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Allergic rhinitis in remission with house dust mite subcutaneous immunotherapy

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Abstract

Background: House dust mite subcutaneous immunotherapy (HDM SCIT) is a therapeutic option for allergic rhinitis (AR) patients who are unable to properly manage symptoms with standard medications.

Objective: This study aimed to determine long-term efficacy and identify predictive factors in the clinical remission of AR patients who completed and discontinued HDM SCIT.

Methods: This study included 240 AR patients, who completed a three-year course of HDM SCIT at two tertiary hospitals and were currently being discontinued. We followed-up the patients to ask about their current symptoms and allergy medication. Clinical remission was defined by patients who no longer required daily intranasal steroid or oral antihistamine. We compared patients in clinical remission to those still taking medication.

Results: The enrolled patients had a median age of 21.0 (11.0–36.0) years at the time they began HDM SCIT. The clinical remission of AR was achieved in 174 (72.5%) patients. Starting HDM SCIT before the age of 15 and not having asthma were identified as significant and independent predictors of remission (aOR 4.44; 95%CI, 1.72–11.50; *p*-value 0.002, and 2.67, 95%CI 1.00–7.12; *p*-value 0.049), respectively, as determined by multivariate logistic regression analysis. There were no significant differences in HDM SCIT duration or sensitization patterns between patients in remission and those on medication after discontinuing HDM SCIT for at least one year.

Conclusions: HDM SCIT exhibited persistent long-term efficacy after treatment discontinuation. Starting HDM SCIT before the age of 15 and without asthma comorbidity might be predictors of AR remission with HDM SCIT.

Key words: Allergic rhinitis, remission, house dust mite, allergen-specific immunotherapy, subcutaneous immunotherapy, long-term efficacy

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Introduction

Allergic rhinitis (AR) is a common condition that affects a large proportion of the population, and its prevalence appears to be increasing. Children with AR have challenges with quality of life, sleep, and work productivity, all of which require time and resources for appropriate therapy.[1] The symptoms of AR are caused by a mucosal inflammatory process triggered by allergens, which includes immunoglobulin E (IgE), and inflammatory mediators.

The diagnosis of AR is based on allergic history, clinical symptoms (sneezing, itching, nasal congestion, and rhinorrhea), physical examination, and the evaluation of specific IgE antibodies through skin prick test (SPT) or serum-specific IgE *in vitro* assay. Management of AR includes environmental exposures control, pharmacotherapy, and considering allergen-specific immunotherapy (AIT) for patients experiencing moderate to severe symptoms that remain uncontrolled with these primary interventions and exhibit evidence of specific immunoglobulin-E sensitization to aeroallergens.[2,3]

AIT is a long-term therapeutic approach uniquely capable of altering the progression of the disease. It is particularly helpful for patients with AR since it modifies the immune response to allergens and provides sustained relief from allergic symptoms.[4] Subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT) are the two main forms of AIT used for AR. SCIT, the more prevalent method with over decades of use in Thailand, consists of two phases. Initially, the build-up phase involves gradually increasing allergen doses until an effective maintenance dosage is reached, typically taking 4 to 6 months. Subsequently, the maintenance phase, wherein patients receive a consistent dose, generally administered range every 2 to 4 weeks, continuously for a minimum of three years. This extended duration is required to achieve clinical and immunological tolerance, ensuring the persistence of clinical benefits and the suppression of type 2 immunity. The clinical efficacy of AIT has been proven to significantly reduce AR symptoms and the requirement of rescue medications.[5,6] Moreover, AIT has been found to be effective in reducing the risk of developing asthma, and in maintaining the therapeutic effects after discontinuation.[7,8]

House dust mites (HDM) are a major source of indoor allergens and a trigger for AR and asthma. The application of SCIT with HDM extract has shown benefits in adults and children suffering from HDM-induced AR.[9] Over the recent years, growing evidence supporting the effectiveness and safety of SLIT for HDM-induced AR.[10] Although several studies demonstrate short- and long-term efficacy in HDM SCIT, the extent of long-term efficacy after treatment completion and discontinuation has not been extensively evaluated. In addition, considering Thailand's tropical climate and high humidity, HDMs are the most common sensitizing allergen in AR patients.[11] The long-term efficacy of HDM SCIT would probably differ from that of SCIT for pollen or grass allergens, especially when compared to studies conducted in Western countries.

Accordingly, this study aimed to clarify remaining questions in HDM SCIT, including its long-term efficacy and the predictive factors for AR remission after HDM SCIT completion and discontinuation, as well as to explore the long-term preventive effect of new asthma development, and patients' satisfaction with HDM SCIT.

Methods

Study design and population

This cross-sectional study included 240 patients diagnosed with AR who completed SCIT treatment from the Allergy and Immunology Unit, Ramathibodi Hospital, Mahidol University, and Banphaeo General Hospital, Thailand between December 1987 and December 2021. The diagnosis of AR was on the basis of clinical symptoms, physical examination, and evidence of HDM (*Dermatophagoides pteronyssinus* and/or *Dermatophagoides farinae*) sensitization, based on a positive skin prick test (SPT) result (defined as a wheal diameter of at least 3 mm) or a positive result on a serum specific IgE test (defined as specific IgE level of at least 0.35 kUA/L). All recruited patients were HDM sensitized, had been on HDM SCIT maintenance treatment for a minimum of three years, and had been discontinued HDM SCIT for a minimum of one year. The patients who were not sensitized to HDM, not completed 3 years of maintenance phase, lost to follow-up, patients who finally switch to SLIT treatment, or who had discontinued HDM SCIT treatment for less than a year were excluded. (**Figure 1**)

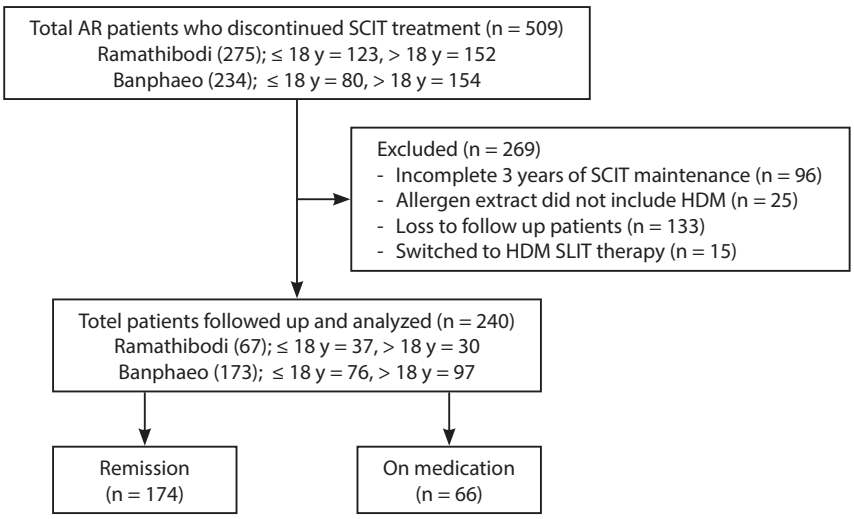

Figure 1. Flowchart of the study.

The ethic approval of this study was obtained from the Ethics Review Board of Ramathibodi Hospital, Mahidol University (COA. MURA2021/1021) and Banphaeo General Hospital (002/65). Verbal inform consents were obtained and recorded from all participants at the telephone follow-up interviews.

Study procedure

A follow-up was conducted either through phone interviews or outpatient clinic visits, assessing patient demographic details, the persistence of symptoms, current medication history, and the patients' opinions regarding HDM SCIT. Participants were required to rate the severity and frequency of their rhinitis symptoms, and a daily medication score was calculated. Additionally, they were questioned about any post-HDM SCIT asthma diagnoses by a physician that required treatment with inhaled corticosteroids. Clinical data (disease duration, sensitization pattern, medication history, comorbidities, and adverse effects of HDM SCIT) were obtained from the medical records.

Immunotherapy

The patients were treated with subcutaneous injections of standardized *Der p* and *Der f* extracts (ALK-Abello Pharm., Inc., Mississauga, Canada). The HDM SCIT treatment protocol consisted of 2 phases, initial build-up phase, followed by maintenance phase. During the build-up phase, there were some differences in the up-dosing protocol. All patients from Banphaeo General Hospital and adult patients at Ramathibodi Hospital followed the conventional protocol, with an up-dosing schedule of up to 16 weeks before reaching a maintenance dose. On the other hand, pediatric patients at Ramathibodi Hospital received up-dosing schedule in a three-day hospitalization under the rush protocol. The details of immunotherapy protocols are shown in **Table 1**. In the maintenance phase, the schedule involved injections every 4 weeks, and the therapeutic maintenance dose varied based on the three allergy units. For the *Dermatophagoides pteronyssinus* (*Der p*) range, it was 300–500 AU, and for *Dermatophagoides farinae* (*Der f*), it was 300–1,000 AU per each 0.5 ml injection.

Table 1. House dust mite Subcutaneous Immunotherapy Protocol.

Pediatric Ramathibodi (Rush protocol)			**Medicine Ramathibodi** (Conventional protocol)			**Ban Phaeo Hospital** (Conventional protocol)		
visit	**Concentration**	**Dosing**	**visit**	**Concentration**	**Dosing**	**visit**	**Concentration**	**Dosing**
Admit d1	1:1000	0.1	1	1:100	0.1	1	1:1000	0.1
		0.2	2		0.2	2		0.2
		0.4	3		0.4	3		0.3
	1:100	0.1	4		0.6	4		0.4
		0.3	5	1:10	0.1	5		0.5
		0.5	6		0.2	6	1:100	0.1
Admit d 2	1:10	0.1	7		0.3	7		0.2
2		0.2	8		0.4	8		0.3
3		0.25	9		0.5	9		0.4
4		0.3	10	1:10	0.07	10		0.5
5		0.35	11		0.1	11	1:10	0.1
6		0.4	12		0.15	12		0.2
7		0.45	13		0.2	13		0.3
8		0.5	14		0.25	14		0.4
9	1:1	0.1	15		0.30	15		0.5
10		0.15	16		0.35	16	1:1	0.1
11		0.2	17		0.40	17		0.2
12		0.25	18		0.45	18		0.3
13		0.3	19		0.5	19		0.4
14		0.35				20		0.5
15		0.4						

Table 1. (Continued)

Pediatric Ramathibodi (Rush protocol)			Medicine Ramathibodi (Conventional protocol)			Ban Phaeo Hospital (Conventional protocol)		
visit	Concentration	Dosing	visit	Concentration	Dosing	visit	Concentration	Dosing
16		0.45						
17		0.5						
*Build-up phase 2 times/week			Every 1 week * 2 weeks			Every 1 /2 /3 week		
Then every 1 /2 /3 week			Every 2 week * 2 weeks			Then every 4 weeks		
Then every 4 weeks			Then every 4 weeks					
*MT Dose: *Der p* 300/ *Der f* 1000 BAU			*MT Dose: *Der p* 500/ *Der f* 500 BAU			*MT Dose: *Der p* 300/ *Der f* 300 BAU		

*Maintenance dosage per injection
Abbreviations: MT: Maintenance, *Der p*: *Dermatophagoides pteronyssinus*, *Der f*: *Dermatophagoides farinae*

Study outcomes

The efficacy of HDM SCIT was evaluated by asking about current AR symptoms and allergy medication use. The symptoms of AR were nasal itching, sneezing, congestion, rhinorrhea, and also eye symptoms. Allergy medication focused on the frequency of medication taken, including antihistamines, intranasal corticosteroids, intranasal decongestant, oral corticosteroids, oral decongestant, and inhaled corticosteroid if indicated in asthma. Patient's preferences were assessed using a preference rating scale ranging from 0 (not satisfied) to 10 (very satisfied), and they were also asked whether they would recommend SCIT to others in the same situation.

Patients were classified into two groups: the remission group, consisting of those who achieved an effective clinical response to SCIT and no longer required daily intranasal steroid or antihistamine to manage symptoms,[12] and the on-medication group, including individuals who still needed medication to control their symptoms despite completion of HDM SCIT treatment.

Statistical analysis

All statistical analyses were performed with SPSS software, version 18.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used for demographic data. The differences between remission and on-medication group were assessed utilizing the independent-sample *t*-test, Mann-Whitney U test, *c*2 test, and Fisher's exact test where applicable. *P*-values less than 0.05 were considered statistically significant. The effects of parameters, including sex, mono/polysensitization, other comorbid atopic diseases, variation in immunotherapy protocols, family history of atopic disease, and history of regular smoking exposure, as predictive factors for remission were analyzed by multiple logistic regression models. Adjusted odd ratios (aOR) with 95% confidence intervals (CI) were reported.

Results

Demographic characteristics

A total of 240 patients, of which 113 (47.1%) were male, were diagnosed with AR with HDM sensitized, had completed the 3-year-HDM SCIT treatment, and had been discontinued HDM SCIT for at least one year. The median age at which patients started HDM SCIT was 21.0 (11.0–36.0) years. When categorized by age range, 109 (45.4%) patients started HDM SCIT after the age of 25, whereas 76 (31.7%) patients started between the ages of 5–12 years. Most of study participants, 234 (97.5%), used both intranasal steroid and oral antihistamine on a daily basis, and 82 (34.2%) had asthma as a comorbidity. The most common sensitization patterns were polysensitization (HDM+ other allergens) (172, 71.7%). Of polysensitization patients, 142 (82.6%) received multiple SCIT allergens (at least 1 allergen combined with HDM). The overall duration of HDM SCIT treatment was 4.5 (3.7, 5.5) years (**Table 2**).

Long-term efficacy of HDM SCIT

Among the 240 patients who completed HDM SCIT, 174 (72.5%) were classified as AR in remission. Considering the time duration after discontinuation of HDM SCIT, 56 (72.7%) patients had a duration of 1–3 years, 100 (41.67%) patients had a duration of 3–5 years, and 63 (26.25%) patients had a duration of more than 5 years. The longest duration after HDM SCIT discontinuation was 16 years, while the shortest time was 1 year. There was no significant difference in the rate of long-term remission between these three groups (**Figure 2a**).

Predictive factors for AR remission

When comparing clinical factors between the remission and on-medication groups, the patients in the remission group started HDM SCIT earlier (16 (11, 33), 31.5 (19.8, 41.3) years, p-value < 0.001). Patients in the on-medication group had more asthma and comorbid atopic diseases,

Table 2. Demographic and characteristics of the study population.

Characteristics	Total study subjects (N = 240)
Age started SCIT (years)	21 (11, 36)
Age distribution	
> 5–12 years	76 (31.7)
> 12–18 years	36 (15)
> 18–24 years	19 (7.9)
≥ 25 years	109 (45.4)
Male	113 (47.1)
Duration of AR* (years)	5 (2, 11)
Asthma comorbid*	82 (34.2)
Other comorbid atopic* (AD, food allergy)	114 (47.5)
Family history of AR/asthma	111 (46.3)
Pre SCIT-Medications*	
- Intranasal steroid with oral antihistamine	208 (86.7)
- Intranasal steroid with oral antihistamine with LTRA	26 (10.8)
- Oral antihistamine (only)	4 (1.7)
- Intranasal steroid (only)	2 (0.8)
Polysensitization	172 (71.7)
- HDM + cockroach	70 (40.7)
- HDM + grass + cockroach	40 (23.3)
- HDM + grass	20 (11.6)
- HDM + cockroach + cat	12 (7)
- HDM + other allergens	30 (17.4)
Received multiple SCIT allergens	142 (59.2)
- HDM + cockroach	75 (52.8)
- HDM + cockroach + grass	27 (19.0)
- HDM + grass	14 (9.9)
- HDM + other allergens	26 (18.3)
Duration of SCIT (years)	4.5 (3.7, 5.5)

Data was presented as N (%) and median (IQR)
*Before start SCIT
Abbreviation: MT: Maintenance, *Der p*: *Dermatophagoides pteronyssinus*, *Der f*: *Dermatophagoides farinae*, AR: Allergic rhinitis, AD: Atopic dermatitis, HDM: House dust mite, SCIT: Subcutaneous immunotherapy

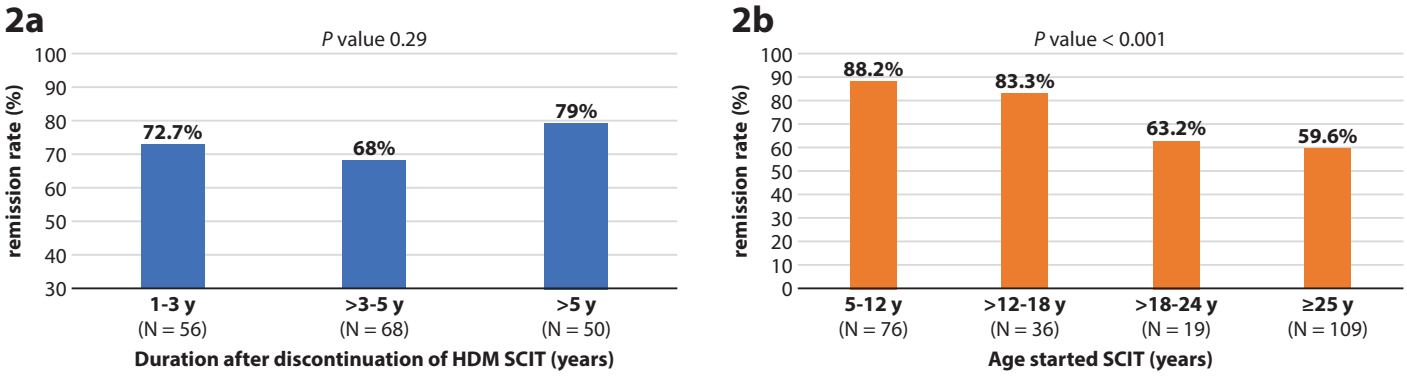

Figure 2. Remission rate by house dust mite immunotherapy (HDM SCIT) in patients with allergic rhinitis (AR) who were sensitized to HDM
2a: Remission rate comparison by years after HDM SCIT discontinuation: 1–3 years, >3–5 years, and > 5 years
2b: Remission rate comparison by age of HDM SCIT initiation: 5–12 years, >12–18 years, >18–24 years, and ≥ 25 years

(*p*-value < 0.001) (**Table 3**). Further analysis was carried out to determine the optimal age at which to begin HDM SCIT in order to achieve a higher remission rate. The results revealed that starting HDM SCIT at a younger age led to significantly higher remission rates (88.2% for ages 5–12, 83.3% for ages >12–18, and 63.2% for ages >18–24, *p*-value < 0.001) (**Figure 2b**).

Multivariate logistic regression analysis revealed that starting HDM SCIT before the age of 15 and not having asthma were identified as significant and independent predictive factors for remission in AR patients receiving HDM SCIT therapy (aOR 4.44; 95%CI, 1.72–11.50; *p*-value 0.002, and 2.67, 95%CI 1.00–7.12; *p*-value 0.049), respectively, after all factors simultaneously adjusted, including sex, sensitization patterns (monosensitization/polysensitization), other comorbid atopic diseases, family history of atopic disease, variation in immunotherapy protocols, history of smoking exposure, and duration of HDM SCIT. The duration of HDM SCIT treatment, sensitization pattern (polysensitization), pet exposure, and HDM SPT wheal size had no association with long-term AR remission (**Table 4**).

Table 3. Comparison between patients in remission and the on-medication group.

Characteristics	Remission (N = 174)	On-medication (N = 66)	*P* value
Age started SCIT (years)	16 (11, 33)	31.5 (19.8, 41.3)	< 0.001
Comorbid asthma*	47 (27.0)	35 (53.0)	< 0.001
Other atopic diseases (AD, food allergy)*	70 (40.2)	44 (66.7)	< 0.001
Duration of AR before start SCIT (years)	5 (2,10)	7.8 (3.0, 17.0)	0.010
Duration of SCIT (years)	4.3 (3.7, 5.4)	5.0 (4.0, 6.1)	0.010

Data was presented as N (%) and median (IQR)
*Before start SCIT
Abbreviation: AD: Atopic dermatitis, SCIT: Subcutaneous immunotherapy

Table 4. Multivariate analysis for predictive factors in remission.

Factors	Adjusted OR*	95%CI	*P* value
Age start SCIT before the age of 15	4.44	1.72 – 11.5	0.002
No asthma comorbid	2.67	1.00 – 7.12	0.04
No other atopic disease (AD, food allergy)	1.53	0.59 – 3.97	0.38
Polysensitization	1.12	0.55 – 2.30	0.75
No family history of atopy	1.64	0.82 – 3.27	0.16
No smoking exposure	0.71	0.34 – 1.46	0.35
Male	1.50	0.74 – 3.05	0.26
Duration of AR before start SCIT	0.99	0.10 – 1.00	0.227

*Adjusted with sex, mono/polysensitization, other atopic diseases, family history of atopic disease, different protocol usage and history of smoking exposure
Abbreviation: AD: Atopic dermatitis, SCIT: Subcutaneous immunotherapy

Adverse events associated with HDM SCIT

During the build-up phase, 46 (19.2%) patients had local reactions and 56 (23.3%) patients had systemic reactions, with 12 of them requiring treatment with adrenaline. During the maintenance phase, there were 63 (26.2%) patients had local reactions and 24 (10%) patients had systemic reactions, with 3 patients receiving adrenaline treatment. The rush protocol of the build-up phase showed a higher rate of systemic reactions than the conventional protocol (54% versus.18%) and all of the reactions met WAO's grade I and II in severity criteria.[13]

New onset of asthma after HDM SCIT

In this study, two patients who began HDM SCIT treatment after the age of 15 developed new onset of asthma, but none of the patients who began HDM SCIT before the age of 15 reported. However, the effectiveness of asthma prevention could not be evaluated due to the lack of control group.

Patients' satisfaction with HDM SCIT

Most patients were satisfied with HDM SCIT therapy with a median scale of 9.0 (8,10). The majority of patients, 210 (87.5%), would recommend HDM SCIT therapy to others; 15 (6.3%) patients were not sure; and 15 (6.3%) would not recommend due to lots of hospital visits, long wait times, unsatisfactory results and overall adverse effects.

Discussion

HDM SCIT is a favorable AR treatment due to its proven benefits. According to studies, patients reported a higher quality of life, reduced nasal symptoms, and decreased medication use.[8,14,15] Long-term treatment has demonstrated the potential to modify the course of allergic disease. However, to the best of our knowledge, there is inadequate evidence to support HDM SCIT's long-term efficacy, especially after treatment discontinuation. Here, we present our data from 240 patients who completed HDM SCIT treatment and had discontinued it for at least one year. Our findings reveal that HDM SCIT leads to AR remission in 72.5% of patients, with sustained effects lasting over 5 years post-discontinuation. Notably, this is the first study that identify significant predictors of post-treatment long-term efficacy in terms of AR remission: starting HDM SCIT before the age of 15 and absence of asthma comorbidity significantly contribute to AR remission. Although our study lacked a control group, a prevalence study in Thailand provides insight into the natural remission of pediatric AR.[16] The study showed similar AR prevalence rates in children aged 6–7 years (15%) and 13–14 years (17.5%), which could imply that the natural remission rate of AR does not show much difference between age groups. Therefore, the clinical improvements observed in our study are likely due to the benefits of HDM SCIT, supporting its efficacy in sustaining clinical improvement for pediatric AR.

Our findings of the AR remission with HDM SCIT are consistent with previous studies. Shin JS et al. reported a 76.6% remission rate using the same remission classification; however, they enrolled adult patients while on treatment (receiving HDM SCIT for at least one year) and post-treatment, whereas our study only assessed post-treatment efficacy, which may more accurately reflect sustained clinical remission.[17] In addition, another pediatric study (which included patients who were still on treatment) showed that 69.7% of patients were effective based on their current medication usage and current symptoms.[12] Only a few studies on the long-term efficacy of HDM SCIT in children have been reported in post-treatment patients. In those studies, they reported data on long-term outcomes less than five years after treatment cessation and found improvements in visual analog scores, rhinoconjunctivitis quality of life questionnaire scores, and total medication scores, contrast to our study, which classified patients as being in remission.[9,18]

International guidelines strongly recommend that allergen immunotherapy should be continued for a minimum of 3 years to achieve disease modification and long-term tolerance.[19] However, symptoms may relapse after discontinuation. The sustained efficacy of HDM SCIT has been a significant concern, especially with limited data on its efficacy years after HDM SCIT cessation. Our data demonstrated that AR remission can maintained in 79% of patients after discontinuation for 5 years. While earlier studies have only followed up for a maximum of 2 years, reporting notable improvements in total nasal symptom scores, daily medication score, and total combined scores.[9,20] In the evaluation of the long-term efficacy of HDM SCIT in asthma patients, assessed up to 3 years post treatment. it was observed that 45% of patients did not have a clinical asthma relapse.[21] The study further indicated a correlation between the duration of HDM SCIT treatment and its duration of efficacy after HDM SCIT cessation. However, this study did not reveal a statistically significant difference in the duration of HDM SCIT treatment between the remission and on-medication groups. Possible reasons for the difference in remission rate include the variations in study participants' age groups, underlying allergic conditions, allergen dosage used in HDM SCIT, and allergen exposure following therapy. Furthermore, variations in the serum HDM-specific IgE of study participants can effect the identification of suitable candidates for undergoing HDM SCIT among patients with HDM-induced allergic rhinitis.[22]

Predicting AR remission in HDM SCIT patients is still challenging, although studies have been performed.[12,17,23] Our study was the first to demonstrate significant predictors based on AR remission in patients who has stopped HDM SCIT. Starting HDM SCIT before the age of 15 and having no asthma comorbidity were found to be significantly correlated with AR remission. The findings align with another study that evaluated clinical improvement and noted that children (age <14 years) tend to achieve better long-term efficacy of HDM SCIT than adults, as evidenced by significant improvements from baseline values in total nasal symptom scores and total combined scores.[9] In contrast, few studies have not found a significant difference in clinical outcomes based on age of starting SCIT.[17,24] Further well-designed long-term studies are required to clarify this aspect. One possible explanation is that children's immune systems are more adaptable,

which may allow for better tolerance and desensitization. While our study identified the absence of asthma as a predictive factor for clinical remission in AR, highlighting the significant difference in the clinical remission of AR symptoms in the specific subgroup of patients without asthma, this does not contradict the established effectiveness of HDM SCIT for asthma. Further studies are needed to explore the benefits of HDM SCIT on asthma control in patients with both AR and asthma.

Studies analyzing the effect of the duration of AR before SCIT treatment on the long-term efficacy have been reported.[9,25,26] Huang, et al., showed that patients who had AR history of less than 10 years resulted in better improvement in a total combined score (TCS) at 2 years after discontinued SCIT.[9] In our study, we found that the duration of AR before receiving HDM SCIT had correlated when comparing the remission group to the on-medication group. However, in multivariate analysis, when adjusting other factors, the duration of AR did not reach statistical significance. Furthermore, other reported predictors of long-term efficacy, such as sensitization status (monosensitization/polysensitization), degree of HDM sensitization (specific IgE level/ wheal size of HDM SPT), smoking exposure, and family history of atopic disease, revealed no significant association in our study.

Allergen-specific immunotherapy has demonstrated effectiveness in preventing new-onset asthma by targeting allergic responses. In our study, we investigated the effect of HDM SCIT on new asthma onset. Notably, only 1.6% of patients who began HDM SCIT after age 15 developed new asthma. However, due to our study's limitations, particularly the absence of a control group, we are unable to definitively attribute this result to HDM SCIT. Further research with larger sample sizes and control groups is required to validate and expand on these findings.

Regarding adverse reactions in HDM SCIT treatment, this study's maintenance phase adverse reaction rate was found to be comparable to previously reported.[27] During the build-up phase, we observed a higher rate of systemic responses.[9,18] This might be due to using a rush protocol in 14.2% of pediatric patients, as contrast to other reports that used a conventional protocol, nonetheless, none of the events were life-threatening. Apart from difference in adverse reactions during the study, we found no other significant differences in treatment efficacy between conventional and rush methods.

The present study has several limitations. First, because it was a cross-sectional study that included a retrospective review, it can have information on recall bias. Second, only current symptoms and medications were used to assess remission; it would be more valuable to have additional results comparing symptom score before and after SCIT treatment. Third, there were no control groups, thus any preventive effect could not be determined. Fourth, the study used two different HDM SCIT protocols, the rush protocol, and the conventional protocol; however, we found no difference in treatment efficacy; we only observed more adverse reactions in patients receiving the rush protocol.

In conclusion, HDM SCIT for 3 years exhibited persistent long-term efficacy, with better clinical outcomes in patients starting SCIT before the age of 15 and without asthma comorbidity. To achieve the best benefits, SCIT should begin in childhood who do not have asthma.

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