Allergic Disease Phenotypes and Their Clinical Correlates: A Real-World Observational Analysis

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ABSTRACT

Background: Allergic diseases present with diverse clinical phenotypes and variable treatment outcomes. Understanding the relationship between these phenotypes and clinical responses to allergen immunotherapy (AIT) in real-world settings is critical for optimizing care and improving adherence. **Objective:** This study aimed to evaluate the clinical and demographic characteristics associated with treatment outcomes in patients undergoing AIT and to explore the relationship between allergic disease phenotypes and adherence in routine practice. **Methods:** In this an observational cross-sectional study, we analyzed data from 109 patients treated with AIT between 2020 and 2022 at a tertiary allergy center. Patients were grouped based on clinical outcome into "improved" or "discontinued." Variables assessed included sex, year of treatment initiation, number and type of allergic diseases, and presence of multiple allergy phenotypes. Associations were tested using Chi-square statistics, with $p < 0.05$ considered significant. **Results:** Of the 109 patients, 66 (60.6%) reported clinical improvement, while 37 (33.9%) discontinued therapy. The most frequent phenotypes were allergic rhinitis (52.3%), urticaria (50.5%), and bronchial asthma (47.7%). Improvement rates were highest among patients with allergic rhinitis (71.9%), asthma (71.2%), and those with four or more coexisting allergies (85.7%), although differences were not statistically significant. Patients with "other allergies" (e.g., drug, insect, or contact allergies) showed less favorable trends, possibly reflecting heterogeneous presentations and unmet diagnostic needs. No significant associations were observed for sex or year of initiation. **Conclusion:** This analysis highlights that clinical improvement in AIT is more strongly associated with adherence and complexity of allergic phenotypes than with demographic factors. Patients with multiple allergic conditions may achieve better outcomes due to increased engagement with care. These findings underscore the need for standardized adherence measures and phenotype-specific management strategies in allergy clinics.

Keywords: Subcutaneous immunotherapy, allergic rhinitis, bronchial asthma, chronic urticaria, food allergy, treatment adherence, hypersensitivity, allergic phenotypes

1. Introduction

Allergic diseases are a group of immunologically mediated conditions characterized by hypersensitivity to typically harmless environmental allergens. These conditions are highly prevalent worldwide and are associated with substantial morbidity, particularly when multiple allergic disorders coexist in the same individual a phenomenon known as allergic multimorbidity. The clinical spectrum includes allergic rhinitis**,** bronchial asthma**,** urticaria, and food allergies, each with distinct yet often overlapping symptomatology that may significantly impair patients' quality of life and functional capacity (Ha *et al*., 2017).

In Egypt, the burden of hypersensitivity disorders is particularly high, shaped by a unique combination of environmental, climatic, and lifestyle risk factors. Many urban and rural areas, suffer from high levels

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of air pollution, due to traffic emissions, industrial activity, and open burning. The situation is exacerbated by frequent dust storms and fluctuating humidity, which increase airborne allergen exposure and respiratory irritation. Furthermore, there is notably high rates of tobacco use, including cigarettes, hookah, and electronic cigarettes (World Bank 2019; WHO 2022). All forms of tobacco smoke contribute to airway inflammation, impaired mucosal defenses, and worsening of allergic symptoms, especially asthma and rhinitis. These environmental and behavioral exposures likely contribute to early sensitization, chronic symptomatology, and allergic multimorbidity in Egyptian patients. Despite this, data exploring the interaction between these factors and clinical response to immunotherapy remain insufficient (Fahmy & Abdelrahman, 2020).

Allergic diseases represent a growing public health issue in Egypt, with multiple studies underscoring their prevalence across different age groups and regions. A study conducted in Cairo reported a 9.4% prevalence of physician-diagnosed asthma among schoolchildren (El-Sayed & Abdelaziz, 2018). Similarly, research in Damanhur city found notable asthma prevalence among school-aged children (El-Sayed & Hassan, 2019). The same study in Damanhur showed a 47.7% prevalence of allergic rhinitis among schoolchildren (El-Sayed & Hassan, 2019). Additionally, research on Egyptian patients with respiratory allergies highlighted the significant role of pollen sensitization in exacerbating allergic symptoms. These statistics underscore the significant burden of allergic diseases in Egypt, highlighting the need for targeted public health interventions and further research to address this growing concern (Fahmy & Abdelrahman, 2020).

Allergic rhinitis commonly manifests as nasal congestion**,** sneezing, rhinorrhea, and pruritus, often with ocular symptoms such as tearing and conjunctival redness (Kakli and Riley 2016). Bronchial asthma, another frequent presentation, is characterized by episodic wheezing, cough, chest tightness, and dyspnea, with variable airflow limitation that may escalate to life-threatening exacerbations. Importantly, rhinitis and asthma often co-exist, reflecting a unified airway inflammatory process and predicting a more severe clinical course (Wu *et al.,* 2019). Urticaria presents as transient, pruritic wheals and/or angioedema, which may be spontaneous or triggered by foods, medications, or physical stimuli. Chronic forms can be particularly distressing due to their unpredictability and impact on emotional well-being (Balp *et al.,* 2018). Food allergies, often mediated by immediate-type hypersensitivity, can range from mild symptoms such as oral pruritus to severe anaphylaxis, especially in atopic individuals with coexisting dermatitis or asthma. Clinical heterogeneity, overlapping diseases, and variable response to treatment present ongoing challenges for personalized management (Small *et al.,* 2018).

Subcutaneous immunotherapy (SCIT) remains the most established form of allergen-specific immunotherapy, particularly in moderate to severe allergic rhinitis, allergic asthma, and venom hypersensitivity. By gradually introducing increasing doses of diluted relevant allergens, SCIT induces immune tolerance and modifies the disease course. Clinically, this translates into reduced symptom severity, decreased medication use, and improved quality of life. However, the effectiveness of SCIT varies significantly among patients. Factors such as baseline symptom severity, the presence of multiple allergic diagnoses, and patterns of allergen sensitization can influence outcomes. For instance, patients with isolated seasonal rhinitis may respond differently than those with perennial rhinitis and coexisting asthma or urticaria (Lin, 2019).

Moreover, adherence to SCIT poses a major challenge, especially in real-world settings where the treatment duration extends over several years and requires regular clinic visits. Severe or persistent symptoms may enhance motivation for treatment, while delayed symptom relief or adverse reactions can increase dropout rates. Identifying clinical predictors of adherence and favorable outcomes is thus essential for optimizing patient selection and improving long-term success (Shamji *et al.,* 2021).

2. Patients and Methods

This is a cross-sectional observational study that was conducted on 109 patients diagnosed with hypersensitivity in the period from 2020 till 2022. Patients with hypersensitivity conditions who were diagnosed by skin prick test (SPT) were recruited from the Chest Outpatient Clinic in the Medical Research Centre of Excellence, National Research Centre and received treatment at a tertiary clinic. Follow up was done monthly to assess clinical outcome. They received SCIT according to their conditions, given daily or twice weekly for a period of minimum 6 months. Patients data included; age, gender, history taking, clinical examination, skin prick tests (SPTs) results, symptom duration and treatment outcome.

All individuals received subcutaneous injections (SCIT) the of the diluted allergens of house dust mites, food, drugs and pollen allergens …etc, in a tertiary clinic and had the follow up done monthly in the Chest Outpatient Clinic in the Medical Research Centre of Excellence, National Research Centre to assess the response to treatment. The study included: Atopic patients aged between 4 and 74 years with a confirmed diagnosis of one or more hypersensitivity conditions (bronchial asthma, allergic rhinitis or urticaria, etc..). Exclusion criteria: Patients who had immunotherapy side effects (such as; headaches, chest tightness, dyspnea, skin rash) those younger than 3 years or older than 75 years old and individuals with severe comorbidities.

2.1. Sample size calculation

The sample size was calculated to detect a significant difference in treatment outcomes between patients who improved and those who discontinued therapy, with a two-sided alpha level of 0.05 and 80% power. Based on previous literature indicating an improvement rate of approximately 65% (Passalacqua *et al.,* 2013), and assuming a minimum detectable difference of 20% between groups, the required sample size was estimated at 94 patients. To account for potential loss to follow-up or incomplete data, the final sample size was increased to 109 patients.

2.2. Ethical Considerations

The study adhered to the principles outlined in the Declaration of Helsinki and received approval from the Ethical Committee of the National Research Centre, Cairo, Egypt. Written informed consent was obtained from all participants or their legal guardians before enrollment in the study.

2.3. Statistical Analysis

Data were coded and analyzed using IBM SPSS Statistics version 28 (IBM Corp., Armonk, NY, USA). Quantitative variables were summarized as means, standard deviations, medians, and ranges (minimum and maximum), while categorical variables were presented as frequencies and percentages. Comparisons between quantitative variables were conducted using the non-parametric Mann-Whitney U test (Chan, 2003a). The Chi-square (χ^2) test was used to assess associations between categorical variablesExact test was used instead when the expected frequency is less than 5 (Chan, 2003b). *P*-values less than 0.05 were considered as statistically significant.

3. Results

Table 1 summarizes the gender distribution of patients included in the study with a total number of patients n=109. Females comprised the majority of patients, accounting for 64 patients (58.7%), while males were 45 individuals (41.3%), suggesting a modest female predominance in the cohort.

Table 1: Gender distribution of the study population

		Count	%
Sex	Male	45	41.3%
	Female	64	58.7%

Table 2 demonstrates the age distribution and duration of therapy. The study population included a broad age range, from 4 to 74 years, with a mean age of 31.44 years (SD = 14.70), and a median age of 32 years. The high standard deviation reflects substantial variability in the ages of participants. Both pediatric and older adult patients were represented.

Duration of Treatment (Months): Mean: 10.00 months, Standard Deviation: 9.73 months, Median: 7.00 months, Minimum: 0.25 months, Maximum: 39.00 months.The average duration of treatment was 10 months, but the median was 7 months, i.e., some patients underwent treatment for much longer periods, pulling the mean higher. The duration ranged from less than a month to over 3 years, reflecting variable adherence or treatment needs.

**Table 2:** Age distribution and duration of therapy

	Mean	Standard Deviation	Median	Minimum	Maximum
Age	31.44	14.70	32.00	4.00	74.00
Duration (months)	10.00	9.73	7.00	0.25	39.00

In terms of allergic manifestations, table 3 shows the distribution of various allergic conditions among patients receiving desensitization therapy between 2020 and 2022. Allergic Rhinitis was the most common condition, reported in 52.3% of patients (57 out of 109). Followed by Urticaria which showed a balanced distribution, reported by 50.5% of patients (55 individuals). Bronchial Asthma was nearly equally common, present in 47.7% of patients (52 individuals). Food Allergy was the least common allergic phenotype in this cohort, affecting only 14.7% (16 individuals). This lower prevalence may reflect underdiagnosis, differing referral patterns, or regional dietary exposures. Other allergic conditions, which may include contact dermatitis, drug allergies, or insect venom hypersensitivity, were reported in 29.4% of patients, (32 individuals), underscoring the heterogeneity of allergic presentations. The nearly equal distribution of allergic rhinitis, asthma, and urticaria supports the concept of allergic multimorbidity, where patients frequently exhibit more than one allergic disorder.

Collectively, these findings highlight the necessity for an integrated approach in managing hypersensitivity disorders, considering that most patients present with more than one clinical manifestation. The data also suggest that allergic rhinitis, urticaria, and asthma are the primary targets for desensitization efforts in this population.

Table 3: Prevalence of allergic conditions among patients undergoing desensitization therapy

		Count	%
Allergic Rhinitis	**Yes**	57	52.3%
	No	52	47.7%
Bronchial Asthma	**Yes**	52	47.7%
	No	57	52.3%
Urticaria	**Yes**	55	50.5%
	No	54	49.5%
Food Allergy	**Yes**	16	14.7%
	No	93	85.3%
Other Allergies	**Yes**	32	29.4%
	No	77	70.6%
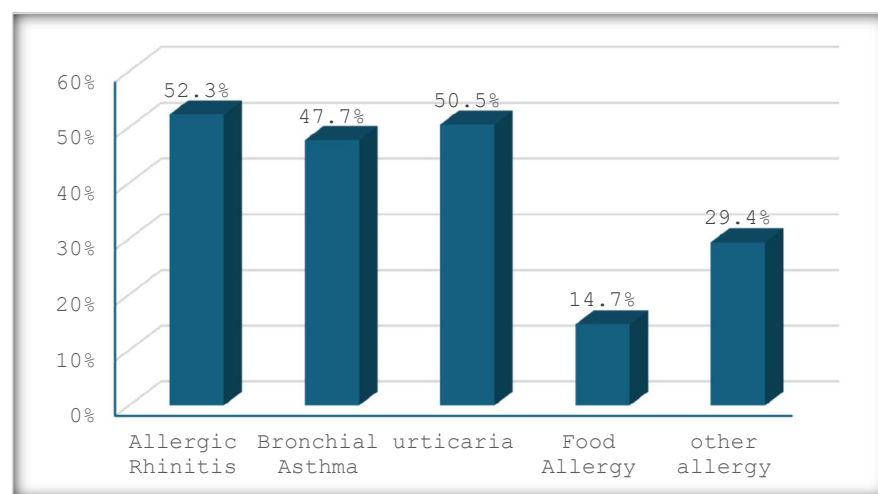
Fig. 1: Different allergic conditions

As shown in figure 1 our cohort study revealed the distribution of allergic conditions, with allergic rhinitis being the most prevalent, affecting 52.3% of patients. This was followed closely by urticaria, present in 50.5% of the cohort, and bronchial asthma, affecting 47.7%. Other allergies were collectively grouped and accounted for 29.4% of the study population, while food allergy was reported in 14.7% of patients.

Table 4 demonstrates a detailed breakdown of isolated and coexisting allergic conditions among patients receiving desensitization therapy, highlighting the heterogeneity and complexity of allergic presentations.

Table 4: Prevalence and patterns of single and coexisting allergic conditions among study participants

Allergy Type or Combination	Count N=109	%
Single Allergic Conditions		
Allergic Rhinitis	8	7.3%
Bronchial Asthma	11	10.1%
Urticaria	19	17.4%
Other Allergies	2	1.8%
Dual Allergic Combinations		
Allergic Rhinitis+Bronchial Asthma	16	14.7
Allergic Rhinitis+Urticaria	5	4.6%
Allergic Rhinitis+Food Allergy	2	1.8%
Allergic Rhinitis+Other Allergies	4	3.7%
Bronchial Asthma+Urticaria	2	1.8%
Bronchial Asthma+Food Allergy	1	0.9%
Bronchial Asthma+Other Allergies	2	1.8%
Urticaria+Food Allergy	3	2.8%
Urticaria+Other Allergy	7	6.4%
Food Allergy+Other Allergy	2	1.8%
Triple Allergic Combinations		
Allergic Rhinitis+Bronchial Asthma+Urticaria	5	4.6%
Allergic Rhinitis+Bronchial Asthma+Others	3	2.8%
Allergic Rhinitis+Bronchial Asthma+Food Allergy	1	0.9%
Allergic Rhinitis+Urticaria+Food Allergy	2	1.8%
Allergic Rhinitis+Urticaria+Others	2	1.8%
Allergic Rhinitis+Food Allergy+Others	1	0.9%
Bronchial Asthma+Urticaria+Food Allergy	1	0.9%
Bronchial Asthma+Urticaria+Others	2	1.8%
Multiple Allergic Combinations (≥4 Conditions)		
Allergic Rhinitis+Bronchial Asthma+Urticaria+Food Allergy	1	0.9%
Allergic Rhinitis+Bronchial Asthma+Urticaria+Others	5	4.6%
Allergic Rhinitis+Bronchial Asthma+Food Allergy+Others	1	0.9%
Allergic Rhinitis+Bronchial Asthma+Urticaria+Food Allergy+Others	1	0.9%

Urticaria only was the most common isolated condition, reported in 17.4% of patients, followed by bronchial asthma only (10.1%) and allergic rhinitis only (7.3%). These findings suggest that although some patients present with a single allergic phenotype, a majority exhibit overlapping conditions, emphasizing the polymorphic nature of hypersensitivity disorders. The most prevalent dual combination was allergic rhinitis with bronchial asthma (14.7%), supporting the well-established link between upper and lower airway inflammation. Other notable combinations included: Allergic rhinitis + urticaria (4.6%), Urticaria + other allergy (6.4%). Several other dyads were observed in smaller proportions (1.8%–3.7%). These combinations underline the frequent co-occurrence of respiratory and dermatologic allergic conditions, consistent with the concept of systemic atopy. Triple and Higher-Order Combinations such as: Allergic rhinitis + bronchial asthma + urticaria were found in 4.6% of patients, demonstrating a triad of airway and skin involvement. Allergic rhinitis + bronchial asthma + urticaria + others occurred in another 4.6%. More complex phenotypes involving four or more allergic disorders (e.g., including food allergy and "others") were rare, each accounting for approximately 0.9% of the sample.

The distribution of allergic conditions observed in this study reveals that a significant number of patients exhibit multisystem involvement. This overlap of clinical manifestations underscores the importance of adopting a comprehensive management approach that addresses the entire allergic profile through individualized diagnosis, monitoring, and treatment to enhance patient adherence and achieve optimal therapeutic outcomes.

Figure 2 illustrates the distribution of patients undergoing desensitization therapy. The highest proportion of patients was recorded in 2021 (45.0%), Both 2020 and 2022 had equal patient proportions, each accounting for 27.5% of the total cohort.
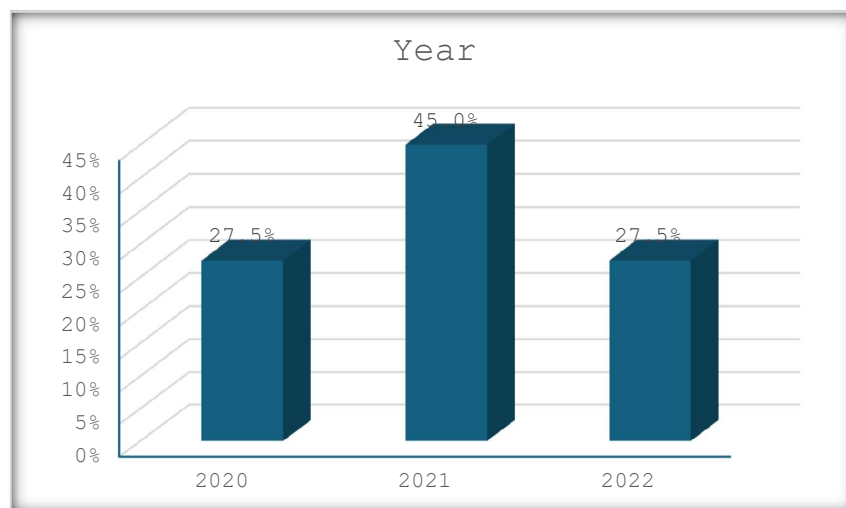
Fig. 2: Yearly trends in allergen immunotherapy utilization

Table 5 shows that among the study cohort, 66.1% of patients (n=72) demonstrated clinical improvement following desensitization therapy, indicating a favorable response to treatment in the majority of cases. Conversely, 33.9% of patients (n=37) discontinued therapy prior to completion. This discontinuation rate highlights a significant challenge in allergen immunotherapy, where long-term adherence is critical for achieving optimal outcomes. Potential contributing factors may include side effects, inconvenience of treatment schedules, lack of perceived benefit, or socioeconomic barriers warranting further investigation.

Table 5: Clinical outcomes of patients undergoing desensitization therapy

		Count	**%**
Outcome	**Improved**	72	66.1%
	Discontinued	37	33.9%

Table 6 compares the age and duration of therapy between patients who improved and those who discontinued desensitization therapy. Patients who improved had a mean age of 30.25 ± 15.19 years, while those who discontinued were slightly older, with a mean age of 33.76 ± 13.57 years. However, this difference was not statistically significant ($p = 0.265$), suggesting that age did not significantly influence treatment outcome or adherence in this cohort.

Regarding the tretament duration; the mean treatment duration was significantly longer in the improved group (13.24 ± 9.63 months) compared to the discontinued group (3.70 ± 6.28 months). This difference was highly statistically significant ($p < 0.001$), indicating that longer duration of immunotherapy is strongly associated with clinical improvement.

Table 6: Comparison of age and treatment duration between improved and discontinued patients

	Outcome										P value
	Improved					**Discontinued**					
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
Age	30.25	15.19	31.00	4.00	74.00	33.76	13.57	35.00	7.00	70.00	0.265
Duration (months)	13.24	9.63	12.00	0.25	36.00	3.70	6.28	1.00	0.25	24.00	*< 0.001

Data are presented as mean ± standard deviation (SD). *P value < 0.05 was considered statistically significant

Table 7 examines associations between patient characteristics and desensitization therapy outcomes (improved vs. discontinued). The comparisons are based on proportions and statistical significance. Females (67.2%) and males (64.4%) showed similar improvement rates. The difference was not statistically significant (p = 0.766), suggesting no association between sex and treatment outcome. Patients with allergic rhinitis (71.9%) and bronchial asthma (71.2%) had higher improvement rates compared to those without these conditions (59.6% and 61.4%, respectively). However, the associations were not statistically significant (p = 0.175 and p = 0.283, respectively). Similarly, urticaria, food allergy, and other allergy showed no significant effect on outcome, though numerically, those with food allergy had a higher discontinuation rate (43.8%). Improvement tended to increase with the number of allergic diagnoses, peaking at 100% in patients with five allergic conditions. Although this trend suggests a potential dose-response relationship, the association was not statistically significant (p = 0.783), likely due to small subgroup sizes. The highest improvement rate was seen in 2020 (73.3%), compared to 63.3% in both 2021 and 2022. Again, the difference was not statistically significant (p = 0.613).

No demographic or clinical variable in this table showed a statistically significant association with treatment outcome. However, patients with multiple allergic conditions and those with respiratory allergies (rhinitis and asthma) demonstrated a numerically higher likelihood of improvement, suggesting that these subgroups may derive greater benefit from immunotherapy.

Table 7: Comparison of patient characteristics by treatment outcome

		Outcome				*P value
		Improved		**Discontinued**		
		Count	Row N %	Count	Row N %	
Sex	**Male**	29	64.4%	16	35.6%	0.766
	Female	43	67.2%	21	32.8%	
Allergic rhinitis	**Yes**	41	71.9%	16	28.1%	0.175
	No	31	59.6%	21	40.4%	
Bronchial asthma	**Yes**	37	71.2%	15	28.8%	0.283
	No	35	61.4%	22	38.6%	
Urticaria	**Yes**	35	63.6%	20	36.4%	0.590
	No	37	68.5%	17	31.5%	
Food allergy	**Yes**	9	56.3%	7	43.8%	0.370
	No	63	67.7%	30	32.3%	
Other allergies	**Yes**	23	71.9%	9	28.1%	0.408
	No	49	63.6%	28	36.4%	
Number of allergic conditions	**One condition**	26	65.0%	14	35.0%	
	Two conditions	27	61.4%	17	38.6%	
	Three conditions	12	70.6%	5	29.4%	0.783
	Four conditions	6	85.7%	1	14.3%	
	Five conditions	1	100.0%	0	0.0%	
Year	**2020**	22	73.3%	8	26.7%	
	2021	31	63.3%	18	36.7%	0.613
	2022	19	63.3%	11	36.7%	

*P values were calculated using the Chi-square test. P value < 0.05 was considered significant

4. Discussion

This study analyzed clinical and demographic data from a cohort of patients who received subcutaneous immunotherapy (SCIT) between 2020 and 2022 in a tertiary center. Using an observational cross-sectional design, we aimed to explore the relationship between baseline clinical manifestations, adherence to (SCIT), and treatment outcomes. Our objective was to identify practical predictors of adherence and response that could inform more personalized immunotherapy strategies and improve care for patients with complex allergic profiles. While Subcutaneous Immunotherapy (SCIT) is well-established as the only disease-modifying therapy for IgE-mediated allergic diseases, treatment success often depends on multiple interrelated variables, including patient characteristics, allergic phenotype, and duration of therapy.

In our study population, females comprised a modest majority (58.7%), while males accounted for 41.3% of the total sample. This female predominance aligns with several previous studies on allergic disease demographics and treatment patterns.

Alining with our finding, Zuberbier *et al.* (2010) found that adult females are more likely than males to report allergic symptoms and seek medical care for hypersensitivity conditions, particularly allergic rhinitis and urticaria. Similarly, Kim *et al.* (2012) reported a higher prevalence of asthma and allergic rhinitis in adult women compared to men in a large Korean population study, attributing this difference to both biological and behavioral factors. Ek *et al.* (2002) also observed that women utilize healthcare services for asthma and allergy management more frequently than men, suggesting that health-seeking behavior may contribute to increased female representation in treatment cohorts.

However, not all studies support a clear gender difference in the epidemiology or treatment of allergic disorders. For example, Kiel *et al.* (2013) analyzed real-world adherence to subcutaneous immunotherapy and found no significant sex-based differences in treatment persistence or clinical outcomes. Similarly, Marogna *et al.* (2010) reported that the efficacy of allergen immunotherapy was comparable in males and females over a multi-year follow-up period. In contrast, Bender *et al.* (2014) suggested that males may be more prone to early treatment discontinuation, often due to time constraints, occupational responsibilities, or lower engagement in chronic disease management programs.

The mean age of our study cohort is 31.4 and it shows a broad age distribution ranging from (4-74) which highlights the applicability of desensitization therapy across a wide age spectrum. The relatively young mean and median ages suggest that hypersensitivity disorders are particularly prevalent or more frequently treated with immunotherapy among young to middle-aged adults.

This age trend is consistent with previous studies, such as that by Marogna *et al.* (2010), who reported a similar mean age (~30 years) among patients undergoing allergen-specific immunotherapy, reflecting early diagnosis and initiation of treatment during productive years. Demoly *et al.* (2006) also observed that immunotherapy is most often initiated in early adulthood, when allergic symptoms begin to significantly impact quality of life and daily functioning.

However, some studies have shown differing age distributions. Balachandran *et al.* (2019) for example, found that older adults (>45 years) were underrepresented in allergen immunotherapy trials, likely due to comorbidities, polypharmacy, or reduced referral rates. This underutilization in older populations may contribute to delayed management and poorer outcomes in those groups. In contrast, the presence of patients as young as 4 years in our cohort aligns with current guidelines supporting the safe use of subcutaneous immunotherapy (SCIT) in pediatric populations, as demonstrated by Aytekin *et al.* (2021), who found SCIT both effective and well-tolerated in children.

In the present cohort, the duration of SCIT varied considerably. The mean treatment duration was 10 months. The range extended from 0.25 to 36 months, highlighting significant variability in patient adherence. The observed treatment durations suggest substantial challenges in maintaining adherence. This pattern aligns with findings from other real-world studies. A retrospective study by Kiel *et al.* (2016) found that only 58.7% of patients maintained SCIT at three years. The primary reasons for discontinuation were treatment frequency (82.2%), prolonged duration (70.9%), and the inconvenience of travel to allergy clinics (67.7%) (Kiel *et al.,* 2013)*.* Similarly, a systematic review by Araujo *et al.* (2022) reported wide variability in persistence (16%–93.7%) and adherence rates (15.1%–99%), with inconvenience being the most frequently cited reason for early termination.

Long-term data from a 30-year retrospective study also indicated poor compliance, with rates ranging from 18% to over 90% depending on the study design. Factors such as lack of perceived efficacy and logistical barriers played major roles in discontinuation (Di Bona *et al.,* 2019).

These findings emphasize the need for strategies to enhance adherence, including patient education on the expected timeline of improvement, proactive management of side effects, and potentially exploring alternative delivery systems such as sublingual immunotherapy (SLIT).

In our cohort, the most prevalent allergic conditions were allergic rhinitis, urticaria, and bronchial asthma, with food allergy and other allergic conditions comprising 29.4% of cases. This pattern reflects the recognized overlap between respiratory and cutaneous allergies and aligns with regional and international data.

Allergic rhinitis was the most common condition, affecting over half of the patients, consistent with El-Ghoneimy *et al.* (2011), who reported similar prevalence in Egyptian adults. The well-established association between allergic rhinitis and asthma was confirmed in our study. According to the Global Initiative for Asthma (GINA, 2021), asthma prevalence in urban Middle East North Africa (MENA) populations, including Egypt, is rising due to air pollution, dust exposure, and smoking factors prevalent in our setting and likely contributing to these rates.

Urticaria prevalence in our sample was notably higher than global estimates, where rates typically range between 0.5% and 1% (Zuberbier *et al.,* 2010). Similarly, food allergy was present in 14.7% of patients, exceeding the global adult average of 2–10% (Tang & Mullins, 2017). This elevated prevalence may reflect referral bias, increased awareness, and underdiagnosis or limited surveillance in the region (Nwaru *et al*., 2014).

Shaheen *et al.* (2012) demonstrated a clear association between urban air pollution and increased allergic disease risk in Cairo's children, while Farag *et al.* (2019) noted that over half of allergic patients had overlapping conditions, reinforcing our findings of multimorbidity. Additionally, Araujo *et al.* (2022) emphasized that patients with multiple allergic disorders are more likely to pursue immunotherapy, suggesting that the broad spectrum of allergic manifestations in our patients may influence their engagement with desensitization treatment. However, some contrasting evidence exists. Global population-based studies report lower prevalence rates of urticaria and food allergies, particularly among adults in non-referral settings (Zuberbier *et al.,* 2010; Nwaru *et al.,* 2014). Furthermore, the World Allergy Organization cautions that self-reported allergies often overestimate true IgE-mediated disease, highlighting the importance of confirmatory diagnostic workups. These discrepancies underscore the need for standardized diagnostic approaches and population-specific data, particularly in regions like Egypt, where allergic diseases are influenced by environmental, cultural, and healthcare system factors. Region-specific epidemiological studies and improved diagnostic accuracy in allergy clinics are essential

In our cohort, other allergies, a category that included less common hypersensitivity manifestations such as contact dermatitis, insect venom allergy, and drug allergies accounted for 29.4% of patients. While each of these conditions may present less frequently in isolation, their collective burden is significant and often under recognized in allergy epidemiology.

This category's clinical relevance lies in its heterogeneous nature, which can contribute to diagnostic challenges and variations in management strategies. For example, contact dermatitis is a prevalent condition influenced by environmental exposures and occupational factors, particularly in developing countries (Zuberbier *et al.,* 2010). Similarly, drug hypersensitivity reactions can complicate chronic disease management and impact patient quality of life, particularly in populations with limited access to allergy testing and desensitization therapies (Demoly *et al.,* 2006).

Patients in this group may also exhibit higher psychological distress and lower adherence to desensitization regimens due to uncertainty about triggers and lack of standardized protocols for immunotherapy in non-respiratory allergic diseases. These factors may affect treatment continuation, though our study did not find a statistically significant association between this group and discontinuation (*P*= 0.408).

Araujo *et al.* (2022) emphasize the need for tailored approaches to immunotherapy in patients with multiple or atypical allergic disorders, noting that clinical outcomes may be improved when treatment plans consider individual allergen profiles and comorbidities. Conversely, Kiel *et al.* (2013) highlight the low persistence of patients with non-airborne allergen sensitivities, possibly due to skepticism about the benefits of immunotherapy in these subtypes.

In our cohort, allergic conditions exhibited considerable overlap, with several patients presenting multiple concurrent allergies. The most common individual diagnoses were urticaria only (17.4%), bronchial asthma only (10.1%), and allergic rhinitis only (7.3%). Combinations such as allergic rhinitis

with bronchial asthma (14.7%) and various other mixed presentations were also frequent, underscoring the complexity and multimorbidity of allergic diseases.

This pattern aligns with existing evidence of coexisting allergic conditions. For example, the coexistence of allergic rhinitis and asthma is well documented, supported by studies like El-Ghoneimy *et al.* (2011) and confirmed in our cohort. The unified airway concept suggests shared pathophysiological mechanisms and environmental triggers that contribute to this overlap (Bousquet *et al.,* 2008). Similarly, the notable prevalence of urticaria, both alone and combined with respiratory allergies, supports findings from Zuberbier *et al.* (2010)*,* who highlighted the frequent coexistence of cutaneous and respiratory allergic disorders.

Moreover, the substantial proportion of patients with multiple allergies, including food allergy and other less common allergic types, echoes reports by Farag *et al.* (2019), which emphasize multimorbidity as a common feature in allergy clinics. Araujo *et al.* (2022) further suggest that patients with multiple allergic conditions are more likely to seek immunotherapy, consistent with the complex allergy profiles observed in our referral-based cohort.

However, some studies report lower rates of multimorbidity and individual allergy prevalence, particularly in population-based samples rather than specialized clinics (Nwaru *et al.,* 2014; Tang & Mullins, 2017). The elevated rates of overlap in our sample may partly reflect referral bias, as patients with more severe or multiple allergic conditions are more likely to be seen in tertiary allergy centers. Additionally, self-reported allergy data, common in many epidemiological studies, can overestimate true IgE-mediated allergy, as cautioned by the World Allergy Organization *(2016).*

The data show that patients who improved had a significantly longer treatment duration (mean 13.24 $\pm$ 9.63 months) compared to those who discontinued early (mean 3.70 $\pm$ 6.28 months), with the difference highly significant ($p < 0.001$). This finding supports the widely accepted view that sustained adherence to allergen immunotherapy or allergy treatments is crucial for achieving clinical benefit. Supporting this finding, Cox *et al.* (2011) demonstrated that longer treatment duration correlates with better symptom control and immunological tolerance, while Canonica *et al.* (2014) emphasized that discontinuation before 3 years often leads to suboptimal outcomes.

Conversely, no significant difference in patient age was observed between the improved and discontinued groups ($P = 0.265$), indicating that age alone may not strongly influence adherence or response in this population. This aligns with findings by Passalacqua *et al.* (2013), who noted that demographic factors such as age had limited impact on treatment continuation, suggesting that behavioral and psychosocial factors may play larger roles.

However, some literature points to conflicting evidence regarding treatment adherence. For example, a study by Dhami *et al.* (2017) found that although longer treatment duration generally improves outcomes, some patients discontinue early due to adverse reactions, cost, or lack of immediate symptom relief, which complicates the association between duration and improvement. Additionally, Bender *et al.* (2009) highlighted that patient motivation and education are pivotal in sustaining long-term therapy, regardless of age or baseline characteristics.

Overall, our findings emphasize the critical importance of encouraging prolonged adherence to allergy treatment to maximize benefits. Identifying and addressing barriers to continuation, such as side effects, cost, or patient expectations, remains essential to improve clinical outcomes.

In our cohort, clinical outcomes defined as improved versus discontinued treatment, did not significantly differ by sex, allergic rhinitis, bronchial asthma, urticaria, food allergy, number of allergic conditions, or year of treatment initiation. For example, improvement rates were similar between males (64.4%) and females (67.2%) ($P = 0.766$), and comparable across allergic conditions, suggesting baseline demographic and clinical factors alone may not strongly predict treatment response or adherence.

This finding aligns with prior research emphasizing the crucial role of adherence rather than patient demographics or baseline allergy phenotype in determining clinical success. Passalacqua *et al.* (2013) reported that persistence in immunotherapy is a stronger determinant of outcome than initial disease characteristics. Bender *et al.* (2009) also highlighted that behavioral and psychosocial factors including patient education and motivation are vital for maintaining adherence and improving outcomes.

Regarding multiple allergies, although no statistically significant differences were found, patients with four or five allergic conditions showed numerically higher improvement rates. Canonica *et al.* (2014) suggested that patients with complex allergic profiles may demonstrate better engagement and adherence, possibly due to increased symptom burden and healthcare interaction.

Conversely, some studies indicate that specific allergy subtypes may impact outcomes. Dhami *et al.* (2017) showed that food allergy patients often have higher discontinuation rates, related to treatment complexity and psychological burden. While our data did not reach statistical significance, the trend toward lower improvement in food allergy patients warrants further investigation.

Regarding temporal trends, our study found no significant differences in outcomes by treatment year. This contrasts with Zhao *et al.* (2018), who reported improvements in adherence over time linked to better patient education and healthcare delivery. This discrepancy may reflect regional differences in healthcare systems or patient populations.

Adding to this, a recent study by Lee *et al.* (2022) emphasized the importance of personalized adherence interventions in allergic disease management, demonstrating that tailored patient education and digital health tools significantly improve persistence and clinical outcomes. Such innovations highlight emerging strategies to overcome adherence barriers.

Our findings underscore that improving clinical outcomes in allergy treatment depends primarily on enhancing adherence and patient support rather than on fixed demographic or clinical factors. Personalized care plans, behavioral support, and consistent follow-up are critical to maximize therapeutic benefit. Patients with multiple allergies, who may be more motivated or monitored, could benefit from targeted interventions to sustain treatment.

The category of other allergies was not significantly associated with treatment outcomes in our cohort. This is consistent with limited data on these allergy subtypes in relation to long-term desensitization or immunotherapy outcomes. While these conditions contribute to the overall allergic burden, they often require distinct management approaches compared to respiratory or food allergies (Alvaro-Lozano *et al* 2020). The heterogeneity and lower prevalence of these allergies in referral clinics may also limit the power to detect outcome differences. Further research is needed to clarify how these diverse allergic conditions influence treatment adherence and clinical improvement.

5. Conclusion

Our study suggests that clinical improvement in allergen immunotherapy is more strongly associated with patient adherence and engagement than with demographic characteristics or individual allergy types. Notably, patients with multiple allergic conditions appeared to have better outcomes, potentially reflecting more frequent healthcare interactions and follow-up. However, the study has limitations, including small sample sizes within certain allergy subgroups and the treatment discontinuation.

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