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A Retrospective Analysis of the Impact of Specific Desensitization Therapy on Atopic Patients

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ABSTRACT

Background: Subcutaneous immunotherapy (SCIT) is a widely recognized, disease-modifying treatment for a range of allergic conditions. By targeting the underlying immune response, SCIT offers a promising approach to reducing hypersensitivity to allergens, thereby improving patients' symptoms and quality of life. **Objective:** This study aimed to analyze the clinical outcomes of patients with atopy who underwent desensitization therapy using SCIT. The focus was on determining the effectiveness of treatment in reducing allergy symptoms. **Patients and Methods:** A retrospective review was conducted on the medical records of 205 patients treated at the Food and Drug Allergy Center over a two-year period, from 2020 to 2022. All patients included in the study had been diagnosed with allergic conditions based on clinical evaluations and Skin Prick Test (SPT) results. They received subcutaneous injections of diluted allergens tailored to their individual sensitivities as identified through SPT. **Results:** Out of the 205 patients included in the study, 193 continued their treatment through the follow-up period. Among these, 124 patients (64.2%) exhibited notable clinical improvement, characterized by reduced allergy symptoms and decreased reliance on rescue medications. Conversely, 69 patients (35.8%) showed no significant improvement in their allergic conditions despite undergoing therapy. Twelve patients (5.9%) were lost to follow-up and discontinued treatment. Statistical analysis revealed that the duration of treatment played a critical role in determining outcomes. Patients who demonstrated improvement had undergone therapy for a significantly longer duration compared to those who did not show improvement (10.66 ± 8.82 months vs. 1.02 ± 1.07 months; $P < 0.001$). This finding emphasizes the cumulative effect of SCIT over time and underscores the importance of maintaining long-term adherence to the treatment protocol. **Conclusion:** Subcutaneous immunotherapy (SCIT) has proven to be an effective method for reducing hypersensitivity to a variety of allergens, particularly when administered over an extended period. The study highlights the necessity of prolonged treatment to achieve optimal outcomes, as patients with longer treatment durations experienced significantly better results. These findings reinforce the value of SCIT as a cornerstone in the management of allergic diseases and the need for strategies to enhance patient adherence to ensure sustained benefits.

Keywords: allergy, subcutaneous immunotherapy, skin prick test, desensitization, atopy, allergic rhinitis, urticaria, bronchial asthma

1. Introduction

Atopic diseases, including allergic rhinitis, asthma, and atopic dermatitis, affect a significant portion of the global population, leading to substantial morbidity and increased healthcare costs. Effective management of these conditions is crucial, and allergen immunotherapy (AIT), also known as specific desensitization therapy, has emerged as a promising treatment option. By targeting the

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underlying immune response to allergens, AIT offers the potential for long-term symptom relief and reduced reliance on pharmacotherapy (Yaneva and Darlenski, 2021).

Allergen immunotherapy involves administering gradually increasing doses of an allergen extract to modify the immune system's response. This approach shifts the immune response from a Th2-dominated (allergic) state to a more balanced Th1 response, addressing the root cause of the allergy. Scientific studies have demonstrated that AIT is effective in reducing symptoms of allergic rhino-conjunctivitis (hay fever) and seasonal asthma triggered by grass, tree pollen, and dust mites. Patients undergoing this treatment often report a reduced need for medication, with benefits that persist beyond the typical three-year treatment period (Durham and Shamji, 2023).

House dust mites (HDMs) play a significant role in persistent allergic respiratory diseases, such as allergic rhinitis (AR) and allergic asthma (AA). These conditions impose a substantial disease burden and elevate healthcare costs, especially in patients with poorly controlled symptoms. Because effective allergen avoidance is often impractical in domestic settings, treatment options for HDM-induced respiratory diseases include symptomatic medications or AIT using purified extracts of HDM bodies, feces, or both (Okasha *et al*., 2021). The efficacy of AIT in managing allergic respiratory conditions is supported by national and international guidelines, with meta-analyses of double-blind, placebo-controlled randomized clinical trials confirming its effectiveness in reducing symptoms, medication use, and bronchial hyper responsiveness (Fox, 2022).

Advancements in AIT, such as sublingual immunotherapy (SLIT) and the integration of biologics, have enhanced patient outcomes and safety. Subcutaneous immunotherapy (SCIT), which involves a series of injections, and SLIT, where daily doses of allergen extract are taken sublingually, have shown promise in managing allergies to grass pollen, tree pollen, dust mites, and insect venom. Moreover, the emerging interest in food desensitization for allergies to peanuts, sesame, tree nuts, wheat, milk, and eggs highlights the expanding scope of AIT (Hesse *et al*., 2022).

The efficacy of AIT in children has been particularly noteworthy, with studies indicating its ability to reduce the progression of allergic diseases. Novel approaches, informed by advancements in immunological mechanisms, aim to further optimize treatment outcomes. However, clinical responses and medication intake in patients with atopy continue to vary, underscoring the need for further studies to refine these therapies and address the small-to-moderate effect sizes observed in some SLIT studies (Burks *et al*., 2018; Pavón-Romero *et al*., 2022).

As the prevalence of atopic diseases continues to rise globally, AIT remains a cornerstone in managing these conditions, offering both symptom relief and the potential to alter the disease trajectory. The current study focuses on assessing the clinical response and medication intake in patients undergoing desensitization therapy, aiming to provide further insights into optimizing treatment strategies (Alvaro-Lozano *et al*., 2020).

2. Patients and Methods

This is a retrospective cross-sectional study, in which the medical records of 205 patients treated between 2020 and 2022 at the Food and Drug Allergy Center were reviewed. The patients were diagnosed with allergic rhinitis, bronchial asthma, or other hypersensitivities caused by factors such as food, drugs, pollens, and viral infections. All participants underwent subcutaneous immunotherapy (SCIT) using diluted allergen extracts (e.g., house dust mites, food, drugs, and pollen allergens), based on the results of their skin prick tests (SPT). The treatment was administered either daily or twice weekly for a minimum duration of six months.

Follow-up assessments were conducted through clinical examination and history taking to evaluate the treatment outcomes. Inclusion criteria included adult atopic patients with bronchial asthma, allergic rhinitis, or urticaria that were poorly controlled with antihistamines. Exclusion criteria included patients younger than six months or older than 75 years, patients with severe comorbidities that could interfere with desensitization, patients who experienced adverse effects from the treatment, and patients participating in other clinical trials.

2.1. Ethical Considerations

This study adhered to the World Medical Association's Code of Ethics and the principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the local Ethics Committee of the National Research Centre in Giza, Egypt.

2.2. Statistical methods

Data were coded and entered using the Statistical Package for the Social Sciences (SPSS) version 28 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize the data, with means and standard deviations for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups were made using analysis of variance (ANOVA) with multiple comparisons post hoc tests for normally distributed quantitative variables. For non-normally distributed quantitative variables, the non-parametric Kruskal-Wallis test and Mann-Whitney test were applied (Chan, 2003a). To compare categorical data, the Chi-square (χ^2) test was used, with the exact test employed when the expected frequency was less than 5 (Chan, 2003b). P-values less than 0.05 were considered statistically significant.

3. Results

Table (1) provides a summary of key demographic and clinical characteristics of 205 patients who underwent subcutaneous immunotherapy (SCIT) for allergic conditions. The mean age of the participants was 31.21±15.39 years, with a median age of 32 years. The age range of patients was from 2 to 74 years, indicating a wide age distribution among the study participants. The average treatment duration was 7.77±8.62 months**,** with a median of 5 months. The treatment duration ranged from 0.25 months to 39 months**,** suggesting varying lengths of treatment among participants. Of the 205 patients, 124 (60.5%) were female, and 81 (39.5%) were male, indicating a higher prevalence of female patients in the study population. Allergic Rhinitis was the most common allergy, affecting 124 (60.5%) of patients. Bronchial Asthma was reported in 94 (45.6%) patients, and Urticaria was present in 106 (51.7%) patients.

Table 1: Demographic and Clinical Characteristics of the Studied Population

Age (years)	Mean±SD	31.21±15.39
	Median (Range)	32.00 (2.00 - 74.00)
Duration of treatment (months)	Mean±SD	7.77±8.62
	Median (Range)	5.00 (0.25 - 39.00)
Sex (n=205) Count (%)	Female	124 (60.5%)
	Male	81 (39.5%)
Type of allergy Count (%) (n=205)	Allergic Rhinitis	124 (60.5%)
	Bronchial Asthma	94 (45.6%)
	Urticaria	106 (51.7%)
	Conjunctivitis	14 (6.8%)
	Angioedema	25 (12.2%)
	Anaphylaxis	6 (2.9%)
	Eczema	15 (7.3%)
	Food Allergy	68 (33.1%)
	Drug Allergy	21 (10.2%)
Other clinical manifestations (n=205)	Hypothyroidism	1 (0.5%)
	Hyperthyroidism	3 (1.4%)
	GERD	1 (0.5%)
	No	200 (97.6%)

SD: Standard deviation

Other types of allergy included Conjunctivitis (6.8%)**,** Angioedema (12.2%)**,** Anaphylaxis (2.9%)**,** Eczema (7.3%)**,** Food Allergy (33.1%)**,** and Drug Allergy (10.2**%)**. These figures highlight the variety of allergic conditions present in the study population. Other Clinical Manifestations**:** Hypothyroidism was present in 1 (0.5%) patient**,** Hyperthyroidism in 3 (1.4**%)**, and GERD (Gastroesophageal Reflux Disease) in 1 (0.5%) patient. The majority of patients, 200 (97.6%), did not have any other clinical conditions that could be linked to their allergies or the treatment.

This table illustrates the diverse range of allergic conditions and the relatively high proportion of female patients in the study, along with the typical age and treatment duration for the cohort.

Figure 1 shows a female predominance among the participating population, with females representing 60.20% of the participants, while males accounted for 39.80%.

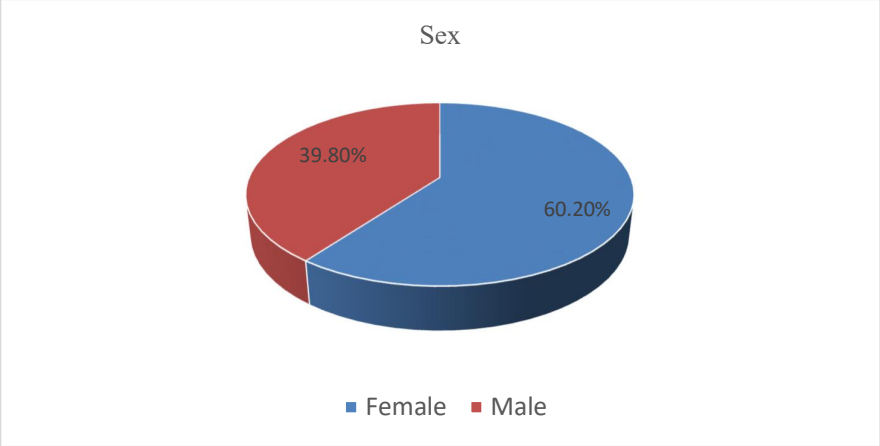

Fig. 1: Gender distribution of the studied population

Figure 2 illustrates the most common types of atopy in our patients, with allergic rhinitis being the most prevalent, followed by urticaria, bronchial asthma, and other forms of allergy.

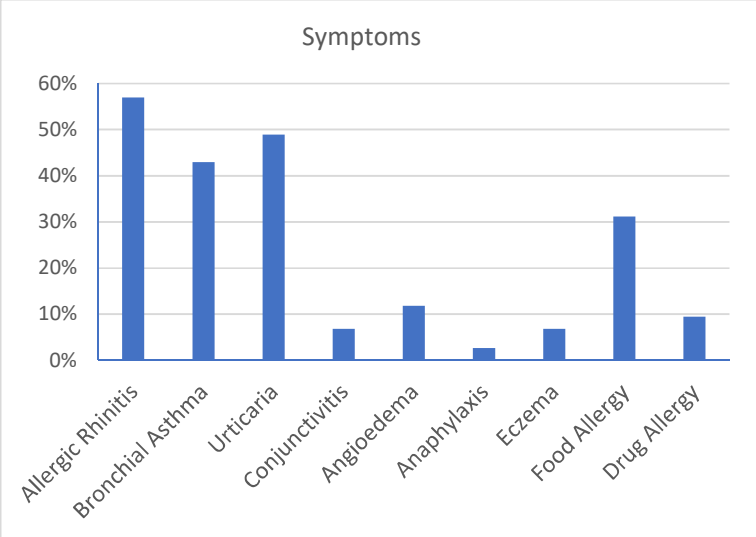

Fig. 2: Variable symptoms of atopy in the participants

As presented in Table 2, the treatment outcomes for the 193 patients who received subcutaneous immunotherapy (SCIT) are as follows: Improved**:** 124 patients (64.2%) experienced improvement after treatment, reflecting a positive clinical response in the majority of the cohort. Discontinued**:** 69 patients (35.8%) either did not show improvement or discontinued the treatment, indicating that a significant portion of patients either did not benefit from the therapy or opted to stop it for unspecified reasons. This distribution highlights that while the majority of patients responded well to the treatment, a substantial minority did not achieve the desired results or chose to discontinue therapy.

Table 2: Treatment outcome

		Count	%
Outcome	Improved	124	64.2%
	Discontinued	69	35.8%

As observed in table 3 the follow-up of treatment for the 205 patients was as follows: Missed follow-up**:** 12 patients (5.9%) missed their follow-up appointments**.** Continued follow-up**:** 193 patients (94.1%) continued with their follow-up appointments. This indicates that the majority of patients adhered to the follow-up schedule, while a small proportion missed their follow-up visits.

Table 2: Follow up of treatment

		Count (%)
Follow up of treatment (n=205)	Missed follow up	12 (5.9%)
	Continued follow up	(4.1%) 193

According to table 4, the causes of missed follow-up among the 12 patients are as follows: Systemic adverse effects: 4 patients (33.3%) missed their follow-up due to experiencing systemic adverse effects related to the treatment. No adverse effects: 8 patients (66.7%) missed their follow-up despite not experiencing any adverse effects from the treatment. This indicates that the majority of patients who missed their follow-up appointments did so without any treatment-related adverse effects, while a smaller group missed follow-ups due to systemic adverse reactions.

Table 4: Cause of missed follow up and treatment outcome in studied patients

		Count (%)
Cause of missed follow up (n=12)	Systemic adverse effects	4 (33.3%)
	No adverse effects	8 (66.7%)

Table (5) compares various factors between the groups of patients who improved and those who did not improve after treatment. Here's the interpretation: Age: The mean age of patients who improved was 29.55±15.49 years, while those who did not improve had a mean age of 33.09±15.33 years. The difference was not statistically significant (P = 0.163), suggesting age did not have a significant impact on treatment outcomes. Sex: Of the patients who improved, 63.5% were female and 65.4% were male in the non-improved group. No significant difference was found (P = 0.786), meaning gender did not significantly affect the outcome. Type of allergy: Allergic Rhinitis: The majority of both improved (64.9%) and non-improved (35.1%) patients had allergic rhinitis, but the difference was not significant (P = 0.835). Bronchial Asthma: More patients with bronchial asthma improved (70.1%) compared to those who did not improve (29.9%), but the difference was not statistically significant (P = 0.123). Urticaria: Slightly more patients with urticaria showed improvement (60.9%) than those who did not improve (39.1%), though the difference was not significant (P = 0.350). Other types of allergies: No significant differences were found for conjunctivitis, angioedema, anaphylaxis, eczema, food allergy, and drug allergy (P values ranged from 0.358 to 1), suggesting that the type of allergy did not strongly influence the treatment outcomes. Duration of treatment: Patients who improved had a mean treatment duration of 10.66±8.82 months, significantly longer than the 1.02±1.07 months for those who did not improve (P < 0.001). This indicates that longer treatment duration was strongly associated with improvement. In summary, the only statistically significant factor related to with age**,** sex**,** or type of allergy.

Based on these data, we conclude that patients who showed improvement had a significantly longer treatment duration compared to those who did not improve (10.66±8.82 vs 1.02±1.07 months; P< 0.001). No significant relationship was observed between treatment outcomes and factors such as age, gender, or type of allergy among the patients studied (Table 5), (Figures 3, 4).

Table 5: Relation between descriptive data with treatment outcome

		Outcome		P value
		Improved (n=124)	Not improved (n=69)	
		Count (%)	Count (%)	
Age	**Mean±SD**	29.55±15.49	33.09 ±15.33	0.163
	Median (Range)	30.00 (3.00 - 74.00)	34.00 (5.00 - 73.00)	
Sex	**Female**	73 (63.5%)	42 (36.5%)	0.786
	Male	51 (65.4%)	27 (34.6%)	
Type of allergy	**Allergic Rhinitis**	72 (64.9%)	39 (35.1%)	0.835
	Bronchial Asthma	61 (70.1%)	26 (29.9%)	0.123
	Urticaria	56 (60.9%)	36 (39.1%)	0.350
	Conjunctivitis	7 (58.3%)	5 (41.7%)	0.758
	Angioedema	15 (65.2%)	8 (34.8%)	0.918
	Anaphylaxis	4 (66.7%)	2 (33.3%)	1
	Eczema	7 (53.8%)	6 (46.2%)	0.550
	Food Allergy	32 (62.7%)	19 (37.3%)	0.794
	Drug Allergy	8 (53.3%)	7 (46.7%)	0.358
Duration of treatment (months)	**Mean ± SD**	10.66±8.82	1.02±1.07	**< 0.001**
	Median (Range)	8.00 (0.25 - 39.00)	0.25 (0.25 - 4.00)	

SD: Standard deviation. P value < 0.05 were considered statistically significant

As illustrated in figure 3 the patients who improved had a longer duration of treatment compared to those who discontinued treatment

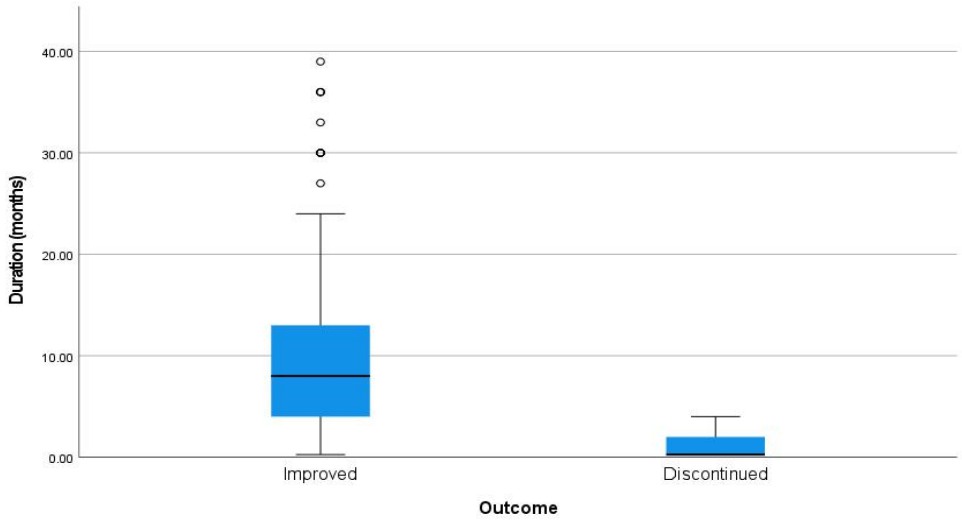

Fig. 3: Relation between treatment duration with treatment outcome

Figure 4 shows that patients who improved underwent a longer duration of treatment compared to those who discontinued their therapy

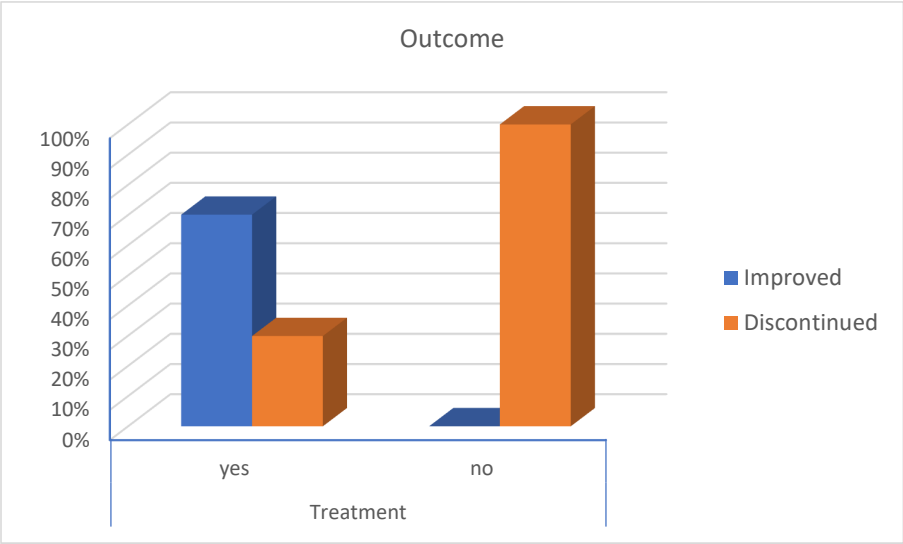

Fig. 4: Relation between receiving treatment and the outcome

Figure 5 demonstrates that 92.8% of the studied population received treatment, while 7.2% did not receive treatment.

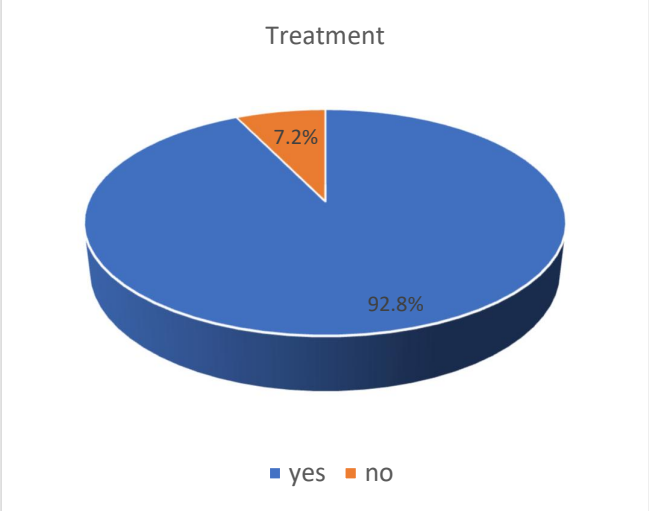

Fig. 5: Patients who received treatment vs patients with no treatment

4. Discussion

The current study aimed to analyze the outcomes of desensitization on clinical response and medication intake among patients with atopy treated at the Food and Drug Allergy Center between 2020 and 2022. To achieve this objective, we reviewed the records of 205 patients with allergic conditions who received subcutaneous immunotherapy (SCIT) through diluted allergen injections based on their skin prick test (SPT) results.

The mean age of the patients in our study was 31.21 ± 15.39 years, ranging from 2 to 74 years. Similarly, in the study by Di Bona *et al*. (2020) on 2200 patients with allergic rhino-conjunctivitis

with or without asthma who underwent SCIT, the mean age was reported as 29.4 ± 11.7 years. Furthermore, Lourenço *et al*. (2020) reported a mean age of 30 ± 13 years in their study. The median age in our cohort was 32 years, which was higher than the median age of 21 years reported in the study by Liu *et al*. (2021). Interestingly, while patient age did not significantly affect treatment outcomes in our study, studies like Agenäs *et al*. (2023) found that older children (aged 11-15) had more persistent nasal symptoms after one year of pollen SCIT. compared to younger children (5.6 vs. 4.2, p = 0.007). The study also found that older children had a higher total symptom score after one year (12.6 vs. 9.8, p = 0.009). The difference can likely be attributed to the younger population in Agenäs *et al*. '(2023) study.

Female predominance was observed in our study, with females comprising 60.5% of the sample. This finding aligns with Lourenço et al. (2020), who reported that 52% of their 323 patients receiving SCIT were female. Similarly, Tat (2018) observed a female prevalence of 53.7% in their study. In contrast, Di Bona et al. (2020) reported a slightly lower proportion of females (49.8%) among their study population of 2200 patients with allergic rhino-conjunctivitis with or without asthma who received SCIT. Additionally, Iwona Dziewa *et al.* (2021) conducted a retrospective study conducted in 2015 on atopic patients revealed that females constituted 82% of the study population. In our study, no significant relationship was found between treatment outcomes and patient gender. This is consistent with the findings of Agenäs *et al.* (2023), who reported no significant difference in symptoms between boys and girls during SCIT treatment in their study of 158 children.

In our study, allergic rhinitis was the most prevalent condition, followed by urticaria and asthma. This finding is consistent with global trends and underscores the importance of prioritizing subcutaneous immunotherapy (SCIT) for allergic rhinitis patients, who often experience significant impairments in their quality of life. Our results align with those of Iwona Dziewa *et al*. (2021), who reported allergic rhinitis as the most common allergy, followed by urticaria and bronchial asthma in their retrospective study of 450 atopic cases. Similarly, Knudgaard *et al*. (2021) observed that allergic rhinitis was the most frequent atopic condition, coexisting in 40.5% of patients with allergic dermatitis, in addition to other allergies. Gao *et al*. (2022) reported comparable findings in a cross-sectional survey of adult residents in Shenmu City, China, where allergic rhinitis had a prevalence of 25.4% (1,182/4,655) and asthma was found in 9.4% (439/4,655) of participants. These results are clinically significant, particularly for patients sensitive to common allergens such as house dust mites and pollen.

Furthermore, as noted by Gao *et al*. (2022) and Knudgaard *et al*. (2021), allergic rhinitis frequently coexists with other atopic conditions, which can complicate treatment. Future research could explore the impact of these comorbidities on the efficacy of SCIT, especially in patients with combined asthma and rhinitis. Additionally, longer treatment periods are critical for achieving optimal desensitization. Studies have demonstrated that extended treatment durations result in reduced nasal symptoms and a decreased need for rescue medications, especially in patients with allergies to common allergens.

During the follow-up of the current study, 12 patients (5.9%) were lost to follow-up and discontinued treatment. The discontinuation rate**s** in our study were lower than those reported in some other studies, which observed higher treatment cessation rates. Supporting our findings, Cox (2021) reported SCIT discontinuation rates ranging from 6% to 84%, while SLIT discontinuation rates varied from 21% to 93%. In a study by Aytekin *et al*. (2022) involving 119 SCIT patients, 47.8% discontinued treatment. Similarly, Lourenço *et al*. (2020) found that 16% of patients stopped SCIT, while in the study by Yang *et al*. (2018) on 311 patients, 19.0% dropped out in the first year, 10.0% in the second year, and 6.4% in the third year.

The primary reasons for treatment discontinuation in our cohort were systemic adverse effects (SAEs) (33.3%) and irregular injection visits (66.7%), the latter of which was primarily influenced by economic factors. This highlights the need for improving patient engagement and adherence through methods such as digital tools (Cao *et al*., 2018). These tools could help address irregular visits by providing timely reminders and monitoring, thus improving long-term adherence. The issue of systemic adverse effects and the economic burden also warrants further exploration.

Conversely, Lourenço *et al*. (2020) identified economic reasons (47.9%) as the most common cause for withdrawal, followed by patients' perception of no clinical improvement (23%) and switching to sublingual immunotherapy (11.6%). In Yang *et al*. (2018), the main reasons for non-

adherence were inconvenience (32.7%), perceived lack of effectiveness (25.5%), improvement in symptoms (22.7%), and adverse effects (14.5%). Aytekin *et al*. (2022) reported that the most frequent cause of discontinuation was a supply issue with immunotherapy preparations in Turkey, followed by irregular injection visits without adverse effects (31.2%).

SAEs were observed in 16.6% of patients. Demoly *et al*. (2016) emphasized that improving patient engagement in allergen immunotherapy requires multidimensional programs to enhance participation, address poor adherence, and ultimately improve health outcomes through better self-management and stronger patient-physician relationships. Additionally, smartphone applications, as shown in the study by Cao *et al*. (2018), may help improve adherence.

The duration of immunotherapy plays a crucial role in its effectiveness. Research shows that longer treatment periods can lead to sustained improvements in allergic symptoms even after the therapy has ended. For example, studies have demonstrated that patients undergoing extended immunotherapy experience significant reductions in nasal symptoms and a decreased need for rescue medications (Eifan *et al*., 2011; Lin, 2023). This long-term efficacy is particularly notable in patients with allergies to house dust mites and other common allergens (Valero *et al*., 2022). Furthermore, the duration of SCIT therapy is essential in achieving sustained non-responsiveness (Des Roches *et al*., 1996). In the current study, patients who improved had a significantly longer treatment duration compared to those who did not (10.66±8.82 months vs. 1.02±1.07 months; $P<0.001$), with the treatment duration in the improvement group reaching 26 months (more than 2 years). Supporting our findings, Ren *et al*. (2023) indicated that children who complete a full course of SCIT may experience continued symptom improvement post-treatment, suggesting the lasting effects of the therapy. Additionally, Cox *et al*. (2011) suggested that a 3-year duration of SCIT may be necessary to achieve sustained non-responsiveness after treatment discontinuation. On the other hand, the study by Scadding *et al*. (2017) showed that two years of SCIT therapy did not lead to sustained improvements in nasal symptom scores following allergen challenge one year after discontinuation, when compared to a placebo.

5. Conclusion

SCIT is a promising therapy for atopic diseases, particularly for patients whose conditions are poorly controlled with medications. However, it requires a prolonged duration of treatment to achieve its cumulative effects. Patients who showed improvement had a significantly longer treatment duration compared to those who did not improve (10.66 ± 8.82 months vs. 1.02 ± 1.07 months; $P<0.001$). Nevertheless, no significant relationship was found between treatment outcomes and factors such as patient age, gender, or type of allergy in our study population.

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