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Evaluation of COVID-19 Vaccination Status and Post-Vaccine Reactions in Adolescents with Allergic Diseases

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ABSTRACT

Objective: Studies examining COVID-19 vaccine reactions and reasons for parental hesitancy to COVID-19 vaccines in allergic adolescents are few. This study aimed to identify post-vaccine reactions and parental vaccine refusal/hesitancy among adolescents with allergic diseases.

Materials and Methods: Between January 2022 and April 2022, a questionnaire was completed by the parents of adolescents who were followed at the Pediatric Allergy outpatient clinic. Vaccination status, characteristics of reactions after vaccination, and the frequency of parental vaccine hesitancy were recorded.

Results: Among 104 patients, 70 were followed for asthma, 64 for allergic rhinitis, 12 for drug allergy, 3 for food allergy, and 1 for chronic urticaria. 63.5% (n=66) of the patients were vaccinated. The rate of vaccination was 52.5% in those with a history of COVID-19 and 70% in those without a history of COVID-19 infection (p=0.07). Eight patients were not vaccinated due to recent COVID-19 infection. Reasons for parental vaccine hesitancy/rejection (n=30) included thinking that the vaccine is harmful (63.3%), not effective (53.4%), or not suitable for children (46.7%). 14 (21.2%) children experienced symptoms within the first 2 hours after vaccination. The most common symptom (n=10) was arm pain. Urticaria and itching were reported in one patient and respiratory symptoms were reported in another patient. Both patients could receive the second dose without any reaction.

Conclusion: Vaccination was more frequent among children without a history of COVID-19 infection. One third of the patients were not vaccinated, and the most common reason for vaccine hesitancy was concern about the adverse effects of the vaccine on human health in the long term and distrust of the vaccine. However, vaccinated allergic children did not experience any serious events.

Keywords: COVID-19, adolescents, vaccination, allergic reactions, vaccine hesitancy

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes COVID-19, was first detected in Wuhan, China in December 2019 (1). On March 2020, the COVID-19 outbreak was declared a pandemic by the WHO (2). Globally, the pandemic has caused nearly 6.9 million deaths to date, and postinfectious conditions such as Multisystem Inflammatory Syndrome in Children (MIS-C) have emerged as a cause of morbidity and mortality among children (3-5).

On May 2021, the emergency use authorization for the Pfizer-BioNTech mRNA COVID-19 vaccine was expanded by the US Food and Drug Administration to include adolescents (6). Although the safety and effectiveness of COVID-19 vaccines have been proven, parents with allergic children may still be hesitant to get their children vaccinated. This may both prevent achieving protective immunity in children with allergies and result in a delay in acquiring herd immunity. In the literature, there are studies evaluating COVID-19 vaccine reactions in some

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allergic diseases such as cutaneous mastocytosis and food allergy in pediatric patients (7, 8). However, there is no study that comprehensively evaluates the frequency and characteristics of COVID-19 vaccine reactions in allergic children.

Today, the Centers for Disease Control and Prevention (CDC) still recommends both the pediatric (>6 years) and adult populations to get one updated Pfizer-BioNTech or Moderna COVID-19 vaccine, regardless of whether they have received any original COVID-19 vaccines (9).

In the present study, we aimed to identify COVID-19 vaccination status, the prevalence and characteristics of post-vaccine reactions, the frequency of parental rejection of COVID-19 vaccination, and the reasons for vaccine rejection among adolescents followed at the Pediatric Allergy Clinic of our center.

MATERIALS and METHODS

A questionnaire was completed between January 2022 and April 2022 by the parents of adolescents who were followed at the Pediatric Allergy outpatient clinic. Informed consent was obtained from the participants, and the study was approved by the Institutional Ethics Committee. The questionnaire was used to collect data on demographic characteristics of the patients, their allergic conditions, medications used, duration of follow-up at the pediatric allergy clinic, previous COVID-19 infection status for both the patients and their family members, vaccination status of the patients for COVID-19, influenza and routine childhood vaccines, characteristics of reactions after COVID-19 vaccination, and parental COVID-19 vaccination status. Symptoms that developed within the first 2 hours after vaccination (immediate) and symptoms that developed within the first 3 days (delayed) were questioned separately. The type of COVID-19 vaccine (Pfizer BioNTech or Sinovac-CoronaVac vaccine) received by the patients was also questioned.

Frequency of parental vaccine hesitancy/refusal and the factors involved (concern about allergic reactions, distrust of vaccines, fear of vaccine) were also noted. A 5-point Likert scale was used to identify the reasons behind vaccine hesitancy/refusal. In the results, the options strongly agree and agree, and the options disagree and strongly disagree were interpreted together.

All analyses were performed using the SPSS Statistics for Windows, version 25.0 (IBM Corp, Armonk, NY). Continuous variables were presented as mean and standard deviation (SD) for normally distributed data. Median and interquartile range (IQR) values were reported for the data that did not follow a normal distribution. Differences between the groups were compared using Student's t-test or chi-square, as appropriate. A p-value of ≤0.05 was considered statistically significant.

RESULTS

During the study period, 104 questionnaires were completed by the parents. 39.4% (n=41) of the patients included in the study were male. The median age was 15.66 years (IQR14.03-17.2). Seventy of the patients (%67.3) were being followed for asthma, 64 (61.5%) for allergic rhinitis, 12 (11.5%) for drug allergy, 3 (2.9%) for food allergy, and 1 (0.9%) for chronic urticaria. 22 patients were receiving subcutaneous allergen immunotherapy (18 pollen, 4 venom).

38.5% (n=40) of the patients had a history of COVID-19 infection but none required hospitalization. 54.8% of patients had at least one family member who had developed COVID-19.

The total rate of vaccination was 63.5% (n=66). 55 patients (83.3%) were vaccinated with the Pfizer BioNTech vaccine and 11 (16.7%) patients with the Sinovac-CoronaVac vaccine. The rate of vaccination was 52.5% in those with a history of COVID-19 versus 70% in those without a history of COVID-19 infection (p=0.07). Three of the four patients who did not know whether they had experienced COVID-19 infection were vaccinated.

Symptoms within the first 2 hours after vaccination were reported in 14 (21.2%) patients (Figure 1). The most common symptom (n=10) was arm pain. Immediate allergic reactions were reported in two patients. Urticaria, erythema, and itching were reported in a patient with allergic rhinitis. Cough, dyspnea, and rhinorrhea were reported after the first dose of the vaccine in the other patient with asthma. Both reactions were reported after vaccination with the Pfizer BioNTech vaccine. It was learned that the patient with allergic rhinitis was treated with an oral antihistamine after getting the first vaccination, and the urticaria lasted for three days. She received her second

vaccination in fractionated doses under surveillance at the pediatric allergy clinic. She was followed for two hours at the outpatient clinic and did not develop any reactions. The parent of the asthmatic patient reported that she had uncontrolled asthma symptoms prior to the first vaccine dose and was treated with her reliever medication (short-acting beta-2 agonist) by her parents after the first dose. She received her second dose without experiencing any reaction.

In the first 3 days after vaccination, 24 patients (36.4%) had symptoms associated with the vaccine. Pain in the arm (n=17), fatigue (n=13), and myalgia (n=9) were the most frequently reported symptoms. The symptoms reported by the patients within the first 2 hours and within the first 72 hours after vaccination are summarized in Figure 1.

38 patients (36.5%) were not vaccinated against COVID-19. The parents of eight of these patients reported that their children were not vaccinated because they recently had COVID-19 infection, but they were considering having them vaccinated within the recommended time interval. The rate of vaccine hesitancy or refusal among parents with allergic adolescents was 28.8% (n=30).

Among the parents (n=30) with vaccine refusal or hesitancy who did not consider vaccinating their children, 63.3% strongly agreed or agreed with the statement "I think the vaccine will have a negative impact on human health in the long term". 53.4% stated that they think the vaccine is ineffective, and 46.7% believed that the vaccine is not suitable for children. 40% of parents thought that their children would have an allergic reaction after getting the COVID-19 vaccine because of having an allergic disease, 60% did not trust the vaccine, and 26.7% had fear of the vaccine. The answers according to the 5-point Likert scale are detailed in Table I.

Table I: Reasons for parental vaccine hesitancy/rejection (n=30).

	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
I think that the vaccine will have a negative impact on human health in the long term, n (%)	13 (43.3)	6 (20)	8 (26.7)	2 (6.7)	1 (3.3)
I believe the vaccine is ineffective, n (%)	8 (26.7)	8 (26.7)	10 (33.3)	2 (6.7)	2 (6.7)
I don't trust the vaccine, n (%)	9 (30)	9 (30)	7 (23.3)	3 (10)	2 (6.7)
I'm afraid of vaccination, n (%)	5 (16.7)	3 (10)	11 (36.7)	6 (20)	5 (16.7)
I think my child will have an allergic reaction after vaccination because he/she has an allergic disease, n (%)	7 (23.3)	5 (16.7)	14 (46.7)	4 (13.3)	0
I think the vaccine is not suitable for children, n (%)	8 (26.7)	6 (20)	7 (23.3)	5 (16.7)	4 (13.3)

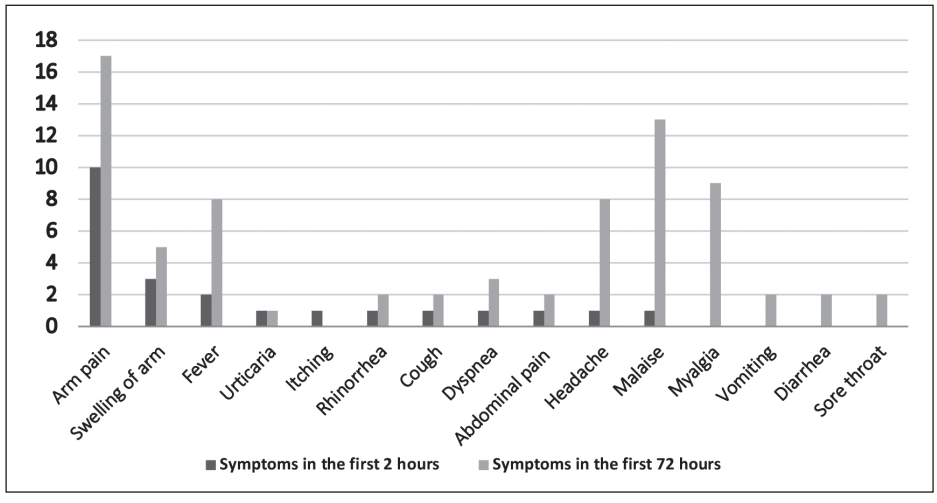

Figure 1. Symptoms after vaccination.

Table II: Parental vaccination status.

	Only one parent vaccinated n (%)	Both parents vaccinated n (%)	Both parents unvaccinated n (%)
Vaccinated adolescents (n=66)	1 (1.5)	65 (98.5)	0
Unvaccinated adolescents (n=30)	6 (20)	20 (66.7)	4 (13.3)
Postponed vaccination due to recent COVID-19 (n=8)	0	6 (75)	2 (25)

Table III: Parental educational status.

	Maternal education level		p value	Paternal education level		p value
	Primary and secondary school n (%)	High school or above n (%)		Primary and secondary school n (%)	High school or above n (%)	
Vaccinated (n=66)	27 (40.9)	39 (59.1)	0.823	13 (19.7)	53 (80.3)	0.016
Unvaccinated (n=30)	13 (43.3)	17 (56.7)		13 (43.3)	17 (56.7)	

In 98.5% of patients who were vaccinated against COVID-19, both parents were vaccinated. None of these patients had both parents unvaccinated. Among those who had not received the COVID-19 vaccine, both parents were unvaccinated in 13.3% (n=4), whereas both parents were vaccinated in 66.6% (n=20). Parental vaccination status is shown in Table II. Although there was no significant difference between the education levels of mothers who had their children vaccinated and those who did not (p= 0.82), paternal education level was higher in the group whose children were vaccinated against COVID-19 (p=0.01) (Table III).

All patients included in the study had their childhood vaccinations according to the routine immunization schedule. 38.5% (n=40) of the patients had received influenza vaccine in previous years.

DISCUSSION

In this survey study, the COVID-19 vaccination rate of allergic adolescents was 63.5%. Vaccination was more frequent among adolescents without a history of COVID-19 infection. The major reason for vaccine hesitancy among parents was the concern about the adverse effects of the vaccine on human health in the long term. Vaccinated allergic adolescents did not experience any serious events and two patients who developed allergic reactions to the first vaccine dose could receive their second dose without any problems.

The latest report from the CDC stated that 68% of the adolescents residing in the USA have received at least one dose of the COVID-19 vaccine, and the vaccination rate varied between 40% and 100% across states (9). In a survey study conducted in China, it was reported that the vaccine coverage rate reached 98.4% among adolescents (10). In our study, the vaccination rate among allergic adolescents was 63.5%.

Vaccine hesitancy and refusal is a growing problem worldwide (11). In a study from Türkiye, the leading factors for routine childhood vaccine refusal and hesitancy among parents were reported as the concern that vaccines could be harmful for children, distrust of vaccines, and the belief that vaccines have no benefit (12). Although the safety and effectiveness of COVID-19 vaccines have been demonstrated, parents still have hesitations about getting their children vaccinated. In studies from different parts of the world, the frequency of COVID-19 vaccination hesitancy among parents varied between 17.9% and 53.5% (13-20). However, there is no study that specifically focused on vaccine rejection among parents of children with allergic diseases.

In the current study, 28.8% of parents had vaccine hesitancy or refusal for their allergic children. It was a remarkable finding that these parents were fully compliant with routine childhood vaccine schedule, and at least one parent had received the COVID-19 vaccine for themselves in 86.7% of the children. On the other hand, in a study from Italy in parents who were highly compliant with common vaccinations, only 26.5% of the parents expressed their willingness to have their children receive the COVID-19 vaccines (21). In the same study, a lower education level was associated with vaccine non-adherence (21). Similarly,

in our study, the father's education level was significantly lower in families with vaccine hesitancy.

In line with our findings, safety issues were the parents' biggest concern with COVID-19 vaccines in previous studies (19-21). Another important consideration was the fear of an allergic reaction to the vaccine (22). Thus, the allergist/immunologist not only plays a role in the delivery of treatment for COVID-19 and the management and prevention of reactions to COVID-19 vaccines but also in dispelling misinformation and addressing parental concerns about allergic and other adverse reactions to COVID-19 vaccines, in order to minimize vaccine hesitancy (23, 24).

Severe allergic reactions to vaccines are rare and these can be caused by the vaccine itself or any of its excipients (25, 26). Although the reported rate of anaphylaxis after vaccination was generally about 1 per million vaccine doses (27), the estimated rate of anaphylaxis was 11.1 cases per million doses after administration of 1,893,360 first doses of the Pfizer-BioNTech COVID-19 vaccine, which is approximately 10-fold higher than other vaccines (28). In a meta-analysis, the overall pooled prevalence estimate of anaphylaxis to BioNTech vaccine was reported to be 9.31 per million doses while the figure for non-anaphylactic reactions was 75.25 per million doses (29). In pediatric studies, the reported overall mean anaphylaxis rate was 12.84 per million vaccine doses (30) but there is no study that focused on hypersensitivity reactions developing in allergic adolescents. In the current study, 1.9% of patients had an immediate hypersensitivity reaction due to COVID-19 vaccines but no cases of anaphylaxis were reported.

Increased referrals to allergists of patients who have had a suspected reaction to vaccines or who are likely to have a reaction to vaccines has led to the development of recommendations to identify which patients require precautions for COVID-19 vaccination (31, 32). Accordingly, in a position paper published by the EEACI/ENDA, only patients with a history of anaphylaxis to injectable drugs, vaccines, or oral/topical products containing PEG; those who experience recurrent anaphylaxis with an undefined trigger; confirmed allergy to PEG derivatives; or suspected or confirmed allergy to any mRNA vaccine are reported to require an allergic work-up (31).

In our study, one patient with allergic rhinitis developed generalized urticaria after the first dose of BioNTech vaccine and received her second vaccine in fractionated doses. Similarly, Rosa Duque et al. reported three pediatric patients with mild allergic rhinitis who had urticaria within 4 h after their first BioNTech vaccine, received their second dose uneventfully by a graded approach or a single full-dose and were observed for at least 1 h after each injection (33). In the EAACI position paper, patients who experienced a grade 1 hypersensitivity reaction after vaccination are recommended to have skin tests with excipients or get vaccinated directly under hospital surveillance (31).

A risk stratification schema was developed to guide individuals with different allergy histories to receive their mRNA COVID-19 vaccine safely (34). Patients with allergic rhinoconjunctivitis; well-controlled allergic asthma, eczema, food, venom or latex allergies; mastocytosis without previous history of anaphylaxis; chronic urticaria or angioedema do not require any allergic work-up before vaccination, and routine vaccination with either 15-minute or 30-minute observation periods is recommended for these patients (31). In the case of uncontrolled asthma, it is recommended to proceed to vaccination after achieving the best possible asthma control, and if asthma control is suboptimal, vaccination is recommended in the hospital setting and under surveillance for at least 60 minutes (35). In our study, an asthmatic adolescent who had uncontrolled asthma symptoms prior to vaccination developed respiratory symptoms within 2 hours of the vaccination. Moreover, although having a reaction after the first dose, she received her second dose without consulting the Pediatric Allergy Clinic, where she was being followed. This clearly shows the importance of evaluating the asthma control status of asthmatic patients considering vaccination (32).

The main limitation of the study is the small number of cases included. Studies with larger patient groups are needed to evaluate post COVID-19 vaccine reactions in adolescents with allergic diseases.

In conclusion, vaccination was more frequent among children without a history of COVID-19. One third of the patients were not vaccinated, and the most common reason for parental vaccine hesitancy was the concern about the adverse effects of the vaccine on human health in the long term and distrust of vaccine. However, the vaccinated allergic children included in our study did not experience any serious events. We believe that our study provides guidance for vaccination of adolescents with allergic diseases.

Conflict of Interest
The authors declare that there is no conflict of interest regarding the publication of this article.

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Author Contributions
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