

The effect of the COVID-19 pandemic on vaccine hesitancy and vaccine refusal in children with food allergies

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ABSTRACT

Objective: Food allergies are an important factor causing hesitancy towards childhood vaccines. This study aimed to investigate the effect of the COVID-19 pandemic on vaccine hesitancy and vaccine refusal in children with food allergies.

Material and Methods: This study was conducted with 104 children and their parents, who applied to the pediatric allergy clinic between October 1, 2020, and March 30, 2021. The children were classified as “fully vaccinated,” “incompletely vaccinated,” and “unvaccinated.” Moreover, fully vaccinated children were divided into two subgroups: “fully vaccinated on time” and “fully vaccinated with a delay.” Their vaccination statuses and histories of COVID-19 were questioned. The Beck Anxiety Scale was applied to the parents in the patient and control groups.

Results: Although there were no unvaccinated children, there were 12 (11.5%) incompletely vaccinated children, 57 (54.8%) children who were fully vaccinated on time, and 35 (33.6%) children who were fully vaccinated with a delay. Logistic regression analysis determined that living outside the city center (OR: 6.9) and having a family history of COVID-19 (OR: 5.8) caused a delay in vaccination. The analysis also revealed that a high anxiety score (OR: 1.8) led to missed vaccinations.

Conclusion: The rate of delay in vaccination administration increased among individuals living outside of a city center and those with a family history of COVID-19 infections. It was also found that the rate of missed vaccinations increases with increased parental anxiety.

Keywords: Allergy, anxiety, COVID-19, food, vaccine refusal.



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INTRODUCTION

The COVID-19 pandemic is a global health crisis that began in 2019, causing significant impacts on healthcare systems and societies worldwide.^[1] While most pediatric COVID-19 cases are mild or asymptomatic, severe cases can occur in children with underlying chronic conditions.^[2] Since there is still no effective treatment, non-medical measures such as lockdowns have become crucial for controlling COVID-19. Immunization practices in all age groups, especially routine childhood vaccinations, have been interrupted, particularly during quarantine periods.^[3] During the COVID-19 pandemic, a decrease in routine vaccinations for children has been reported in some countries. This situation creates the risk of the recurrence of vaccine-preventable diseases, especially in children.^[4]

Vaccines significantly contribute to saving millions of children's lives and preventing diseases and disabilities each year. However, increasing "vaccine hesitancy" among parents can lead to delays in vaccinating and/or vaccine rejections at varying times.^[5] Vaccine hesitancy is a complex and multifaceted phenomenon, encompassing a wide spectrum of context-dependent attitudes and beliefs. Multiple factors influence parental decision-making, including knowledge, sources of information, risk perception, trust, and individual experiences, among others. It is known that parents' beliefs about their children's diseases and their perceptions of health and disease risks have an important effect on their decisions about vaccinating their children.^[6] Studies have shown that mothers of children with food allergies experience more anxiety and stress than mothers of children without chronic diseases.^[7] The presence of a food allergy in a child may cause their parents to hesitate about vaccinating, experience anxiety, or refuse some childhood vaccines, especially those possibly contaminated with food allergens, to avoid the risk of anaphylaxis or other factors. In this context, changes in vaccine hesitancy can be observed in parents of children with food allergies during the COVID-19 pandemic.

This study aimed to determine the vaccination statuses of children with food allergies during the COVID-19 pandemic and to ascertain the effect of the COVID-19 pandemic process on the vaccination hesitancy and vaccine refusal of parents of children with food allergies.

MATERIAL AND METHODS

This descriptive study with analytical implications, conducted within the framework of the Declaration of Helsinki protocol, was carried out in the pediatric allergy clinic of our hospital over a 6-month period from October 1, 2020, to March 30, 2021.

Study Population

The population of this study consisted of children aged 0–18 years diagnosed with food allergies by a pediatric allergist and their parents. Children with chronic diseases other than food allergies were excluded from the study. Parents who did not volunteer to participate in the study and parents with any chronic disease (hypertension, diabetes, obesity, malignancy, etc.) were excluded from the study (chronic diseases were excluded because they may cause anxiety in both the family and the child and/or may create a prejudice against the vaccine). If there was a history of a diagnosed anxiety disorder in a parent or child being

considered for either the food allergy group or the control group, both the child and parent were excluded from the study.

The following criteria were used for the diagnosis of a food allergy:

- i. Clinical history: the onset of symptoms following food consumption.
- ii. The diameter of the swelling measured by the skin prick test is ≥ 3 mm more than the negative control and/or the allergen-specific IgE level result is ≥ 0.35 kU/L (Non-IgE-mediated food allergies did not meet this criterion).
- iii. A remission of symptoms with the elimination of the suspected allergen and/or a positive oral provocation test result.

A control group (only one parent, either the mother or the father) was formed to compare the vaccination status and the anxiety level of the parents. Additionally, the opinions of the parents of the children in the control group about vaccination were questioned. The control group consisted of parents and children aged between 0 and 18 years who did not have any acute or chronic diseases and were admitted to the well-child outpatient clinic of our hospital for routine childhood examinations.

In this study, the vaccination statuses of children according to the national vaccination calendar were classified as "fully vaccinated," "incompletely vaccinated," and "unvaccinated." "Fully vaccinated" defined a child who received all vaccinations on the national calendar according to their age. "Unvaccinated" defined a child who did not receive any of the vaccines on the national vaccination calendar. "Incompletely vaccinated" defined a child who did not receive one or more of the vaccines that should be administered according to the intervals specified in the national vaccination calendar. In addition, fully vaccinated children were divided into two subgroups: "fully vaccinated on time" and "fully vaccinated with a delay." If the vaccine, which should be administered to a child according to the calendar age, was administered within one month, the patient was included in the "fully vaccinated on time" group. If the vaccine was administered with a delay of at least 1 month, the child was included in the "fully vaccinated with a delay" subgroup. "Vaccination refusal" indicates a refusal to have vaccinations.

Questionnaire

The questionnaire was conducted using the face-to-face interview technique with parents. The questionnaire form included the demographic characteristics of the patients, which food allergies are present and anaphylaxis history, the age at which the diagnosis of atopy was made, the history of COVID-19 in the family and in the immediate environment, the child's vaccination status with the vaccines in the Turkish Ministry of Health extended vaccination program, the presence of missing and delayed vaccines, the parent's general attitude about the vaccines, and the parent's level of knowledge and thoughts. In addition, the results of the skin prick tests and serum allergen-specific IgE levels were obtained from the hospital files.

The Beck Anxiety Scale (BAS), designed to measure the severity of anxiety, was developed by Beck, Epstein, Brown, and Steer and consists of 21 items. The total score of the scale includes items determining some cognitions of anxious temperament, autonomic hyperactivity, and motor tension. The scale was translated into Turkish by Nesrin Ahin, and the validity and reliability study of the Turkish

Table 1: Demographic characteristics of children and parents according to type of food allergy

	IgE	Non IgE	IgE and non IgE
Sex (F/M)	41/26	9/10	12/6
Age (months) (median and interquartile range)	19.7 (14.2–25.3)	15.3 (12–25.6)	16.8 (13.4–35)
Mother's education level, n (%)			
University and above	13 (19.4)	4 (21.1)	4 (22.2)
High school and below	54 (80.6)	45 (78.9)	14 (77.8)
Father education level, n (%)			
University and above	18 (26.9)	8 (42.1)	6 (33.3)
High school and below	49 (73.1)	11 (57.9)	12 (66.7)
Place of living, n (%)			
Town center	41 (61.2)	13 (68.4)	11 (61.1)
Provincial	26 (38.8)	6 (31.6)	7 (38.9)

F: Female; M: Male.

Table 2: Clinical characteristics of patients according to food allergy type

	IgE		Non IgE		IgE and non-IgE		p
	n	%	n	%	n	%	
History of anaphylaxis	19	28.4	0	0	2	11.1	0.01
History of elimination	13	19.4	10	52.6	5	27.8	0.01
Regular follow-up in the pediatric allergy clinic	60	89.5	17	88.8	16	88.9	>0.05
Family history of allergic disease	8	11.9	3	15.8	2	11.1	>0.05
Missing vaccine	9	13.4	1	5.3	2	11.1	>0.05
Delayed vaccine	25	37.3	5	26.3	5	27.7	>0.05

version was conducted by Mustafa Ulusoy.^[6] BAS was applied to the parents in the patient and control groups. The total score obtained from the scale indicates the severity of the anxiety experienced by the individual. Scores between 0 and 7 indicate minimal anxiety; 8–15 indicate mild anxiety; 16–25 indicate moderate anxiety; and 26–63 indicate severe anxiety.

Statistical Analysis

The data obtained with the prepared data form were recorded in the database created with SPSS (Statistical Package for Social Sciences) for Windows 22.0 (SPSS Inc., Chicago, IL), and statistical analysis was performed. Numerical data with a normal distribution were presented as mean±standard deviation, and data without a normal distribution were presented as median and min–max values. Categorical data were expressed as frequencies and percentages. The Shapiro-Wilk test was used to assess the conformity of the parameters to the normal distribution. Chi-square and Fisher's Exact tests were used to analyze the categorical variables. Continuous parameters were tested for a normal distribution, and for normally distributed parameters, an independent

group t-test was used for two-group comparisons and a multi-group comparison. On the other hand, the Mann-Whitney U test was used in paired group comparisons, and multiple group comparisons were used for non-normally distributed variables. Factors causing delay and deficiency in vaccination were analyzed by logistic regression analysis, and the fully vaccinated group was accepted as the reference category. A p-value<0.05 was accepted as statistically significant.

Results

This study was conducted with 104 children and their parents who were admitted to the pediatric allergy clinic within 6 months with newly diagnosed food allergies or who were followed up with a diagnosis of a food allergy. The control group consisted of 104 children and their parents.

Of the patients in the food allergy group, 67 (64.5%) had an IgE-mediated food allergy, 19 (18.3%) had a non-IgE-mediated food allergy, and 18 (17.3%) had both non-IgE and IgE-mediated food allergies. The demographic characteristics of the patients according to their types of food allergies are given in Table 1.

Anaphylaxis was present in 21 of the patients (20.2%). The clinical characteristics of the patients according to the types of food allergies are given in Table 2.

Parents in both the patient and control groups stated that they did not refuse any vaccine for their children. In this study, while no unvaccinated patients were detected in the patient group, 12 (11.5%) were incompletely vaccinated, 57 (54.8%) were fully vaccinated, and 35 (33.6%) were fully vaccinated with a delay. On the other hand, in the control group, no unvaccinated patients were detected, and 8 (7.6%) were incompletely vaccinated, 87 (83.7%) were fully vaccinated on time, and 9 (8.7%) were fully vaccinated with a delay. There was no statistically significant difference ($p>0.05$) between the two groups in terms of missing vaccines; however, a statistically significant difference ($p=0.001$) was found in terms of complete vaccination with a delay.

Of the parents who stated that their child was fully vaccinated with a delay, 22 (21.2%) reported difficulty reaching the health center during the quarantine process, and 13 (12.5%) deliberately delayed the vaccine's administration due to indecision or hesitancy during the pandemic.

It was found that 12 (11.5%) of the cases had a missing vaccine in their routine vaccination schedule. The reason for this deficiency was attributed to "having difficulty reaching the health center during the quarantine period" by 9 (75%) patients and "not wanting to be vaccinated during the COVID-19 pandemic" by 3 (25%) patients.

Fourteen participants (13.5%) had a family history of COVID-19, and 32 (30.8%) stated that their close relatives had a history of COVID-19 infections.

The rates of delayed ($p<0.05$) and missing ($p<0.05$) vaccines were statistically significantly higher in those with a family history of COVID-19. It was observed that delayed ($p=0.21$) and missing ($p=0.5$) vaccine cases were not statistically more prevalent in patients who had neighbors and close relatives with a history of COVID-19.

The mean score calculated using the BAS was 3.1 (standard deviation: 1.59) in the food allergy group and 0.67 (standard deviation: 1.06) in the control group, with a statistically significant difference between the two groups ($p<0.05$). Additionally, no difference in anxiety scores was found between the three food allergy groups ($p=0.27$).

The responses given by the parents to questions about their views on childhood vaccines during the pandemic are presented in Table 3. A statistically significant difference was found between the patient and control groups regarding concerns about vaccines containing egg and cow's milk proteins ($p<0.05$ and $p<0.05$, respectively).

According to the multivariate logistic regression analysis, living outside the city center (OR: 6.9) and having a family history of COVID-19 (OR: 5.8) were found to cause a delay in vaccination (Table 4). The analysis also indicated that a high anxiety score (OR: 1.8) led to incomplete vaccination (Table 5).

DISCUSSION

This study revealed that 11.5% of children with food allergies were incompletely vaccinated, and 33.6% were fully vaccinated with delays. Moreover, it was found that the rate of delays in vaccinations

increased for patients living outside of a city center and those with a family history of COVID-19 infection. Additionally, in cases of increased parental anxiety, the rate of incomplete vaccinations significantly rose.

The restrictions implemented after the first COVID-19 case was reported in our country on March 11, 2020, such as the closure of kindergartens and schools, the prohibition of gatherings in public places, and intercity travel restrictions, led to healthcare-related challenges in the pediatric age group. For children with or suspected to have food allergies, many family health centers refrain from administering certain vaccines and refer patients to specialized centers.^[9] Furthermore, parents may exhibit vaccination hesitancy if their children have food allergies. The presence of a food allergy can influence both the physician's attitude towards vaccinating a child and the family's anxiety, potentially leading to vaccination hesitancy. As the COVID-19 pandemic impacts every facet of our lives, it may also have influenced the attitudes of parents towards vaccinations for their children with food allergies.

In Türkiye, the number of families who do not want their children to be vaccinated increased to 980 in 2013, 5,400 in 2015, and 12,000 in 2016. The number of cases related to vaccine refusal reached 23,000 as of 2018.^[10] However, no vaccine rejection was detected in any of the parents in this study. Health care providers are most frequently cited as sources of information by families, including parents of unvaccinated children. Clinicians should listen to parents' concerns and, if necessary, discuss the risks of vaccination.^[11] The fact that 89.4% of the patients were regularly followed up in the allergy outpatient clinic may have had a preventive or reducing effect on vaccination hesitancy in a group with high parental anxiety due to the children having food allergies.

Twenty-two (21.2%) of the parents who stated that the vaccine was administered with a delay in routine childhood vaccines during the COVID-19 period mentioned that they deliberately delayed the vaccine because of difficulty reaching the health center during the quarantine process. On the other hand, 13 parents (12.5%) stated that they deliberately delayed the vaccine because they were undecided or hesitant during the pandemic process. It was observed that 12 (11.5%) of the cases had missed vaccines in the routine vaccination schedule. The reason for this deficiency was attributed to "having difficulty reaching the health center during the quarantine period" by 9 (75%) patients and "not wanting to be vaccinated during the COVID-19 pandemic" by 3 (25%) patients.

When examining the factors affecting vaccination delays in fully vaccinated children, it was observed that having a family history of COVID-19 and living outside of a city center increased the likelihood of delays in vaccinations, regardless of other confounding factors. The distance from health institutions and transportation difficulties are major reasons why children may not be vaccinated on time. In a study conducted in our country, home visits were made to reach 350 children aged between 1.5 and 5 years who were absent from vaccinations, revealing that 39 families did not have their children vaccinated due to the long distances from the health institute.^[12] It was considered that individuals living outside city centers, especially under pandemic restrictions, might find it challenging to access health institutions, potentially causing delays in the vaccination process.

Table 3: Parents' opinions about vaccination and COVID-19

	Patient group						Control g.	
	IgE		Non IgE		IgE and non-IgE		n	%
	n	%	n	%	n	%		
Do vaccine-related side effects worry you?								
Yes	42	62.7	12	63.2	11	61.1	62	59.6
No	14	20.9	4	21	4	22.2	21	20.2
No idea	11	16.4	3	15.8	3	16.7	21	20.2
Are you concerned about the content of the vaccines?								
Yes	45	67.2	12	63.2	11	61.1	59	56.7
No	15	22.4	3	15.8	3	16.7	25	24
No idea	7	10.4	4	21	4	22.2	20	19.2
Are you concerned about the egg protein in vaccines?								
Yes	40	59.7	4	21	8	44.4	18	17.3
No	14	20.9	5	26.3	3	16.7	64	61.5
No idea	13	19.4	10	52.6	7	38.9	22	21.2
Are you concerned about the milk protein in vaccines?								
Yes	38	56.7	8	42.1	7	38.9	15	14.4
No	17	25.4	6	31.6	4	22.2	69	66.3
No idea	12	17.9	5	26.3	7	38.9	20	19.2
How has your attitude towards childhood vaccines changed with the pandemic process?								
Positive	41	61.2	11	57.9	8	44.4	64	61.5
Negative	12	17.9	6	31.6	4	22.2	22	21.1
No idea	14	20.9	2	10.5	6	33.3	18	17.3
Do you think that having a food allergy will increase your child's risk in the period of COVID-19?								
Yes	36	53.7	10	52.6	11	61.1	58	55.8
No	14	20.9	1	5.3	1	5.6	20	19.2
No idea	17	25.4	8	42.1	6	33.3	26	25
Do you think that applying to a health institution for vaccination may increase your child's and/or your risk of COVID-19?								
Yes	30	44.8	10	52.6	8	44.4	46	44.2
No	14	20.9	1	5.3	4	22.2	22	21.2
No idea	23	34.3	8	42.1	6	33.3	36	34.6
Do you think that the risk of transmission by an infectious agent is an obstacle to being vaccinated?								
Yes	17	25.4	3	15.8	4	22.2	47	45.2
No	7	10.4	7	36.8	3	16.7	9	8.7
No idea	43	64.2	9	47.4	11	61.1	48	46.1
Do you know that having COVID-19 after vaccination will not affect the course of the disease?								
Yes	25	37.3	5	26.3	7	38.9	27	26
No	10	14.9	5	26.3	2	11.1	12	11.5
No idea	32	47.8	9	47.4	9	50	65	62.5
Do you know that the vaccine can be administered 10 days after a positive result or 14 days after contact isolation?								
Yes	18	26.9	3	15.8	4	22.2	28	27
No	32	47.8	12	63.2	12	66.7	48	46.2
No idea	17	25.4	4	21.1	2	11.1	28	27
Do you think that routine childhood vaccinations can protect your child against COVID19?								
Yes	18	26.9	3	15.8	1	5.6	28	27
No	25	37.3	8	42.1	5	27.8	39	37.5
No idea	24	35.8	8	42.1	12	66.7	37	35.5
Do you know that routine pre-vaccination testing for COVID-19 is not recommended or required?								
Yes	38	56.7	16	84.2	4	22.2	56	53.8
No	3	4.8	1	5.2	2	11.1	6	5.8
No idea	26	38.8	2	10.5	12	66.7	42	40.4

Table 4: Factors causing delay in routine childhood vaccinations in children diagnosed with food allergies during the COVID-19 pandemic (according to logistic regression analysis results)

Factors*	Univariate analysis			Multivariate analysis		
	OR	95% CI	p	OR	95% CI	p
History of anaphylaxis	3.75	1.36–10.31	0.01			
Elimination diet	7.32	2.80–19.12	<0.001			
Living outside the city center	10.5	4.02–27.38	<0.001	6.97	2.33–20.81	<0.001
Going to a regular allergy clinic	0.23	0.08–0.64	0.005			
Having a family history of COVID-19	8.12	3.16–20.81	<0.001	5.85	1.82–18.83	0.003

*: According to univariate analysis results, p<0.05 values are given in the table. OR: Odds ratio; CI: Confidence interval.

Table 5: Factors causing missing vaccines in routine childhood vaccinations in children diagnosed with food allergies during the COVID-19 pandemic (according to logistic regression analysis results)

Factors*	Univariate analysis			Multivariate analysis		
	OR	95% CI	p	OR	95% CI	p
History of anaphylaxis	5.57	1.57–19.77	0.008			
Elimination diet	20.55	4.13–102.13	<0.001			
Living outside the city center	8.14	1.68–39.35	0.009			
Going to a regular allergy clinic	0.08	0.02–0.31	<0.001			
Administration of the vaccine in the hospital	9.33	2.54–34.18	<0.001			
Anxiety score	2.36	1.56–3.56	<0.001	1.8	1.1–2.9	0.011

*: According to univariate analysis results, p<0.05 values are given in the table. OR: Odds ratio; CI: Confidence interval.

While no case of vaccine rejection was detected in this study, 12 children with missing vaccinations were identified. The missing vaccines could be due to families’ personal preference to reject vaccines or the restrictions experienced during the pandemic and transportation issues. When examining the factors affecting under-vaccination status, a high rate of anxiety was found to increase the likelihood of missing vaccines, regardless of other confounding factors.

Children’s illnesses are a significant source of anxiety for parents, with potential hospitalization, the disease itself, disease-related limitations, economic strain, and increased care needs all contributing factors, particularly for mothers.^[13] Chronic conditions like food allergies also induce parental anxiety. A pre-pandemic study in Russia found moderate to high anxiety in one out of every five mothers whose child had a food allergy.^[14] Another study, examining the impact of food allergies on anxiety and quality of life in parents of children with food allergies during the COVID-19 pandemic, found no difference in anxiety levels between mothers of children aged 0–1.5 years in the case and control groups. However, in the case group, mothers of children aged 1.5–8 years had higher anxiety levels compared to the control group (p<0.05). The study also indicated that high anxiety might delay food allergy testing and treatment.^[15] Similarly, our study found that

the anxiety levels of parents of children with food allergies were statistically significantly higher than those in the control group. Moreover, it was observed that parental anxiety influenced their vaccination preferences. These results suggest that the anxiety experienced by families of children with chronic conditions like food allergies adversely affects vaccine acceptance during the COVID-19 pandemic.

It was observed that delayed (p<0.05) and missing vaccines (p<0.05) were statistically significantly higher in those with a family history of COVID-19. It has been recommended that routine vaccinations for COVID-19-positive children be postponed to prevent the risk of COVID-19 transmission to healthcare workers and others. While none of the patients in our study had a COVID-19 infection, the isolation due to close contact at home might have delayed their access to health institutions for vaccinations.

Concerns regarding vaccines containing egg and cow’s milk proteins were noted in the patient group and were statistically significantly higher than in the control group. This concern may stem from the fact that some vaccines in the country contain egg and cow’s milk proteins.

No statistical difference was found in the missing vaccination rates between children with food allergies and the control group. Generally, parents of children with food allergies may exhibit hesi-

tancy towards certain vaccines; however, in our clinic, families are adequately informed, and vaccines are administered with necessary precautions. This might explain the lack of detected difference. The rate of delayed vaccine administration was found to be higher in the food allergy group compared to the control group. Delays in vaccine administration can occur in the food allergy group for various reasons. In our country, routine childhood vaccinations are typically administered in family medicine units, but children with food allergies are often referred to pediatric allergy clinics for some vaccines, which can lead to delays. Additionally, parental hesitancy and anxiety due to their child's food allergy may contribute to delayed vaccination.

Üzüm et al.^[16] reported that 53.6% of participants in a study conducted in our country believed that routine vaccines could have side effects. In our study, 67.3% of parents expressed concerns about vaccine-related side effects, a higher rate possibly linked to their children's food allergy diagnoses. Furthermore, 65.4% of participants were concerned about vaccine content, which may also be related to food allergy diagnoses in children.

Our study has limitations, including its single-center design. Our results could not be compared with other studies, as there are no studies in the literature focusing specifically on vaccine rejection in children with food allergies.

CONCLUSION

In conclusion, our study revealed that vaccination delays occur in children with food allergies, particularly for those residing outside city centers and with a family history of COVID-19 infections during the pandemic. However, these factors are not exclusive to children with food allergies and could also impact healthy children. Furthermore, our study indicated that increased parental anxiety leads to incomplete vaccinations. It is crucial to thoroughly inform families to alleviate the anxiety of parents with children who have food allergies. Addressing transportation issues, especially during quarantine periods, could prevent potential grievances. Although the WHO declared the end of the COVID-19 pandemic on May 5, 2023,^[17] the findings from this study can serve as a guide for vaccination strategies in future pandemics.

Statement

Ethics Committee Approval: The Ankara Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 10.12.2020, number: 93471371-514.10).

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