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ORIGINAL ARTICLE

COVID-19 vaccination hesitancy among patients admitted to the immunology and allergy clinic with drug allergies

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Abstract

The aim of our study was to determine the factors responsible for COVID-19 vaccination acceptance and hesitancy in patients with drug allergies. We prepared a survey to understand the thoughts, hesitancies and experiences about COVID-19 vaccination and COVID-19 infection in patients with drug allergies and statistically examined the results. A survey study was applied to 76 patients who were admitted to Ankara University Internal Medicine Allergy and Immunology Department with drug allergies. 38 patients who were vaccinated and 38 patients who weren't were compared. Among the 38 patients who were vaccinated, 34 (89.5%) chose Biontech vaccine, 4 (10.5%) chose Sinovac vaccine. Among the patients who weren't vaccinated, 28 (73.7%) explained they weren't vaccinated because of drug allergies. Educational statuses were statistically significantly different (p=0.026) among vaccinated and non-vaccinated patients, lower in vaccinated patients. Vaccinated patients thought the vaccine reduced the possibility of COVID-19 infection and complications, which was significantly different (p<0.01). Non-vaccinated group significantly feared the possible allergic reaction to the COVID-19 vaccine, more than the vaccinated group (p=0.028). Fear of the possible side effects of the COVID-19 vaccine (p<0.001) and the thought of the COVID-19 vaccine being associated with unpredictable effects were significantly more evident in the non-vaccinated group (p<0.001). In conclusion, our study analyzed multiple factors in drug allergy patients regarding vaccine acceptance, rejection, and hesitancy for the first time in literature, similar studies with larger samples can also contribute to the literature in the future.

Keywords: COVID-19, COVID-19 vaccines, drug Hypersensitivity, vaccination hesitancy

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Introduction

COVID-19 infection, caused by the Sars-CoV-2 virus, emerged in the Wuhan city of China in December 2019 and quickly spread worldwide after a month, causing World Health Organization to declare COVID-19 a pandemic on the 11th of March 2020. As of February 2023, COVID-19 has caused roughly 750 million cases and 7 million deaths worldwide, with 17 million cases and 100 thousand deaths in Turkey [1]. As of February 2023, there are 242 vaccine candidates, 821 vaccine trials and 50 vaccines that have gone through Phase 3 and were approved [2].

Vaccine hesitancy was a very important issue even before the COVID-19 pandemic, so much so that in 2019 World Health Organization added vaccine hesitancies to the ten threats to global health [3]. COVID-19 vaccine acceptance and hesitancy is a complex subject, and its complexity is increased by the new variants and newly developing vaccines. Therefore, identifying factors that induce vaccine acceptance and hesitancy is very important in order to overcome vaccine hesitancy [4]. In a review about COVID-19 vaccine acceptance and hesitancy which was published in July 2022, vaccine motivators were listed as high perception of COVID-19 infection risk (loved ones experiencing COVID-19, chronic diseases, old age), trust for the healthcare system, social responsibility; while factors inducing vaccine hesitancy were listed as low perception of COVID-19 infection risk, poor experiences with other vaccines, disinformation, fear of the vaccine side effects, distrust against vaccine effect [5]. It was also shown in previous literature that among people with allergies, allergic asthma and the families of child-adolescent patients with allergies and allergic asthma, vaccine hesitancy is very common [6]. Therefore, it is particularly crucial to thoroughly and carefully inform these groups about the COVID-19 vaccines in order to raise vaccine extensity and reduce the spread of the COVID-19 pandemic.

In this study, we aimed to understand the thoughts and experiences about the COVID-19 vaccine and determine factors inducing COVID-19 vaccine hesitancy (age, marital status, educational status, chronic diseases, anaphylaxis, COVID-19 infection history, concerns about COVID-19 infection) among patients who were admitted to Ankara University Internal Medicine Allergy and Immunology Department with drug allergies.

Materials and Methods

This study was approved by the Ankara University Faculty of Medicine Human Research Ethics Committee (I05-271-22).

Study Design

This study has been conducted among 76 patients who were older than 18 years and were admitted to the Ankara University Internal Medicine Allergy and Immunology Clinic May 2022 to September 2022. We prepared a survey to analyze demographic information, attitudes and behaviors about vaccines, COVID-19 vaccines, thoughts and experiences about COVID-19 infection. Patients were informed that their participation to our study was voluntary and written informed consent was obtained from patients who participated in this study.

Statistical Analysis

Statistical analyses were conducted with the IBM® SPSS® Statistics Version 25 program. Normal distribution of variables was examined visually (histogram, probability graphs) and analytically (*Kolmogorov-Smirnov*/*Shapiro-Wilk* tests). Descriptive analyses were reported with medians and quartiles for numeric variables which were not normally distributed, and frequency tables for ordinal and categorical variables. For numeric variables which were not normally distributed *Mann Whitney U* test was used, while for categorical variables Chi-Square test or *Fisher* test were used. *P* values below 0.05 were considered statistically significant.

Results

Characteristics and Survey Answers of All Participants

Our study included 76 drug allergy patients. Characteristics and survey answers of all participants are summarized in Table 1.

Table 1: Characteristics, survey answers and statistics of all drug allergy patients, non-vaccinated and vaccinated groups.

	All drug allergy patients (n=76)	**Non-vaccinated patients (n=38)**	**Vaccinated patients (n=38)**	**p value**
Gender*				0.62[a]
Female	52 (68.4)	25 (65.8)	27 (71.1)	
Male	24 (31.6)	13 (34.2)	11 (28.9)	
Age				0.78[b]
Mean±SD	40.6±13.4	40.2±14.1	41±12.7	
Median value	40 (22)	41 (27)	39 (21)	
Age*				0.55[a]
18-25	14 (18.4)	9 (23.7)	5 (13.2)	
26-35	18 (23.7)	7 (18.4)	11 (28.9)	
36-45	15 (19.7)	7 (18.4)	8 (21.1)	
46-65	29 (38.2)	15 (39.5)	14 (36.8)	
Marital status*				0.64[a]
Single	30 (39.5)	14 (36.8)	16 (42.1)	
Married	46 (60.5)	24 (63.2)	22 (57.9)	
Educational status*				**0.026**[a]
Primary school	9 (11.8)	1 (2.6)	8 (21.1)	
Middle school	6 (7.9)	6 (15.8)	0 (0)	
High school	26 (34.2)	13 (34.2)	13 (34.2)	
College	29 (38.2)	16 (42.1)	13 (34.2)	
Masters	2 (2.6)	1 (2.6)	1 (2.6)	
Doctorate	4 (5.3)	1 (2.6)	3 (7.9)	
Working status*				0.11[a]
Unemployed	39 (51.3)	23 (60.5)	16 (42.1)	
Employed	37 (48.7)	15 (39.5)	22 (57.9)	
Chronic disease*				0.49[a]
None	53 (69.7)	25 (65.8)	28 (73.7)	
One chronic disease	14 (18.4)	9 (23.7)	5 (13.2)	
Multiple chronic diseases	9 (11.8)	4 (10.5)	5 (13.2)	
Chronic disease*				0.45[a]
None	53 (69.7)	25 (65.8)	28 (73.7)	
Present	23 (30.3)	13 (34.2)	10 (26.3)	
Which drug group caused the reaction?*				0.51[a]
Analgesic	36 (47.4)	19 (50)	17 (44.7)	
Antibiotic	25 (32.9)	10 (26.3)	15 (39.5)	
Muscle relaxant	8 (10.5)	4 (10.5)	4 (10.5)	
Contrast material	2 (2.6)	2 (5.3)	0 (0)	
Other	5 (6.6)	3 (7.9)	2 (5.3)	
Allergy with antibiotics*	25 (32.9)	10 (26.3)	15 (39.5)	0.22[a]
Allergy with analgesics*	36 (47.4)	19 (50)	17 (44.7)	0.65[a]
Did you experience anaphylactic shock?*				0.43[a]
No	57 (75)	27 (71.1)	30 (78.9)	
Yes	19 (25)	11 (28.9)	8 (21.1)	
How was the drug used?*				0.75[a]
Oral	58 (76.3)	30 (78.9)	28 (73.7)	
Intravenous (IV)	10 (13.2)	5 (13.2)	5 (13.2)	
Intramuscular (IM)	8 (10.5)	3 (7.9)	5 (13.2)	
Allergy with oral drug*	58 (76.3)	30 (78.9)	28 (73.7)	0.59[a]
Allergy with IV drug*	10 (13.2)	5 (13.2)	5 (13.2)	1.00[a]
Allergy with IM drug*	8 (10.5)	3 (7.9)	5 (13.2)	0.71[c]
Were you hospitalized with drug allergy?*				0.81[a]
No	52 (68.4)	27 (71.1)	25 (65.8)	
Yes, inpatient care	11 (14.5)	6 (15.8)	5 (13.2)	
Yes, emergency room	11 (14.5)	4 (10.5)	7 (18.4)	
Yes, intensive care unit	2 (2.6)	1 (2.6)	1 (2.6)	
Hospitalization with drug allergies*	24 (31.6)	11 (28.9)	13 (34.2)	0.62[a]
Have you ever had COVID-19?*	38 (50)	20 (52.6)	18 (47.4)	0.65[a]
If you had COVID-19, were you hospitalized?*, n=38	2 (5.3)	1 (5)	1 (5.6)	>0.99[c]

If you had COVID-19, were you hospitalized in intensive care unit? *, n=38	1 (2.6)	1 (5)	0 (0)	>0.99[c]
If you had COVID-19, did you have a reaction with the medication for COVID-19? *, n=38	2 (5.3)	0 (0)	2 (11.1)	0.22[c]
Have any of the people you know had COVID-19? *				1.00[a]
No	14 (18.4)	7 (18.4)	7 (18.4)	
Yes	62 (81.6)	31 (81.6)	31 (81.6)	
Do you know anybody who died from COVID-19? *				1.00[a]
No	56 (73.7)	28 (73.7)	28 (73.7)	
Yes	20 (26.3)	10 (26.3)	10 (26.3)	
Are you anxious about getting COVID-19? *				1.00[a]
No	50 (65.8)	25 (65.8)	25 (65.8)	
Yes	26 (34.2)	13 (34.2)	13 (34.2)	
Do you think COVID-19 leads to serious complications? *				0.065[a]
No	34 (44.7)	21 (55.3)	13 (34.2)	
Yes	42 (55.3)	17 (44.7)	25 (65.8)	
Do you think you would get really sick if you had COVID-19? *				0.15[a]
No	48 (63.2)	27 (71.1)	21 (55.3)	
Yes	28 (36.8)	11 (28.9)	17 (44.7)	
Are you afraid of getting COVID-19? *				0.34[a]
No	48 (63.2)	26 (68.4)	22 (57.9)	
Yes	28 (36.8)	12 (31.6)	16 (42.1)	
Do you think COVID-19 vaccine reduces the risk of getting COVID-19 or its complications? *				**<0.001**[a]
No	36 (47.4)	28 (73.7)	8 (21.1)	
Yes	40 (52.6)	10 (26.3)	30 (78.9)	
Have you ever had a reaction with a vaccine? (other than the COVID-19 vaccine) *				>0.99[c]
No	75 (98.7)	37 (97.4)	38 (100)	
Yes	1 (1.3)	1 (2.6)	0 (0)	
Do you know anybody who had an allergic reaction to the COVID-19 vaccine? *				0.48[c]
No	67 (88.2)	32 (84.2)	35 (92.1)	
Yes	9 (11.8)	6 (15.8)	3 (7.9)	
Are you afraid of an allergic reaction to the COVID-19 vaccine? *				**0.028**[a]
No	25 (32.9)	8 (21.1)	17 (44.7)	
Yes	51 (67.1)	30 (78.9)	21 (55.3)	
Have you had the COVID-19 vaccine? *				NA
No	38 (50)	NA	NA	
Yes	38 (50)	NA	NA	
If you had the COVID-19 vaccine. which vaccine did you choose? *, n=38				NA
Sinovac	4 (10.5)	NA	NA	
Biontech	34 (89.5)	NA	NA	
Why did you choose the vaccine you had? (written answers)* , n=38				NA
More protective	24 (36.2)	NA	NA	
Less side effects	4 (10.5)	NA	NA	
I trust it more	3 (7.9)	NA	NA	
Physician recommendation	3 (7.9)	NA	NA	
Effective	1 (2.6)	NA	NA	
European recommendation	1 (2.6)	NA	NA	
mRNA vaccine	1 (2.6)	NA	NA	
Live virus vaccine	1 (2.6)	NA	NA	
Did you get the vaccine immediately when it was possible? *, n=38				NA
No	3 (7.9)	NA	NA	
Yes	35 (92.1)	NA	NA	
If you had the vaccine later, what was the reason?*, n=3				NA
Pregnancy	1 (33.3)	NA	NA	
No time	1 (33.3)	NA	NA	
Fear of side effects	1 (33.3)	NA	NA	

What was the positive factor that persuaded you to get the COVID-19 vaccine? (written answers) [*], n=14				NA
Protection	4 (28.6)	NA	NA	
Precaution	2 (14.3)	NA	NA	
People who were vaccinated had a milder disease	2 (14.3)	NA	NA	
Fear	1 (7.1)	NA	NA	
Necessity	1 (7.1)	NA	NA	
Having a chronic disease	1 (7.1)	NA	NA	
High antibody response	1 (7.1)	NA	NA	
To avoid infecting other people	1 (7.1)	NA	NA	
Statements from the government	1 (7.1)	NA	NA	
If you weren't vaccinated, is it because of your drug allergy?[*], n=38				NA
No	10 (26.3)	NA	NA	
Yes	28 (73.7)	NA	NA	
Is it because of another reason? (written answers)[*], n=12				NA
Fear from vaccine side effects[*]	11 (91.7)	NA	NA	
Post-vaccine embolism in family[*]	1 (8.3)	NA	NA	
If you had the COVID-19 vaccine, did you experience an allergic reaction? [*], n=38				NA
No	35 (92.1)	NA	NA	
Yes	3 (7.9)	NA	NA	
Would you get the COVID-19 vaccine once you have been informed thoroughly? [*]				0.16[a]
No	44 (57.9)	25 (65.8)	19 (50)	
Yes	32 (42.1)	13 (34.2)	19 (50)	
Are you afraid of the possible side effects of the COVID-19 vaccine? [*]				**<0.001**[a]
No	21 (27.6)	3 (7.9)	18 (47.4)	
Yes	55 (72.4)	35 (92.1)	20 (52.6)	
Sinovac	4 (10.5)	NA	NA	
Biontech	34 (89.5)	NA	NA	
Why did you choose the vaccine you had? (written answers)[*] , n=38				NA
More protective	24 (36.2)	NA	NA	
Less side effects	4 (10.5)	NA	NA	
I trust it more	3 (7.9)	NA	NA	
Physician recommendation	3 (7.9)	NA	NA	
Effective	1 (2.6)	NA	NA	
European recommendation	1 (2.6)	NA	NA	
mRNA vaccine	1 (2.6)	NA	NA	
Live virus vaccine	1 (2.6)	NA	NA	
Did you get the vaccine immediately when it was possible? [*], n=38				NA
No	3 (7.9)	NA	NA	
Yes	35 (92.1)	NA	NA	
If you had the vaccine later, what was the reason?[*], n=3				NA
Pregnancy	1 (33.3)	NA	NA	
No time	1 (33.3)	NA	NA	
Fear of side effects	1 (33.3)	NA	NA	
What was the positive factor that persuaded you to get the COVID-19 vaccine? (written answers) [*], n=14				NA
Protection	4 (28.6)	NA	NA	
Precaution	2 (14.3)	NA	NA	
People who were vaccinated had a milder disease	2 (14.3)	NA	NA	
Fear	1 (7.1)	NA	NA	
Necessity	1 (7.1)	NA	NA	
Having a chronic disease	1 (7.1)	NA	NA	
High antibody response	1 (7.1)	NA	NA	
To avoid infecting other people	1 (7.1)	NA	NA	
Statements from the government	1 (7.1)	NA	NA	
If you weren't vaccinated, is it because of your drug allergy?[*], n=38				NA

No	10 (26.3)	NA	NA	
Yes	28 (73.7)	NA	NA	
Is it because of another reason? (written answers)*, n=12				NA
Fear from vaccine side effects*	11 (91.7)	NA	NA	
Post-vaccine embolism in family*	1 (8.3)	NA	NA	
If you had the COVID-19 vaccine, did you experience an allergic reaction? *, n=38				NA
No	35 (92.1)	NA	NA	
Yes	3 (7.9)	NA	NA	
Would you get the COVID-19 vaccine once you have been informed thoroughly? *				0.16[a]
No	44 (57.9)	25 (65.8)	19 (50)	
Yes	32 (42.1)	13 (34.2)	19 (50)	
Are you afraid of the possible side effects of the COVID-19 vaccine? *				**<0.001**[a]
No	21 (27.6)	3 (7.9)	18 (47.4)	
Yes	55 (72.4)	35 (92.1)	20 (52.6)	

*n (%), NA: not applicable, aChi-Square, bMann-Whitney U, cFisher's Exact Test

68.4% of all participants were female, 31.6% of them were male. Mean age was 40.6±13.4, median value was 40 (22). Most common drug group that caused reactions among our study group was analgesics (47.4%), and drugs that caused reactions in the study group were most commonly used orally (76.3%).

In our study group, 50% of the drug allergy patients experienced COVID-19 infection, among them 5.3% required hospitalization, 2.6% needed intensive care. 5.3% of the patients had a reaction with COVID-19 medication (favipravir).

Among the 38 patients who were vaccinated, 34 (89.5%) chose Biontech vaccine, 4 (10.5%) chose Sinovac vaccine. Reasons for patients to prefer the indicated vaccine were listed as: more protective (Biontech), less side effects (Sinovac), safety (Biontech), physician recommendation (Biontech), effective (Biontech), European recommendation (Biontech), mRNA vaccine (Biontech), live virus vaccine (Biontech, which is misinformation). 14 of the vaccinated patients answered our question about the positive factor that persuaded them to get vaccinated, and these factors were listed as: Protection, precaution, people who were vaccinated experienced a milder disease, fear, necessity, having a chronic disease, high antibody response, to avoid infecting other people, statements from the government. 92.1% of vaccinated patients didn't experience an allergic reaction after the COVID-19 vaccine.

While 28 (73.7%) of the non-vaccinated patients indicated that they were not vaccinated because of their drug allergies, 10 patients (26.3%) indicated they were not vaccinated because of other reasons. These reasons were indicated as fear from vaccine side effects and familial history of post-vaccine embolism.

Comparison of the Vaccinated and Non-Vaccinated Groups

Comparison and statistics of the vaccinated and non-vaccinated groups are shown in Table 1.

There was no significant difference between non-vaccinated and vaccinated groups in regard to gender (p=0.62), age (p=0.78), marital status (p=0.64), working status (p=0.11), chronic diseases (p=0.45), hospitalization requiring drug allergies (p=0.62), COVID-19 infection history (p=0.65), hospitalization with COVID-19 infection (p>0.99), knowing someone who had COVID-19 infection (p=1.00), knowing someone who died because of COVID-19 infection (p=1.00). Educational status was significantly lower in the vaccinated group (p=0.026)

Vaccinated patients thought the vaccine reduced the possibility of COVID-19 infection and complications, which was significantly different from the non-vaccinated patients (p<0.01). Non-vaccinated group feared the possible allergic reaction to the COVID-19 vaccine, significantly more than the vaccinated group (p=0.028). Fear of the possible side effects of the COVID-19 vaccine (p<0.001) and the thought of the COVID-19 vaccine being associated with unpredictable

effects were significantly more evident in the non-vaccinated group (p<0.001).

Discussion

As a perspective published in New England Journal of Medicine indicated, COVID-19 vaccines emerged as a hope to "give us our world back" [7]. Therefore, vaccination hesitancy is an important topic to be addressed in order to universalize the COVID-19 vaccines and attaining herd immunity. It was established in previous research that families of young individuals with allergies and allergic asthma have COVID-19 vaccine hesitancy, so it is crucial to address concerns of individuals with allergies [6,8,9]. The aim of our study was to determine the factors responsible for COVID-19 vaccination acceptance and hesitancy in patients with drug allergies.

While 28 (73.7%) of the non-vaccinated patients indicated that they were not vaccinated because of their drug allergies, 10 patients (26.3%) indicated they weren't vaccinated because of their fear of vaccine side effects or post-vaccine embolism in their families. Previous research also indicated that fear of vaccine side effects is an important factor for vaccine hesitancy [10]. It is very important to thoroughly explain the side effects of the vaccine, probability of these side effects and risk-benefit ratio of the COVID-19 vaccine. As for vaccine hesitancy due to allergies, it should be shared with patients that Biontech COVID-19 vaccine has an anaphylaxis probability of 4.7 among 1 million cases and there is no mortality with anaphylaxis when patients were observed [11]. In our study, among 38 drug allergy patients who were vaccinated, 3 of them (7.9%) had post-vaccine reaction, but these reactions were skin reactions, and none of these patients had anaphylaxis. European Academy of Allergy and Clinical Immunology (EEACI) stated in 2021 that allergy to drugs, food, insect venoms or inhalant allergens is not a contraindication for COVID-19 vaccines [12].

There was no difference in gender, marital status, working status between vaccinated and non-vaccinated groups. Although older age has been indicated as a factor inducing vaccine acceptance in previous research [13], there was no difference in age between non-vaccinated and vaccinated groups, this may be due to the lack of geriatric individuals among our drug allergy patients.

While in previous literature it was shown that lower educational status was associated with lower vaccination rates [14], in our study educational status was significantly different between non-vaccinated and vaccinated groups (p=0.026), with lower educational status being higher in the vaccinated group. This can be due to the fact that our sample is smaller, or due to the fact that higher educated individuals may have higher vaccination hesitancy because of their more frequent usage of social media, which can lead to misinformation [15,16].

Although it was shown in the literature that individuals with chronic diseases had higher vaccine acceptance rates [13], in our study there was no significant difference in regard to chronic diseases between vaccinated and non-vaccinated groups.

Vaccinated patients thought the vaccine reduced the possibility of COVID-19 infection and complications, which was significantly different (p<0.01). Non-vaccinated group significantly feared the possible allergic reaction to the COVID-19 vaccine, more than the vaccinated group (p=0.028). Fear of the possible side effects of the COVID-19 vaccine (p<0.001) and the thought of the COVID-19 vaccine being associated with unpredictable effects were significantly more evident in the non-vaccinated group (p<0.001). These results were compatible with previous research that vaccine acceptance was highly associated with trust towards the COVID-19 vaccine effectivity and safety [17].

In our study group, patients who chose the inactivated Sinovac vaccine made this decision based on the thought that the vaccine had fewer side effects than the Biontech vaccine. The most common side effect related to the inactivated vaccine is pain at the site of the injection. Fever, headache, fatigue, myalgia were also reported as mild side effects [18]. As for the Biontech vaccine, most common side effects were pain at the site of the injection, fatigue, muscle pain, local swelling, headache, joint pain, fever, lymph node swelling

[19]. In terms of allergic reactions, in a phase 1-2 clinical trial of Sinovac reported only one case of acute hypersensitivity [18], another phase 1-2 clinical trial reported one case of anaphylaxis, which was grade 1 severity [20]. A phase 3 trial of Sinovac conducted in Turkey reported one grade 3 allergic reaction, which required hospitalization but resolved within 24 hours [21]. Among the 17.5 million doses of Biontech and Moderna mRNA vaccines, only 66 anaphylaxis cases were reported, which was interpreted as 4.7 cases per 1 million doses for Biontech vaccine [21]. A study conducted with elderly patients in our country showed that the probability of allergic reactions was similar with Biontech and Sinovac vaccines [22]. Neither Sinovac nor Biontech caused mortal allergic reactions or anaphylaxis cases, all reported allergic reactions mentioned during phase studies or real-life studies resolved uneventfully [18,19].

With our survey study, we analyzed multiple factors regarding vaccine hesitancy among 76 drug allergy patients, for the first time in literature. Most important limitation of our study was the number of participants. Some of our results were incompatible with previous research, this may be due to the participant number, but also can be due to the changes in individuals' experiences, thoughts and behaviors between the beginning of the COVID-19 pandemic to our study timeline, which was two years after the start of the COVID-19 pandemic. Similar studies among drug allergy patients involving multiple centers and larger groups of participants may also contribute to the literature in the future.

Conclusion

In conclusion, our study analyzed multiple factors regarding vaccine acceptance, rejection and hesitancy among drug allergy patients for the first time in literature. Our results show that informing patients with drug allergies thoroughly, answering questions about the side effects and effectiveness of the COVID-19 vaccines are crucial in order to overcome vaccine hesitancy. Similar studies with larger samples and involving multiple centers can also contribute to the literature in the future.

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Conflict of interest

The authors have no competing interests to disclose.

Data availability statement

The authors confirm that the datasets for this article are included within the article, raw data that for our study is available from the corresponding author, upon request.

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