

ORIGINAL ARTICLE

An Italian 15-year single-center retrospective study on the distribution of peach fruit and pollen-related to peach fruit allergens in a population of north Italy

Peach fruit and peach-related allergens distribution

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Summary

Background. Peach allergy is a common cause of food allergy in Mediterranean populations, often linked to pollen sensitization. Longitudinal data on peach and inhalant allergen sensitization remain limited, especially in pediatric cohorts. This retrospective study evaluated allergen sensitization patterns in 9,986 patients attending IRCCS San Gerardo dei Tintori, Monza, from 2010 to 2024.

Methods. Extract-based specific IgE levels were measured for peach fruit (*Prunus persica*, f95) and seven major inhalant allergens involved in cross-reactivity, including birch (*Betula verrucosa*, t3), ragweed (*Ambrosia artemisiifolia*, w1), and timothy grass (*Phleum pratense*, g6). **Results.** The most prevalent IgE sensitizations were to timothy grass (g6, 11%), ragweed (w1, 11%), and birch pollen (t3, 10%). Distinct sensitization profiles were observed between adults and children. Among 352 f95-positive patients, 50 (14.2%) (26 adults, 24 pediatrics) were monosensitized to peach, suggesting potential primary sensitization independent from pollen cross-reactivity. Longitudinal analysis revealed stable sensitization to major pollens but a marked increase in f95 positivity occurred after

2019, particularly in subjects aged 7–12 years. **Conclusions.** The identification of monosensitized pediatrics highlights the need for molecular diagnostic approaches to distinguish between secondary cross-reactivity and primary food allergy. These findings showed evolving sensitization trends, likely influenced by environmental or exposure-related factors, dietary and lifestyle. The study supports the need for continued epidemiological monitoring and the integration of molecular allergology in clinical practice to enhance personalized allergy management.

Key words

Peach; pollen, allergy; paediatric population; adult population; food; cross-reactivity.

IMPACT STATEMENT

Peach sensitization increased after 2019, particularly in children, with 7% monosensitized, indicating primary allergy. Stable pollen trends and emerging patterns highlighted the need for molecular diagnostics and continued epidemiological monitoring.

1.Introduction

Allergic diseases, including respiratory and food allergies (FA), have emerged as prevalent conditions with an increasing global incidence, affecting approximately 3–10% of children and up to 10% of adults worldwide (1-3). The global prevalence of FA shows significant variability, ranging from 0.14% in India to 5.6% in Switzerland, though self-reported figures in Europe can reach up to 35.0% (1-7). This heterogeneity is influenced by a complex interplay of intrinsic factors, such as age, genetics, and ethnicity, and extrinsic variables, including geographical area, dietary habits, and diagnostic methodologies (1-3). Among the various mechanisms involved, IgE-mediated reactions remain the most clinically significant. Accordingly, the recent European Academy of Allergy and Clinical Immunology (EAACI) guidelines recommend diagnosing IgE-mediated FA through a combination of clinical symptoms and the presence of specific IgE against the suspected food

(2,6,7,10). In Europe, and also in Northern Italy, the allergenic profile is dominated by sensitization to aeroallergens, which serve both as a primary cause of respiratory disease and as a driver of Pollen-Food Allergy Syndrome (PFAS) through cross-reactivity (4).

About 400 allergenic proteins from over 170 different foods have been identified as triggers of IgE-mediated reactions. Many of these proteins share structural homologs with pollen allergens, such as *Betula verrucosa* and *Phleum pratense*, which often act as the primary sensitizing agents (4,6,7,10).

A prominent example of this interplay is the peach (*Prunus persica*), a member of the *Rosaceae* family (4,11). The peach allergy exhibits significant geographical and molecular heterogeneity. In Northern and Central Europe, it is frequently secondary to birch pollen sensitization, typically presenting as mild oral symptoms (4). Conversely, in Mediterranean countries, fruit allergies often occur independently of pollinosis and are associated with more severe systemic reactions (4,7,11,12). These severe phenotypes are frequently linked to Lipid Transfer Proteins (LTPs). Notably, while LTP sensitization is a hallmark of Mediterranean fruit allergy, it is now recognized as a clinically relevant sensitizing allergen in Northern Europe as well, complicating the traditional geographical diagnostic paradigms (13).

Despite the high prevalence of aeroallergens and their link to food cross-reactivity, longitudinal data on the distribution of specific pollen sensitizations and their relationship with peach fruit remain limited, particularly in pediatric cohorts. The aim of this study was to perform a retrospective analysis of allergen distribution patterns in the population attending the IRCCS San Gerardo dei Tintori, Monza, located in Lombardy, in Northern Italy, over a fifteen-year period, from 2010 to 2024. The assessment of a broad spectrum of allergens, specifically f95 (*Prunus persica*), t3 (*Betula verrucosa*), t9 (*Olea europaea*), t23 (*Cupressus sempervirens*), w1 (*Ambrosia artemisiifolia*), w3 (*Ambrosia trifida*), w6 (*Artemisia vulgaris*), and g6 (*Phleum pratense*), could facilitate a better understanding of specific IgE prevalence in this region and a comprehensive overview of immunological profiles. Furthermore, it provides an evidence-based foundation for targeted public health interventions and allergy management strategies.

2. Materials and Methods

2.1. Study Design and Population

A retrospective study was performed to assess the distribution of allergen sensitization in subjects attending IRCCS San Gerardo dei Tintori, Monza, between January 1, 2010, and December 31, 2024. Data were extracted from the Laboratory database. The prevalence of sensitization to eight allergens (one food f95 (*Prunus persica*), and eight pollens, t3 (*Betula verrucosa*), t9 (*Olea europaea*), t23 (*Cupressus sempervirens*), w1 (*Ambrosia artemisiifolia*), w3 (*Ambrosia trifida*), w6 (*Artemisia vulgaris*) and g6 (*Phleum pratense*), was determined by calculating the percentage of individuals who tested positive for each specific allergen.

The local ethics committee did not require informed consent because all subjects' data were de-identified.

2.2. Determination of specific IgE

Sera were collected by venous blood sampling and stored at 2-8 °C. Specific IgE of the eight allergen sources were quantified by ImmunoCAP technology following the manufacturer's recommendations (Thermo-Fisher Scientific Phadia, AB Uppsala, Sweden). We used a cut-off value of >0.15 kUA/L for specific IgE positivity to identify low-level sensitizations, allowing us to capture a comprehensive overview of the population's immunological profile s where low levels can be relevant or predictive of future allergic disease (14).

2.3. Statistical analysis

Statistical analyses were performed using Microsoft Excel 2016 (Microsoft, Redmond, WA, USA). The chi-square (χ^2) test was used to compare the results obtained in the different groups, and it was performed using MedCalc for Windows, version 19.4 (MedCalc Software, Ostend, Belgium).

Concentration values reported as > 100 mg/L were assigned the values 100 kUA/L. A p value < 0.05 was considered statistically significant.

Results

A total of 9,986 patients were included in the analysis, with a median age of 30 years (range: 1–96 years). Females represented 56% ($n = 5,642$) of the cohort. Adults (aged 18–99 years) comprised 55% of the population (1,772 males and 3,684 females), whereas pediatric patients (aged 0–17 years) constituted the remaining 45% (2,572 males and 1,958 females).

The most prevalent sensitizing allergens identified were timothy grass (*Phleum pratense*, g6; 11%), ragweed (*Ambrosia artemisiifolia*, w1; 11%), and birch pollen (*Betula verrucosa*, t3; 10%), followed by olive pollen (*Olea europaea*, t9; 4%), cypress pollen (*Cupressus sempervirens*, t23; 4%), peach fruit (*Prunus persica*, f95; 4 %), and wormwood pollen (*Artemisia vulgaris*, w6; 2%).

Analysis of allergen sensitization revealed distinct patterns between adult and pediatric populations, particularly in multiple sensitization and monosensitization profiles to inhalant allergens and the peach fruit allergen (Table 1). Sensitization analysis among *Asteraceae* allergens—including ragweed (w1), giant ragweed (w3), and mugwort (w6)—demonstrated limited overlap, with 89 subjects sensitized to both w1 and w3, and 22 to both w3 and w6. While 557 individuals exhibited simultaneous sensitization to timothy grass (g6) and birch pollen (t3), only 29 showed concurrent sensitization to timothy grass and cypress pollen (t23), indicating a lower frequency of association between the latter allergens. Birch pollen (t3) also showed substantial overlap with ragweed (w1), with 631 patients sensitized to both allergens.

Among the 352 subjects (214 adults, 138 paediatrics) sensitized to the peach fruit allergen (f95), the most frequently associated sensitizations were to birch pollen (145 patients, 41.2%), followed by ragweed (118 patients, 33.5%), and timothy grass (79 patients, 22.4%). Additional associations were observed with olive pollen (75 patients, 21.3%), mugwort (45 patients, 12.8%), cypress (34 patients, 9.7%), and giant ragweed (15 patients, 4.3%). Age stratification of peach-sensitized pediatric subjects

revealed the highest prevalence among children aged 7–12 years (68 cases, 49%), followed by those aged 13–17 years (39 cases, 28%), and those aged 0–6 years (31 cases, 21%) ($p < 0.05$). Notably, 50 patients (14.2%) were monosensitized exclusively to peach, without sensitization to other allergens. Among these monosensitized individuals, the 24 pediatric cases (0–17 years) were more common in males (14 males vs. 10 females), while in the 26 adults (18–99 years), females predominated (16 females vs. 10 males).

Longitudinal data from 2010 to 2024 revealed dynamic trends in sensitization rates, also considering pre- and post-pandemic Covid-19 period, when the patients had more difficult access to allergy clinic (Figure 1). Sensitization to the peach declined from 15% (54/352) cases in 2010 to 3% (12/352) in 2019, followed by a rise, with 7% (26/352) cases in 2023 and 10% (36/352) in 2024 ($p < 0.05$). Birch and ragweed were the most frequently detected allergens, with 948 and 998 positive cases, respectively, showing relative stability over time. Timothy grass also showed a consistently high prevalence, with 1,050 positive cases and a minor upward trend in recent years. In contrast, less prevalent allergens such as giant ragweed and mugwort exhibited lower and stable sensitization rates.

Discussion

This retrospective longitudinal analysis of allergen sensitization in nearly 10,000 subjects over 15 years provides significant insights into the complex interplay between inhalant and food allergens, with a particular focus on peach fruit allergen and predominant pollens such as birch, ragweed, and timothy grass. The persistent prevalence of these pollens corroborated prior epidemiological studies that identified them as major inhalant allergens in different populations (15).

The presence of sensitization to birch pollen and peach fruit allergen suggested the critical role for cross-reactive panallergens, including LTPs, PR-10 and profilin proteins, in driving allergic sensitization (15,16). Our identification of a subset of monosensitized subjects to peach fruit allergen may align with the hypothesis of primary sensitization through allergens such as LTPs, as described in previous literature (4,16). However, as our study utilized allergen extracts, we cannot definitively attribute these sensitization patterns to specific molecular components. Review data from Hassan and

Venkatesh and Miralles-Lopez highlighted LTPs as major causative agents in Mediterranean fruit allergy, offering a potential framework for our observations (17,18). It is noteworthy that in our population, peach-sensitized individuals showed significant co-sensitization to olive and mugwort pollens. Evidence suggests that primary sensitization to these pollens, specifically via allergens such as Ole e 7 and Art v 3, may act as a relevant driver for LTP-mediated fruit allergy, further complicating the sensitization profile in our Northern Italian population. Although we observed a pediatric subgroup monosensitized to peach, the absence of clinical data prevented us from determining the actual prevalence of clinical allergy versus asymptomatic molecular sensitization, that is a well-known challenge in Mediterranean regions (19). Nevertheless, our findings highlighted the critical need to differentiate between IgE sensitization and clinical allergy through comprehensive diagnostic evaluation in future prospective studies.

Geographical variability in peach allergy prevalence and clinical phenotypes has been well documented. D'Aiuto and coauthors reported a notably high burden of LTP-mediated peach allergy in Southern Italy, frequently associated with systemic reactions. These regional differences likely arise from environmental, genetic, dietary and botanical factors that influence sensitization patterns and reinforce the imperative for region-specific epidemiological data to assist clinicians in diagnosis (7). Our study, although conducted in Northern Italy, within a Mediterranean context, confirmed such regional sensitization trends and highlighted the importance of geographic considerations in allergens profiling.

The observed increase in peach allergen sensitization among children aged 7 to 12 years aligned with the emerging recognition of pediatric fruit sensitization as a significant clinical health problem. Olivieri and colleagues delineated the clinical role of LTP allergy in children, underlining that while sensitization is frequent in Mediterranean populations, not all sensitized children develop symptomatic allergy. Their multicenter study across Italian pediatric allergy centers reported a clinically significant proportion of LTP-sensitized children with either no symptoms or mild Pollen-Food Allergy Syndrome, reinforcing the need for diagnostic tools that can accurately discriminate

between mere IgE sensitization and clinically relevant LTP allergy (22). Ando and coauthors demonstrated that Component-Resolved Diagnostics (CRD) targeting peach allergen-specific IgE can effectively assess and distinguish the risk of local from systemic allergic phenotypes, offering substantial clinical utility in guiding prognosis and therapeutic decisions (23). Our data, revealing diverse mono- and polysensitization profiles, support the integration of CRD in routine allergy diagnostics to enable personalized management strategies, including dietary guidance behavioral advice and immunotherapy. This perspective is reinforced by Indolfi et al., who conducted a 10-year retrospective study in a large Italian pediatric cohort, observing a significant increase in sensitization to LTPs, particularly the Pru p 3 peach allergen. Their analysis revealed a predominance of mono- and oligo-sensitized profiles in school-aged children, further supporting the concept that LTP sensitization may occur independently of broader polysensitization patterns. Moreover, they emphasized the clinical variability among sensitized subjects and the importance of comprehensive phenotypic characterization to guide appropriate clinical management (24).

Furthermore, while recent research has identified Pru p 7 as a major contributor to severe peach allergy linked to cypress pollen (25,26), the frequent co-sensitization to peach and cypress observed in our database can only be considered suggestive of such a molecular link. Without specific Pru p 7 IgE data, we cannot confirm this distinct molecular profile in our cohort. Nevertheless, these trends emphasize the importance of considering geographic exposure to specific pollens when interpreting peach sensitization.

Lastly, the complex polysensitization networks involving *Asteraceae* allergens alongside multiple tree and grass pollens, underscored the heterogeneity of allergic sensitization and its implications for treatment. Molecular allergology remains indispensable for dissecting these intricate profiles assessing and helping to stratify risk and tailoring and monitoring immunotherapeutic interventions (4).

Our findings reflect the complexity of allergen sensitization in this large Northern Italian cohort over 15 years. The recent Olivieri, Scadding, and Skypala's review on LTP allergy proposed a diagnostic

algorithm that stratified LTP-sensitized individuals by clinical risk, incorporating factors such as co-sensitization to stable proteins, geographic and age-related exposure, and presence of cofactors (e.g., exercise, NSAIDs) that may amplify allergic response (27). This model not only could enhance diagnostic accuracy but also improve personalized therapeutic interventions, including dietary counseling, immunotherapy planning, and follow-up scheduling based on individual clinical risk. Future multicenter, prospective studies are essential to validate these models and establish standardized, evidence-based guidelines for managing LTP-related peach allergy in children.

Some limitations of this study must be acknowledged: (1) the work was retrospective and performed in a single center, and a larger number of subjects is needed to confirm our results; (2) CRD analysis was not performed due to the lack of available data for most of the study period. In fact, from 2010 to 2020, CRD was rarely used in routine clinical practice. In contrast, following the COVID-19 pandemic, clinicians increasingly prescribed molecular allergen diagnostics, likely due not only to greater expertise but also to the accumulation of scientific evidence highlighting the fundamental role of CRD in allergy diagnosis.

Collectively, our findings underlined significant age-related and geographical heterogeneity in sensitization trends, reinforcing the complexity of managing peach-sensitized subjects in a Mediterranean context. Our data support the integration of molecular diagnostics and clinical phenotyping into routine practice to accurately differentiate between asymptomatic cross-reactivity and high-risk clinical allergy, particularly in pediatric subjects. Future research should aim to elucidate environmental and genetic determinants of sensitization dynamics, refine CRD-based phenotyping, and enhance clinical management of pediatric and adult peach fruit allergy.

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Author contributions: JI and AS wrote the manuscript; JI, AS, and MC designed the study; FB, CD, EZ, and NN performed the sample analysis; JI, AS, and MC critically revised the manuscript. All authors read and approved the final draft for submission.

Competing interests: None declared.

Informed consent: The local ethics committee did not require informed consent because all subjects' data were de-identified.

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Data Statement

The datasets used during the current study are available from the corresponding author on reasonable request.

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Table 1: Number of patients sensitized to individual allergens and Co-Sensitized to allergen pairs based on specific IgE levels (>0.15 kU/L)

Allergen	f95 <i>(Prunus persica)</i>	t3 <i>(Betula verrucose)</i>	t9 <i>(Olea europaea)</i>	t23 <i>(Cupressus sempervirens)</i>	w1 <i>(Ambrosia artemisiifolia)</i>	w3 <i>(Ambrosia trifida)</i>	w6 <i>(Artemisia vulgaris)</i>	g6 <i>(Phleum pratense)</i>
f95	352	145	75	34	118	15	45	79
t3		948	268	197	631	53	145	557
t9			386	126	271	26	131	266
t23				317	261	27	70	29
w1					998	89	193	574
w3						105	22	57
w6							214	135
g6								1,050

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Figure's legend

Figure 1: Trends in f95 (*Prunus persica*), t3 (*Betula verrucose*), t9 (*Olea europaea*), t23 (*Cupressus sempervirens*), w1 (*Ambrosia artemisiifolia*), w3 (*Ambrosia trifida*), w6 (*Artemisia vulgaris*) and g6 (*Phleum pratense*) sensitization from 2010 to 2024.

