

# Deciphering Barriers to Immunotherapy: A Comparative Study of Patient Choices in Dust Mite Allergy Management

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## Abstract

**Background:** Immunotherapy is still underutilized as an etiologic treatment for house dust mite allergic patients. The reason behind it needs to be explored to improve its availability and effectiveness in treating allergic children.

**Objective:** This study aims to determine the differences in non-clinical and clinical characteristics between pediatric dust allergy patients who received immunotherapy and those who did not receive immunotherapy.

**Method:** This research is a cross-sectional analytical study that aims to compare specific variables that have been determined between HDM allergy patients who underwent immunotherapy and pediatric patients with HDM allergy who did not get immunotherapy. The study involved a total of 180 pediatric patients with HDM allergies who visited the allergy outpatient clinic at the Department of Pediatrics, Dr. Soetomo General Hospital during the period of January 2018 to December 2021. Data for the study were collected from the existing medical records, followed by data processing and comparative analysis.

**Result:** The total sample was collected as many as 180 pediatric dust allergy patients with 90 patients receiving immunotherapy and 90 patients not receiving immunotherapy. The data analysis using Chi-square test found a significant difference ( $p < 0.05$ ) between the two groups regarding the clinical diagnosis of rhinitis, clinical diagnosis of sinusitis, skin prick test results for pet and food allergen, local side effects and systemic side effects. However, no significant differences ( $p > 0.05$ ) were found in the non-clinical characteristics between two sample groups.

**Conclusion:** There were significant differences in the clinical diagnosis of rhinitis, clinical diagnosis of sinusitis, skin prick test result, local side effects and systemic side effects among pediatric patients with HDM allergy who undergo immunotherapy compared to those who only received standard treatment.

Keywords: Characteristics ; Children ; Dust allergy ; House dust mites ; Immunotherapy; Non-Immunotherapy ; Profile

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## 1. Introduction

The global rise in house dust mite allergy prevalence, including in Indonesia, poses a significant health challenge [1,2]. Although symptoms rarely become life-threatening, they adversely affect the quality of life for patients and their caregivers [3]. Allergen immunotherapy (AIT) emerges as an effective solution for paediatric dust mite allergies, offering long-term clinical and immunological tolerance, thereby improving children's quality of life and potentially preventing allergy progression [4,5]. Despite its advantages, immunotherapy remains underutilized as a modality for modifying allergy etiological causes, with many paediatric patients choose not to do it.

Patients who choose not to get allergen immunotherapy shots must depend on medications to manage allergies symptoms, particularly in children where persistent symptoms create a lifelong reliance on drugs. However, conventional treatments are often insufficient in controlling allergies symptoms. Besides that, pharmacotherapy can't prevent the progression of the disease and has to be administered repeatedly as long as symptoms prevail, which often means life-long [6]. Immunotherapy is advised for such cases. If allergy symptoms are not controlled properly, it will have a negative impact on the patient's life. Allergies significantly disrupt children's growth and development, impacting productivity, quality of life, and imposing economic burdens [7,8]. Additionally, they contribute to frequent school absences, which have long-term effects on children's education [3].

Pediatric dust allergy patients' low participation in immunotherapy may result from various supply and demand-related factors. Regarding availability, healthcare services offering immunotherapy facilities remain sparse, with immunotherapy facilities mainly in Malang and Surabaya City, East Java. Patient reluctance stems from parental misunderstanding about immunotherapy's effectiveness and safety, leading to fear and doubt. Additionally, preferences for quicker drug treatments over the discomfort and prolonged nature of immunotherapy sessions contribute to this problem [4].

Investigating the reasons behind the non-participation of dust-allergic pediatric patients in immunotherapy programs is crucial. Understanding these reasons can pave the way for solutions to work up their participation. This research aims to identify barriers to participation in dust allergy immunotherapy among patients and offer recommendations to improve its availability and effectiveness in treating allergic children. Additionally, it explores the manifold benefits and safety aspects of immunotherapy in children, seeking to alleviate patient hesitancy and fears surrounding its selection as a treatment for dust allergies in children.

## 2. Materials and Methods

This was an observational analytical study conducted in Dr. Soetomo General Academic Hospital, Surabaya, from January 2018 until December 2021. The population of this study were pediatric patients who suffered house dust mite allergy in the allergy outpatient clinic at the Department of Pediatrics, Dr. Soetomo General Hospital Surabaya. The sample in this study were patients who met the inclusion criteria, which were pediatric patients aged 5-18 years old, had a positive skin prick test result for house dust mites allergen, and were treated at the allergy outpatient clinic in 2018-2021. The exclusion criteria were patients with incomplete medical record data.

The minimal sample size required in this study was 43 patients. This study used the quota sampling by taking the samples who met the inclusion and exclusion criteria until it exceeds the minimum required sample size. The subjects were assessed based on the non-clinical data -including gender, address, parental education and occupation – and clinical data regarding type of clinical diagnosis, skin prick test result, and side effect.

The research instrument used in this study was the medical record of allergic pediatric patients at Dr. Soetomo General Hospital Surabaya who met the inclusion criteria. The data was analyzed using SPSS. Because all the variables are categorical, the normal distribution test was not performed. Statistical analysis was carried out using the Chi-square test to see whether there were differences in the two sample groups. There is a significant difference if the test carried out produces a p value of less than 0.05. For variables with an expected cell count < 5 more than 20% of cells, the comparison test used is the Fisher's Exact Test.

### 3. Results

A total of 180 samples were obtained which were then grouped based on the type of therapy the samples received. The first group consisted of 90 pediatric dust allergy patients who underwent pharmacotherapy treatment without participating in an immunotherapy program, while the second group consisted of 90 pediatric dust allergy patients who underwent an immunotherapy program for house dust mite allergens.

Table 1. Non-Clinical Characteristics of The Patients

Characteristics	Immunotherapy Group (n=90)	Non-Immunotherapy Group (n=90)	p-value
Gender			
Male	67 (74.4)	64 (71.1)	0.615
Female	23 (25.5)	26 (28.8)	
Geographic Region			
Surabaya	31 (34.4)	34 (37.7)	0.366
East Java (outside Surabaya)	51 (56.6)	43 (47.7)	
Outside Java	8 (8.8)	13 (14.4)	
Parent's Last Education			
JHS	3 (3.3)	3 (3.3)	0.893
SHS	7 (7.7)	4 (4.4)	
Bachelor	30 (33.3)	32 (35.5)	
Master	47 (52.2)	49 (54.4)	
Doctoral	3 (3.3)	2 (2.2)	
Parent's Occupation			
Government Employee	35 (38.8)	34 (38.8)	0.999
Entrepreneur	30 (33.3)	31 (34.4)	
Labor	5 (5.5)	5 (5.5)	
Etc	20 (22.2)	20 (22.2)	

Table 1 shows stratification according to non-clinical aspects of the patients. Of all the patients in the both groups, they were predominantly male in the immunotherapy group (74.4%) and non-immunotherapy group (71.1%). The geographical distribution of the region where they come from is: Surabaya 34.4%, East Java (Outside Surabaya) 56.6%, as well as from outside Java (8.8%). While the non-immunotherapy group comes from Surabaya (37.7%), East Java (Outside Surabaya) 47.7% and Outside Java 14.4%.

Comparative analysis was also carried out to determine whether there were differences in parental education and parental occupation between patients who received immunotherapy and those who did not receive immunotherapy. For the parental education variable, the Fisher exact test method was used because the calculation results showed that 40% of cells had expected cell count less than 5. And for the parental occupation, the Chi-squared test was used. That comparative test showed that there is no significant difference in parents' last education and parent occupation between two groups. The majority of patients' parents had master's degrees and worked as civil servants. It can be concluded that there are no significant differences in non-clinical aspects between the two sample groups.

Table 2. Clinical Characteristics of The Patients

Characteristics	Immunotherapy Group (n=90)	Non-Immunotherapy Group (n=90)	p-value
<b>Primary Clinical Diagnosis</b>			
Asthma	44 (48.8)	33 (36.6)	0.097
Rhinitis	13 (14.4)	84 (93.3)	<0.001
Chronic cough	40 (44.4)	56 (62.2)	0.17
Sinusitis	0 (0)	7 (7.7)	0.007
Eczema	10 (11.1)	7 (7.7)	0.445
Urticaria	3 (3.3)	2 (2.2)	0.65
Conjunctivitis	1 (1.1)	0 (0)	1.0
GI problem	2 (2.2)	0 (0)	0.155
<b>Skin Prick Test</b>			
House dust mite	90 (100)	90 (100)	-
Pet	89 (98.8)	81 (90)	0.009
Food	88 (97.7)	79 (87.7)	0.01
<b>Side Effect</b>			
Local	18 (20)	0 (0)	<0.001
Systemic	11 (12.2)	0 (0)	0.002

The Chi-square test on the primary clinical diagnosis of the patients showed 2 variables that significantly differences between two groups. Rhinitis and sinusitis were significantly different in the immunotherapy and non-immunotherapy groups ( $p < 0,005$ ). Both of those diagnoses are more frequently found in the non-immunotherapy group (Table 2). For other diagnoses, such as asthma, chronic cough, eczema, urticaria, and GI problems, there were no significant differences ( $p > 0.005$ ). Asthma was the most common clinical diagnosis in the immunotherapy group (48,8%), while in the non-immunotherapy group the most frequent diagnosis was rhinitis (62,2%).

In Table 2, it can be seen that the occurrence of local and systemic side effects was significantly different in the immunotherapy and non-immunotherapy groups. Among 90 patients who received immunotherapy, there were 18 patients (20%) who experienced local side effects. Meanwhile, among the 90 patients in the non-immunotherapy group, none of them experienced local or systemic reactions.

Table 2. Allergen Distribution of Patients

Allergens count	n	%
1	7	3.8
2	9	5
3	164	91.1

For the skin prick test results, Chi-square test showed two allergens that significantly differ between two groups, namely food and pet allergens. The distribution shows that in the immunotherapy group, positive skin prick test results for food and pet allergens were significantly higher compared with patients who did not participate in the immunotherapy program. Table 3 shows how the patient's number of sensitization is distributed. Of the total samples, it was found that the majority of samples had polysensitization and were sensitive to two (5%) or even three (91.1%) allergens. The number of patients who were only sensitive to one allergen (monosensitization) was 7 patients (3.9%).

#### 4. Discussion

The study outcomes revealed no significant gender disparity between dust-allergic pediatric patients engaged in immunotherapy and those undergoing pharmacological therapy alone ( $p = 0.615$ ). Similar findings were noted by research conducted in Surabaya indicating no notable gender differences among pediatric patients receiving or not receiving immunotherapy [9]. Nonetheless, males constituted a higher percentage in both groups (74.4% in the immunotherapy group and 71.1% in the non-immunotherapy group). While gender remains an unmodifiable risk factor in childhood hypersensitivity reactions, boys exhibit a doubled asthma risk early on [10]. However, as sexual development ensues, more girls tend to suffer from allergies compared to boys, suggesting a shift in this trend. Hormones like testosterone in males seem protective, whereas estrogen in females exacerbates allergic asthma symptoms [11].

Domicile comparisons among pediatric dust allergy patients in the immunotherapy and non-immunotherapy groups didn't yield significant differences ( $p = 0.366$ ). Echoing findings from another research shows no substantial domicile disparities were observed between groups receiving or not receiving Subcutaneous Immunotherapy (SCIT) [12]. A majority (88.3%) of patients hailed from East Java Province, with a significant portion seeking treatment in Surabaya, comprising 31 patients in the immunotherapy group and 34 in the non-immunotherapy group. Many patients traveled from beyond the city and even the island to access treatment at Dr. Soetomo Surabaya, indicating limited availability of immunotherapy services, currently concentrated in Surabaya and Malang City, East Java.

Educational variables among parents or guardians of pediatric patients receiving or not receiving immunotherapy showed no significant differences ( $p = 0.893$ ). Notably, 53.3% of parents of dust-allergic pediatric patients held Master's degrees. Correspondingly, research in Denmark suggests that families with higher education levels are more inclined to opt for immunotherapy for dust allergies [5]. Higher-educated parents tend to possess heightened health awareness, promptly seeking medical assistance when their child exhibits symptoms.

Similarly, no significant discrepancies in parental employment variables were detected between dust-allergic pediatric patients undergoing immunotherapy and those who were not ( $p = 0.99$ ). Work profiles aligned across both groups, with civil servants/TNI/Polri constituting the most prevalent employment category, followed by self-employed individuals. Employment aspects often correlate with education levels, impacting health-related knowledge and awareness. Research in Makassar suggests a higher prevalence of positive SPT results for aeroallergens in children from higher socio-economic families compared to those from lower socio-economic backgrounds, further highlighting socio-economic influences on allergic diseases [13]. Immunotherapy should not impose an economic burden on dust allergy patients because this treatment is covered by BPJS (Indonesia's health insurance program). However, there are indirect costs that patients have to pay. Such as transportation costs, reduced productivity of patients and their families, loss of working hours

for parents or guardians of patients to take their children to treatment every week. These are the things that patients must consider before choosing this treatment approach.

The preference for pharmacotherapy over immunotherapy among pediatric dust allergy patients, especially those with rhinitis and sinusitis diagnoses, prompts various considerations. Patients may opt for pharmacological treatment due to manageable symptoms or they may consider the symptoms of rhinitis or sinusitis that are occurring as not something serious so there is no need to spend more effort through an immunotherapy program to cure their child's allergies. Individual preferences and the perceived invasiveness of immunotherapy also factor in, alongside the associated costs—despite coverage by BPJS, indirect expenses for completing a series of immunotherapy session may impact their decision. Apart from the many factors above, if immunotherapy facilities are easily accessible, immunotherapy should be the main therapy option chosen by patients if they want to cure dust allergies. Many studies state that immunotherapy has reliable effectiveness [14,15,16]. Immunotherapy is known to induce long-term clinical and immunological tolerance and can improve children's quality of life. Immunotherapy is also a promising intervention to prevent the development of allergic diseases [5]. Moreover, immunotherapy can reduce medical expenses of treatment for pediatric dust allergy patients [12].

In our statistical analysis, we examined skin prick test results to compare differences between the immunotherapy and non-immunotherapy groups. Significantly higher positive test outcomes for food ( $p = 0.009$ ) and pet allergens ( $p = 0.01$ ) were noted in the immunotherapy participants, aligning with another studies indicating pet allergens as prevalent among patients (94.4%), followed by food allergens (92.8%) [16]. Moreover, our findings demonstrated that 96.1% of patients tested positive for multiple allergens, commonly observing sensitivities to both food and pet allergens. This trend of polysensitization among dust allergy patients undergoing immunotherapy is consistent with previous studies indicating a shift from monosensitization to polysensitization over time. Notably, polysensitization correlates with increased allergic disease severity, affecting 27.5–74.3% of allergic patients in the US and Europe [17,18]. Despite polysensitization's prevalence, it shouldn't impede immunotherapy, as it has shown beneficial outcomes in both monosensitized and polysensitized patients [17,19].

In examining side effects, our Chi-square test revealed significant differences between the immunotherapy and non-immunotherapy groups, with higher incidences of both local and systemic side effects in the immunotherapy participants ( $p < 0.005$ ). Specifically, 32.2% of immunotherapy patients experienced side effects, predominantly local (20%). These findings align with prior research highlighting a higher frequency of side effects among immunotherapy-receiving dust allergic patients compared to those on pharmacological therapy alone [20]. This underscores the importance of monitoring and managing potential side effects in patients undergoing immunotherapy. According to practice guidelines, administering Allergen Immunotherapy (AIT) in settings equipped to handle adverse reactions and monitoring patients for 30 minutes post-therapy is essential [21]. The choice of care location, such as a hospital-supervised facility, might enhance safety and treatment compliance [4]. Patients perceive clinical settings with trained personnel, appropriate equipment, and medications as preventive against serious side effects, potentially influencing their treatment decisions [19]. Safety concerns arise from the weekly allergen injections during a year-long immunotherapy course, potentially leading to side effects, prompting hesitation among patients in choosing this treatment path for their children's allergies. These varied factors influence patient choices and warrant comprehensive consideration in treatment planning for pediatric dust allergies. Immunotherapy, while not entirely risk-free, is generally considered safe and well-tolerated [19].

## 5. Conclusion

Significant differences were found between the immunotherapy group and the non-immunotherapy group in clinical characteristics, namely clinical diagnosis of rhinitis, clinical diagnosis of sinusitis, skin prick test results, and the occurrence of side effects. Meanwhile, no differences were found in non-clinical characteristics between two groups.

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