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Factors influencing adherence with subcutaneous immunotherapy among pediatric patient in Surabaya, Indonesia, during and after the COVID-19 pandemic

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Abstract: Adherence is the most critical issue for subcutaneous immunotherapy (SCIT) as treatment for house dust mite allergy. During the COVID-19 pandemic there was a decline in the attendance at immunotherapy clinics. This study aims to identify factors influencing immunotherapy adherence in Dr. Soetomo's hospital during and after the pandemic. A retrospective cohort study was conducted between August 2023 and December 2023. The study sample included all patients allergic to house dust mite diagnosed and treated with SCIT under 18 years at the Child Allergy Clinic Facility, Department of Child Health Sciences, Dr. Soetomo General Academic Hospital Surabaya, who were then interviewed using questionnaire and Google Sheet. Data were analyzed using Chi square test with significance set at $p<0.05$. Structural Equation Modeling (SEM) and Partial Least Squares SEM (PLS-SEM) were used with Smart PLS software. Influencing factors including the risk of systemic reaction, distance to health facilities, injection discomfort, child perception, parental perception, costs and insurance, fears of getting infected with COVID-19, suspected immunotherapy services discontinued, and child positive of COVID-19 are not relate to immunotherapy adherence ($p>0.05$). Environment factor, including concern about lack of transportation during lockdown and concern relate to family members exposed to COVID-19 influenced immunotherapy adherence.

Keywords: *Adherence, Child, COVID-19, Health, Immunotherapy.*

1. Introduction

Adherence is a key issue for subcutaneous immunotherapy (SCIT) in treating house dust mite allergy [1]. Adhering to immunotherapy significantly reduces clinical symptoms and the need for symptomatic treatment. Studies in Indonesia, SCIT significantly reduces symptoms in 73.8% of children with allergic asthma. Non-adherence can increase the recurrence of respiratory symptoms, including asthma [2].

Moreover, adherence to immunotherapy impacts the cost-effectiveness of treatment. Studies suggest that immunotherapy can save up costs compared to pharmacotherapy alone. Factors contributing to non-adherence include discomfort from injections, perceived ineffectiveness, symptom improvement, and relocation. Adverse reactions and costs or lack of insurance also play roles in non-adherence [3].

During the COVID-19 pandemic, there was a decrease in the uptake of immunotherapy due to fears of infection, transportation issues, and changes in healthcare services. Fear of infection was the most common reason for discontinuing immunotherapy [4]. Further research is needed to understand the factors affecting adherence with SCIT, particularly during and after the pandemic, to develop effective policy guidelines.

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Research on the factors affecting adherence to SCIT remains limited. Such data are essential for developing policy guidelines. Therefore, more studies are needed to identify the factors influencing immunotherapy adherence during and after the pandemic.

2. Methods

2.1. Study Design

The research design used was a retrospective cohort study. The sample group was observed for six months during the pandemic. This study was conducted to gather information from patient records regarding patient adherence to immunotherapy and the factors influencing it. The research focused on patients with house dust mite allergies undergoing SCIT at Dr. Soetomo General Academic Hospital from August 2022 to December 2022. Data collection was carried out using questionnaires through interviews and electronically.

2.2. Population and Sample

The research sample consisted of patients with house dust mite allergies undergoing SCIT at Dr. Soetomo General Academic Hospital who met the inclusion criteria consist of under 18 years of age, diagnosed with house dust mite allergy, and undergoing SCIT. Patients were excluded from the study if they did not consent to participate, if their parents had children with special needs, or if the questionnaire data were incomplete

The sample size was determined using total sampling calculated with Lemeshow's formula. With a type I error set at 5%, the significance level ($Z\alpha$) is 1.96, and with a type II error set at 20%, the power of the study ($Z\beta$) is 0.84. Based on these calculations, a minimum of 74 participants was required for each group.

2.3. Data Collection

Data from pediatric patients meeting the inclusion criteria were collected using data collection sheets. Follow-up data collection involved examining factors influencing patient adherence to immunotherapy, including patient data, patient records, and factors affecting immunotherapy adherence. These factors included the risk of systemic reactions, distance from home to the healthcare facility, injection discomfort, family and child perceptions of immunotherapy effectiveness, costs and health insurance, fear of COVID-19 infection, suspected suspension of immunotherapy services during the pandemic, transportation issues during lockdown, family members infected with COVID-19, and patients testing positive for COVID-19. The collected data were presented in tabulated form, graphs, and tables at the end of the study.

2.4. Data Analysis

The results of this study were analyzed using several statistical tests, including tests for variable effect relationships with the chi-square ($\chi 2$) test and the Mann-Whitney U test. To test our hypotheses, we employed Structural Equation Modeling (SEM). If the data were normally distributed, we used Covariance-Based SEM (CB-SEM) with AMOS software. If the data were not normally distributed, we used Partial Least Squares SEM (PLS-SEM) with SmartPLS software. We estimated Confirmatory Factor Analysis (CFA) with unidimensionality for each scale and checked the reliability validity of each variable. Items with values less than 0.500 were removed. Since our variables are reflective, indicator reliability was assessed using factor loadings and Cronbach's alpha. A Cronbach's alpha value greater than 0.700 was considered to indicate reliability and accuracy.

2.5. Research Ethics

Any collection of research subjects must obtain written consent from parents or guardians. The ethical feasibility of research was issued by the Health Research Ethics Committee of Dr. Soetomo

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General Academic Hospital Surabaya on 12nd September 2023 with number 0771/KEPK/IX/2023. The confidentiality of research subjects is well maintained by not mentioning names, but writing by initials. The data from this research is only used for research purposes.

3. Results

In this study, data were collected from 150 patients undergoing immunotherapy, divided into two groups: 75 patients during the pandemic and 75 patients after the COVID-19 pandemic. The sample characteristics are presented in Table 1.

Table 1.
Characteristics before and during the COVID-19 pandemic.

Characteristics	After the COVID-19 pandemic		During the COVID-19 pandemic	
	n	%	n	%
Child's gender				
Male	36	48.0%	37	49.3%
Female	39	52.0%	38	50.7%
Caregiver's gender				
Male	12	16.0%	4	5.3%
Female	63	84.0%	71	94.7%
Parental education				
Elementary school	2	2.7%	0	0%
Middle school	5	6.7%	1	1.3%
High school	39	52.0%	64	85.3%
Diploma	6	8.0%	5	6.7%
Bachelor's degree	22	29.3%	5	6.7%
Master's degree	1	1.3%	0	0%
Parental occupation				
Unemployed	2	2.7%	0	0%
Homemaker	51	68.0%	63	84.0%
Employee	18	24.0%	12	16.0%
Entrepreneur	2	2.7%	0	0%
Other	2	2.7%	0	0%
Place of origin				
Surabaya	47	62.7%	58	77.3%
Outside surabaya	28	37.3%	17	22.7%
Compliance with immunotherapy				
Yes	63	84%	60	80%
No	12	16%	15	20%

The characteristics included gender of children and caregiver, parents' education, parents' occupation, and city of origin. During the pandemic, most subject were female (50.7%), with the majority of caregivers also being female (94.7%). After the pandemic, most subjects were female (52%), with the majority of caregivers also being female (84%). The majority of parents' education level was high school during the pandemic (85.3%) and remained high school after the pandemic (52%). Most parents' occupations during the pandemic (84%) and after the pandemic (68%) were homemakers, with some being employees. The majority of patients were from Surabaya during the pandemic (77.3%) and after the pandemic (62.7%). Most patients adhered to immunotherapy; however, during the COVID-19 pandemic, 20% of patients were non-compliant, while after the pandemic, 16% were non-compliant.

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Table 2.
Comparison of Patient Compliance Before and After the COVID-19 Pandemic.

Factor	During COVID-19 pandemic			After COVID-19 pandemic		
	Compliant	Non-compliant	p-value	Compliant	Non-compliant	p-value
Risk anafilaksis awarness						
Yes	25 (41.7)	7 (46.7)	0.953	32 (50.8)	6 (50.0)	1.000
No	35 (58.3)	8 (53.3)		31 (49.2)	6 (50.0)	
Distance from home to health facility						
Yes	19 (31.7)	4 (26.7)	1.000	17 (27.0)	4 (33.3)	0.729
No	41 (68.3)	11 (73.3)		46 (73.0)	8 (66.7)	
Injection discomfort						
Yes	14 (23.3)	3 (20.0)	1.000	17 (27.0)	4 (33.3)	0.729
No	46 (76.7)	12 (80.0)		46 (73.0)	8 (66.7)	
Child's perception						
Yes	7 (11.7)	2 (13.3)	1.000	9 (14.3)	4 (33.3)	0.204
No	53 (88.3)	13 (86.7)		54 (85.7)	8 (66.7)	
Parental perception						
Yes	19 (31.7)	7 (46.7)	0.430	16 (25.4)	4 (33.3)	0.723
No	41 (68.3)	8 (53.3)		47 (74.6)	8 (66.7)	
Cost and insurance						
Yes	8 (13.3)	1 (6.7)	0.677	17 (27.0)	3 (25.0)	1.000
No	52 (86.7)	14 (93.3)		46 (73.0)	9 (75.0)	
Concerns about contracting COVID-19						
Yes	54 (90.0)	12 (80.0)	0.372	14 (22.2)	5 (41.7)	0.167
No	6 (10.0)	3 (20.0)		63 (84.0)	12 (16.0)	
Suspected immunotherapy service suspension						
Yes	59 (98.3)	14 (93.3)	0.362	18 (28.6)	6 (50.0)	0.182
No	1 (1.7)	1 (6.7)		45 (71.4)	6 (50.0)	
Transportation issues during lockdown						
Yes	54 (90.0)	14 (93.3)	1.000	18 (28.6)	6 (50.0)	0.182
No	6 (10.0)	1 (6.7)		45 (71.4)	6 (50.0)	
Family infected with COVID-19						
Yes	57 (95.0)	14 (93.3)	1.000	16 (25.4)	5 (41.7)	0.299
No	3 (5.0)	1 (6.7)		47 (74.6)	7 (58.3)	
Child tested positive for COVID-19						
Yes	60 (100.0)	15 (100.0)	0.75	27 (42.9)	5 (41.7)	1.000
No	-	-		36 (57.1)	7 (58.3)	

The comparison in Table 2 shows that factors influencing patient adherence included the risk of systemic reactions, distance from home to healthcare facilities, injection discomfort, children's perceptions, parents' perceptions, costs and insurance, fear of COVID-19 infection, suspected suspension of immunotherapy services, transportation issues during lockdown, family members infected with COVID-19, and children testing positive for COVID-19. According to the chi-square statistical test, there were no significant differences in these factors affecting patient adherence during the COVID-19 pandemic compared to after the pandemic ($p>0.05$).

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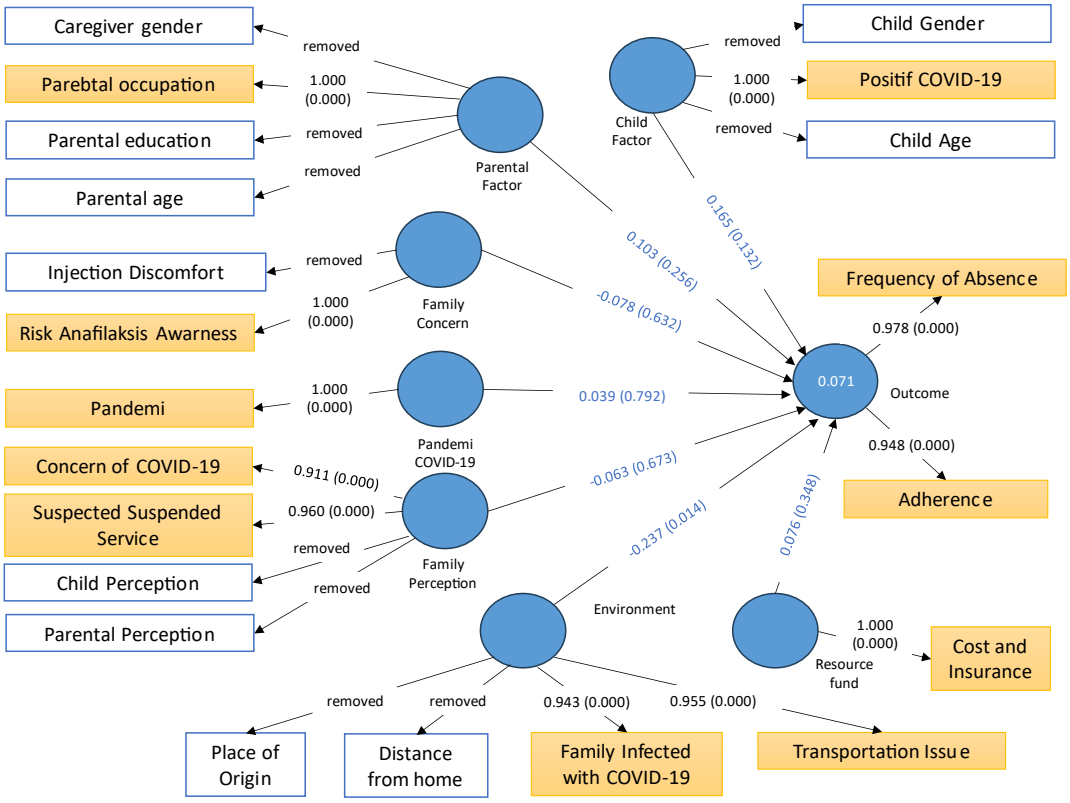

Figure 1.
Multivariate analysis (PLS-SEM analysis).

This data was not normally distributed, so we used Partial Least Squares SEM (PLS-SEM) with SmartPLS software. We estimated Confirmatory Factor Analysis (CFA) with unidimensionality for each scale and assessed the validity and reliability of each variable. Items with values less than 0.500 were removed. Since our variables are reflective, the reliability indicators were factor loadings and Cronbach's alpha. Reliability or accuracy is indicated by a Cronbach's alpha value greater than 0.700, and significance is indicated by $p<0.05$.

The multivariate analysis results in Figure 1 showed that the influencing factors, including children testing positive for COVID-19, parents' occupation, fear of anaphylaxis risk, suspected suspension of immunotherapy services, and fear of contracting COVID-19, did not affect immunotherapy adherence. However, environmental factors ($p=0.014$), such as concerns about transportation availability during lockdown ($\alpha=0.955$) and worries about family members contracting COVID-19 ($\alpha=0.943$), did influence adherence to immunotherapy.

4. Discussion

This study involved 150 patients undergoing immunotherapy, divided into two groups of 75 patients each, one during the pandemic and the other after the COVID-19 pandemic. The majority of respondents were female, with 52% after the pandemic and 50.7% during the pandemic. Another study explored the relationship between gender and COVID-19 diagnosis and testing practices, finding no significant difference between males and females in healthcare-seeking behavior [5].

The relationship between caregivers and patients significantly impacts their financial burden, especially for underage patients, as they cannot bear their costs. This burden is exacerbated when patients have chronic illnesses, limiting caregivers' career opportunities and leaving them focused on

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daily expenses. The necessity for caregivers to be constantly available for patients makes career advancement challenging. While feminine traits like nurturing may enhance caregiving (e.g., being fully present, recognizing children's feelings, providing physical affection), this devotion leaves little time for work, disrupting therapy costs. Female caregivers report higher levels of stress, anxiety, fatigue, low self-esteem, and pessimism compared to male caregivers, further increasing their burden [6].

Most parents of children with HDM allergy who attended the clinic post-pandemic were housewives (64% after the pandemic and 86% during the pandemic) [7]. Research on caregivers' employment, especially housewives, is limited, despite their traditional role as primary caregivers for children with chronic illnesses. Unpaid and socially undervalued work significantly impacts stress levels, particularly for housewives caring for children with special health needs. Without training or experience, housewives face caregiving burdens that affect their health perceptions and psychosocial balance [8].

Most patients in this study were from Surabaya, with 62.7% post-pandemic and 77.3% during the pandemic. This data suggests that patients in Surabaya have better access to immunotherapy services. The distance to healthcare facilities impacts the utilization of health services. In the Netherlands, immunotherapy can be administered in specialized centers and general practitioners' clinics. Dutch research shows higher adherence with immunotherapy among patients treated by general practitioners than allergy specialists, indicating the importance of convenient access [9].

The study showed that patient adherence with immunotherapy during (84%) and after the COVID-19 pandemic (80%) was not significantly different. Education on immunotherapy adherence at Dr. Soetomo General Academic Hospital was provided during each prick test, maintaining high adherence rates. The pandemic affected healthcare service utilization, but it did not significantly impact immunotherapy adherence in this study, suggesting that continuous education and support can mitigate such barriers [10].

As is well known, factors influencing adherence levels encompass all aspects that can have both positive and negative impacts, leading sufferers to move from less compliant to non-compliant. These factors include understanding the instructions given, the education level affecting the ability to comprehend and follow instructions, beliefs, attitudes, and personality contributing to motivation and perception towards treatment, as well as social support playing a crucial role in providing motivation and practical help during the treatment process [10]. This study encompasses several factors generally affecting immunotherapy adherence during and after the COVID-19 pandemic, allowing us to observe changes in these influencing factors' trends after the pandemic. Comparing patient adherence during and after the COVID-19 pandemic shows that factors such as the risk of systemic reactions, distance to healthcare facilities, injection discomfort, child and parent perceptions, costs and insurance, fear of COVID-19 infection, suspicion that immunotherapy services were halted, transportation issues during lockdown, family infection with COVID-19, and children testing positive for COVID-19 all play a role. This study found no significant difference in patient adherence factors during and after the COVID-19 pandemic ($p>0.05$).

This study found that anxiety about the risk of systemic reactions during and after the pandemic did not affect patient adherence with immunotherapy ($p>0.05$). The risk of systemic reactions can appear within 30 minutes [11] including asthma or allergic rhinitis in children, and even anaphylactic reactions [12]. Injections are administered in the upper arm and usually take place monthly until the maintenance phase (three years). Billions of immunotherapy injections are given as scheduled, with minimal, though not nonexistent, fatal risks. Local allergic rhinitis, marked by hyperemia and swelling (edema) around the injection site, is commonly reported, occurring in 26%-82% of patients from 0.7%-4% of injections. Large lesions (>10 cm) or local granulomas may occur due to aluminum hydroxide, suggesting a dose reduction or switching to another adjuvant. Local allergic rhinitis does not significantly increase the risk of systemic reactions [13].

In children, the prevalence of severe systemic reactions is very low, about <0.1% of injections. A survey in the USA indicated that non-fatal systemic reactions occurred in 0.15% of injections and 0.7%

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of patients receiving immunotherapy. Between 2008 and 2017, there were only seven fatal cases from 54.4 billion injection visits. However, in Italy, systemic reactions occurred in up to 5% of cases, with four patients requiring epinephrine injections, but no fatalities reported. Uncontrolled asthma was identified as a major risk factor for severe and fatal systemic reactions, with 50% of asthma attacks involving severe complications. Other influencing risk factors include pollen season, a history of severe reactions, being in the build-up phase of therapy, and injection administration errors [13].

Research at Dr. Soetomo General Academic Hospital indicated that systemic and local reactions occurred in 17.9% of patients, with systemic reaction incidence at 8.38%, accounting for 0.53% of total immunotherapy injections. All patients reporting reactions did so within 30 minutes post-injection, and initial therapy yielded a good and quick response. The most common reactions were urticaria, followed by rhinoconjunctivitis. This study also found that anaphylaxis occurred in 0.091% of 1098 patients and 0.0033% of 30,774 injections [14]. The fear of systemic reactions did not impact immunotherapy adherence, likely because immunotherapy was conducted in a Type A hospital with complete facilities and responsive healthcare personnel.

Distance to healthcare facilities did not affect patient adherence with immunotherapy during and after the pandemic ($p>0.05$). This is likely because most patients visiting Dr. Soetomo General Academic Hospital polyclinic were from Surabaya. However, in other regions, distance can affect adherence. This study's differing results may be due to patient education, easy transportation, and consistent treatment schedules [15]. In Indonesia, immunotherapy practices are still limited, mainly available in urban areas. Expanding allergy services to primary healthcare and improving accessibility through healthcare provider training and specialized allergy programs in tertiary services are essential [16].

This study showed that injection discomfort did not affect patient adherence during and after the pandemic ($p>0.05$). Another study in contrary suggests that injection discomfort affects immunotherapy non-adherence [17]. Another study showed that patients receiving SCIT had lower adherence rates compared to sublingual immunotherapy, suggesting that the administration route impacts adherence [18]. However, regular visits to healthcare providers might provide motivation and alleviate concerns about immunotherapy [19].

This study indicated that child and parent perceptions did not influence SCIT adherence ($p>0.05$). Patient perception can play a crucial role in predicting self-efficacy in disease management and treatment adherence [20]. Improving patient perception through education and psycho-educational interventions is vital. In allergy management, it is crucial to convey that allergies require time, awareness, and not just medication for recovery. Misunderstandings about immunotherapy, such as believing it cures all allergies when it primarily addresses house dust mite allergy, can lead to dissatisfaction and treatment drop-out [16]. Costs and insurance status did not affect immunotherapy adherence during and after the pandemic ($p>0.05$), as the service is covered by BPJS. This finding contrasts with previous research indicating that costs and lack of insurance affect adherence [21]. The difference may be due to the BPJS insurance system, making immunotherapy affordable. Patients' awareness that immunotherapy is more cost-effective than medication also contributes to adherence [1]. Immunotherapy at Dr. Soetomo General Academic Hospital is supported by BPJS, so patients' main costs relate to transportation and meals, not the therapy itself. Although allergen extracts for immunotherapy are not readily available in Indonesia and often need to be imported, Dr. Soetomo General Academic Hospital has been producing standardized house dust mite allergen extracts for 25 years, making them more accessible and affordable [16].

Studies has explored how the COVID-19 pandemic impacted healthcare delivery, fear of infection, adherence to medical treatment, and adherence with preventive instructions among children and adolescents with Inflammatory Bowel Disease (IBD). The findings indicated that high levels of fear of COVID-19 infection affected treatment adherence [22]. Similarly, Celik, et al. [23] evaluated the impact of anxiety among patients and parents on adherence with SCIT in a pediatric allergy and immunology clinic in Turkey during the COVID-19 pandemic, finding that 20.5% cited fear of COVID-

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19 transmission as the primary reason for non-adherence. However, this study found no significant concerns during and after the pandemic ($p>0.05$).

During the pandemic, most patients suspected that immunotherapy services were halted. This suspicion did not significantly affect patient adherence with immunotherapy procedures ($p>0.05$), likely due to effective education about immunotherapy provided after each prick test session, maintaining adherence even during the pandemic. This contrasts with a study by Aytekin, et al. [24] where 29% of participants dropped out of the program due to uncertainty after their immunotherapy was canceled, as hospitals were reportedly only accepting emergency cases [23]. The difference in results is attributed to the effectiveness of doctor-patient communication, ensuring that patients continued their immunotherapy despite suspicions of service cessation.

Dr. Soetomo General Academic Hospital, where this study was conducted, is an Academic Medical Center and the largest hospital in Indonesia in terms of bed count and resident numbers. Located in Surabaya, it serves as a referral center for patients from eastern Indonesia. Approximately 30-40% of patients come from Surabaya, with the remaining 60-70% from other parts of eastern Indonesia. During the COVID-19 pandemic, Surabaya was under lockdown, which nearly turned the city into a ghost town. Although the pediatric allergy clinic remained open, some healthcare workers at Dr. Soetomo General Academic Hospital faced difficulties commuting to work, leading to slower and quieter clinic operations [25]. This study found that travel restrictions (lockdown) impacted immunotherapy adherence during the COVID-19 pandemic, with most patients being Surabaya residents. Similar travel restrictions in Turkey affected smaller regions across the country, with Aytekin et al. reporting that 22.7% of patients had to discontinue their immunotherapy due to the inability to travel to therapy locations during the lockdown [24].

In the multivariate analysis, environmental factors ($p=0.014$), including concerns about transportation during lockdown ($\alpha=0.955$) and worries about family members contracting COVID-19 ($\alpha=0.943$), were found to significantly affect adherence to immunotherapy. These factors likely contributed to a decline in clinic visits. A cohort study at Dr. Soetomo General Academic Hospital examined non-COVID-19 patients using BPJS insurance, comparing subgroups treated during the pandemic with those treated before the pandemic. The study found a 41.4% decrease in pediatric inpatient admissions ($p=0.000$), an increase in severity by 0.08, and an increase in disease complexity by 0.31 ($p=0.00$), along with a reduction in case numbers ($p=0.045$). The decline in pediatric inpatient admissions was attributed to healthcare workforce reductions, patient insecurity, public activity restrictions, and fear of COVID-19 infection, leading people to avoid seeking healthcare [26]. The ECIEN-2020 study also showed decreased emergency department visits, pediatric inpatient admissions, and increased severity and complexity of pediatric inpatient cases during the COVID-19 lockdown [27].

The decline in outpatient and inpatient visits during the pandemic due to lockdown policies also appears to have affected immunotherapy adherence. Research in Turkey observed that the COVID-19 pandemic significantly impacted adherence to subcutaneous allergy immunotherapy (SCIT), with fear of COVID-19 infection being a primary reason for discontinuing therapy. Changes in health priorities and restricted access during the pandemic also disrupted regular immunotherapy schedules for children. Travel restrictions in Turkey during the pandemic impacted small regions nationwide, finding that up to 22.7% of patients had to stop their immunotherapy because they could not travel to therapy locations during the lockdown [24].

This study shows that COVID-19 infection among family members affects patients' adherence to immunotherapy. However, a COVID-19 infection in patients themselves does not seem to influence their adherence. Patients confirmed with COVID-19 undergo self-isolation and only visit the hospital in emergencies, leading to decreased adherence to immunotherapy visits [28]. This trend was also observed in Turkey, where concerns about family members contracting COVID-19 were a reason for dropout.[25] During the pandemic, COVID-19-positive patients were not allowed in pediatric clinics, and

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fear among patients was 100%. This fear remains notable post-pandemic, reaching 42%, despite the pandemic being declared over.

5. Conclusion

Based on the results and discussion above, the following conclusions can be drawn: Family perceptions of the effectiveness of immunotherapy did not affect adherence to immunotherapy during the COVID-19 pandemic. Similarly, children's perceptions of the effectiveness of immunotherapy, injection comfort, costs and health insurance factors, and the risk of systemic reactions did not influence adherence during this period. However, concerns about the lack of transportation facilities during lockdown and having family members with COVID-19 did affect adherence to immunotherapy during the COVID-19 pandemic.

6. Limitations

This study is limited by the sample size and the presence of confounding variables that were not fully controlled. The sample was drawn from the Dr. Soetomo General Academic Hospital polyclinic, meaning the majority of participants were residents of Surabaya and its surrounding areas. Data collection during the pandemic faced challenges as some patients did not return to the clinic and could not be contacted.

6.1. Implication and Directions for Future Research

The results of this study indicate new trends in immunotherapy adherence post-pandemic. Factors that typically influenced adherence before the pandemic seem less impactful now. During the pandemic, adherence was more affected by transportation difficulties during lockdown and concerns about family members contracting COVID-19. Although future lockdowns are unlikely, policies must ensure good immunotherapy adherence during such times, as it significantly affects adherence. Patient education is crucial, especially since some patients still worry about family members contracting COVID-19 even though the pandemic is officially over. This concern should be specifically addressed in patient education before starting immunotherapy sessions.

Further research is needed in other regions of Indonesia, as adherence factors are influenced by patient knowledge, immunotherapy schedules, and social support for patient adherence. Future studies are recommended to collect data using a long-term observational approach, starting from the consent to undergo immunotherapy until the completion of the immunotherapy procedure.

Transparency:

The authors confirm that the manuscript is an honest, accurate, and transparent account of the study; that no vital features of the study have been omitted; and that any discrepancies from the study as planned have been explained. This study followed all ethical practices during writing.

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Abbreviations:

SCIT- Subcutaneous immunotherapy, COVID-19-Coronavirus Disease 2019, SEM- Structural Equation Modeling, PLS- Partial Least Squares, PLS-SEM- Partial Least Squares Structural Equation Modeling (PLS-SEM)

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