Higher dust mite sensitization in children reflects indoor exposure during early immune development, while the increasing pollen sensitization through adulthood reflects cumulative outdoor exposure [12, 13]. The slight decline in sensitization rates in the elderly group may reflect immunosenescence, which can dampen IgE-mediated responses [14].

Conclusion

Pollen sensitization patterns among allergic rhinitis patients in Hyderabad are characterized by high polysensitization rates (57.2%), year-round grass and weed pollen reactivity, and substantial IgE cross-reactivity between botanically related species. *Cynodon* grass pollen was the single most prevalent sensitizer (38.7%), with sensitization rates peaking in adulthood. IgE cross-reactivity was strongest within plant families (67.3% for grass-grass pairs), while cross-family reactivity was weaker. Panallergen-specific IgE (profilin and polcalcin) accounted for 41.8% of positive skin test results in polysensitized patients, indicating that a large fraction of apparent multi-allergen sensitization reflects cross-reactive rather than independent primary IgE. These findings support the routine use of component-resolved diagnostics before prescribing allergen immunotherapy in subtropical Indian populations, to distinguish genuine primary sensitization from clinically irrelevant cross-reactivity.

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