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The Percentage of Hesitation and Factors Associated with Acceptance or Refusal for COVID-19 Vaccination: Does Education About Vaccines by Allergist Affect Personal Decision?

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The Percentage of Hesitation and Factors Associated with Acceptance or Refusal for COVID-19 Vaccination: Does Education About Vaccines by Allergist Affect Personal Decision?

~~Role of Education About Vaccines by Allergist in Determining Personal Decisions for COVID-19 Vaccination of People Admitted to Allergy Clinic~~

The Percentage of Hesitation and Factors Associated with Acceptance or Refusal for COVID-19 Vaccination: Does Education About Vaccines by Allergist Affect Personal Decision?

Original Article

Running Head: The Percentage of Hesitation and Associated Factors with Acceptance or Refusal for COVID-19 Vaccination and The Effect on Vaccination Status of Allergy Patients

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ABSTRACT

Background and aim: As the impact of coronavirus disease (COVID)-19 arises worldwide, the effect of vaccines is protecting its importance. The aim of this study was to investigate the vaccination perspectives of patients and learn how many patients were persuaded to get vaccinated with the effect of the education provided by allergists.

Materials and Methods: A cross-sectional study was carried out among 200 adult patients in the outpatient clinic between February 2021 and January 2022. Patients filled out the anti-vaccination scale form and a questionnaire form developed by allergists. The training about COVID-19 vaccines has been given to the patients who did not consider getting vaccinated. The patients were called by phone and questioned whether they have been vaccinated or not, after 22 weeks.

Results: Sixty point five percent of 200 patients participants were considering getting vaccinated. Patients who did not consider getting vaccinated comprised 45.7% of women and 31% of men. While 52.4% of primary school graduates considered getting vaccinated, 75% of high school graduates and 60.8% of higher education graduates were considering getting vaccinated. Major reasons for rejecting vaccination were concerns about side effects and allergy. While the majority of women (47.2%) who did not want to get vaccinated were concerned about vaccine side effects, the majority of men (34.6%) did not want to get vaccinated because they did not trust the efficacy of the vaccine.

Vaccination rates have been increased with the training we provided to our patients who did not consider getting the vaccine. 76 patients could be reached by phone and 81.6 % of them were vaccinated, and 18.4% were not.

Conclusion: The vaccination rates of allergy patients who did not consider getting vaccinated were increased with the information provided by allergists. So, the allergists should give more attention for giving information and increasing the vaccination rates of covid-19.

Key Words: COVID-19, Vaccination, Allergy, Education

INTRODUCTION

Coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus (SARS-CoV-2), was declared a pandemic by the World Health Organization (WHO) on March 11, 2020.(1) Various studies are underway to prevent and treat the disease. Vaccines are the most effective tools developed to control the COVID-19. The importance of vaccines in the prevention of infectious diseases has been known for years. Various vaccine studies are going on in the world and in our country to struggle with the COVID-19 pandemic. Both inactivated (Sinovac) and mRNA (BioNTechPfizer) vaccines are still being used in Turkey.(2)

COVID-19 vaccines have various benefits like preventing the disease, allowing the disease to have mild symptoms, and reducing hospitalization rates. (3,4) Despite its various known benefits, vaccine hesitancy is increasing in our country as well as in the world. It has been shown that vaccine hesitancy, which encompasses delay, reluctance, or refusal to receive a vaccine despite availability, is a significant threat to the effectiveness of vaccination programs. (5)

According to the study conducted simultaneously in Turkey and the United Kingdom (U.K.), 3% of the people in participating countries refused to get vaccinated and one out of three people in Turkey were unsure about receiving the COVID-19 vaccine. (6) Vaccine hesitancy is caused by multiple factors. One of the major causes of vaccine hesitancy and delay in vaccination is anxiety about adverse effects. (7)

Most of the allergic diseases were not considered during the studies conducted on patients affected by COVID-19 and their comorbidity-related risks, so it is still not clear that allergic diseases are associated with a higher risk of testing positive for SARS-CoV-2 or severe clinical outcomes from COVID-19. We have more data about asthma than other allergic diseases in the literature. Asthma may not be associated with an increased risk of COVID-19 because, it had been shown that patients with COVID-19 had a pooled prevalence of asthma similar to that of the general population (8.3% vs 4.3–8.6%, respectively) in a systematic review. The meta-analysis was conducted in 116 of the 119 included studies and did not show a higher risk of poor COVID-19-related outcomes. (8,9) Patients with allergic diseases are also recommended to get vaccinated against COVID-19 to protect themselves from the negative consequences of the disease, as well as the whole society. However, the tendency to avoid vaccines arises worldwide because it's believed that vaccines may have allergic side effects. (10) It is quite normal for patients who have known allergies to worry about these side effects. As allergists, we must protect our patients' health by providing accurate information on the issue they are concerned about.

We could not find another study that investigates the rates of vaccination after giving accurate information to the patients who did not want to get vaccinated.

The aim of this study was to investigate the vaccination perspectives, and vaccine hesitancy scores and learn how many patients who did not want to get vaccinated could be persuaded to get vaccinated with the effect of the education we provided. This study is the first study that we could detect examining the rates of vaccination of patients before and after giving them accurate information about COVID-19 vaccines by the allergists.

METHODS

Study design

Patients older than 18 years, who are not health-care workers applied to Allergology department of Manisa Celal Bayar University Hospital, Turkey, between February 2021 and January 2022 were randomly selected and included in the study prospectively. None of them refused the study. Written informed consent forms were signed by the participants before the study, and the study was approved by Manisa Celal Bayar University Ethics Committee (Decision number: 2021/ 721). The consent form was taken from the patients, and a questionnaire form was filled out to inquire about demographic information, reasons for applying to the hospital, comorbidities, known allergy, allergen type, the history of anaphylaxis, the history of allergy with any vaccine, approach to getting the COVID-19 vaccine, and the reason for not consider getting vaccinated. Patients filled out the anti-vaccination scale form. (11) The information about COVID-19 vaccines have been given to the patients who consider getting vaccinated. The information consisted of a five-minute oral presentation dispensed by an allergist targeted to inform patients about the effects and side effects of vaccines. Patients were informed that there was no evidence of an increased risk of anaphylaxis in those with previous severe but unrelated allergic reactions. (12) The patients were called by phone and questioned whether they have been vaccinated or not, after 22 weeks.

Vaccine Hesitancy in the Turkish Language

It was developed by Kilincarslan et al. in 2020, and its validity and reliability study was conducted. The scale consists of long and short forms. In this study, the short form of the scale was used. The short form was consisting 12 items in three domains. These domains are: "Vaccination benefit and protective value", "Vaccination repugnance", and "Solutions for not getting vaccinated". The Cronbach's alpha reliability coefficients were calculated to determine the internal consistency of the three factors. The Cronbach's alpha reliability coefficients of the three factors and the total scale ranged between 0.71 and 0.86 and correspond to high-reliability levels. (11) Thus, higher scores indicate that the person has more hesitancy. There is no cut-off point for the Vaccine Hesitancy Scale.

Statistical Analysis

The data obtained were evaluated by descriptive statistics (number, percentage distribution, mean, median, standard deviation, etc.), continuous numerical variables, t-test in independent groups (Mann Whitney u test if normal distribution conditions are not met), one-way analysis of variance (Kruskal Wallis test if normal distribution conditions are not met). Categorical variables were evaluated using the chi-square test, and Fisher's exact test. A value of $p < 0.05$ was considered statistically significant.

RESULT

A total of 200 patients participated in the study, with a mean age of 38.25 (± 12.9) years, 58% were women and 65.5% were married. Educational status, comorbidities like diabetes mellitus, hypertension, asthma, rheumatological, oncological, thyroid diseases, known allergy, the history of anaphylaxis, and the allergy history with any vaccine of the patients participating in the study are given in Table 1. According to the allergen type, there were 8 (6.0 %) patients with venom allergy, 70 (52.2%) patients with pollen allergy, 30 (22.4%) patients with pollen+mite mixed allergy, 19 (14.2%) patients with mite allergy and 7 (5.2%) patients with food allergy.

The percentage of the patients who were considering getting vaccinated was 60.5% in the study. There was no difference in terms of patients' approaches to getting the COVID-19 vaccine according to their marital status, comorbidity, known allergy, the history of anaphylaxis, and the history of allergy to any vaccine ($p > 0.05$). However, there was a difference according to gender distribution ($p = 0.035$). Patients who did not consider getting vaccinated comprised 45.7% of women and 31% of men. When the patients' approaches to getting vaccinated according to their education levels were examined, it was found that the vaccination request rates of high school and higher education graduates were higher than the primary school graduates ($p = 0.047$). While 52.4% of primary school graduates considered getting vaccinated, 75% of high school graduates and 60.8% of higher education graduates were considering getting vaccinated. Patients with a history of anaphylaxis (55.3%) were less likely to consider getting the COVID-19 vaccine than those without (61.7%), but this difference was not statistically

significant. Similarly, the majority of the patients (61.8%) without a history of allergy to any vaccine were considered to have the COVID-19 vaccine more than those with a history of allergy to any vaccine (57.1%). However, this difference was not statistically significant because of the insufficient number of participants (Table 1).

Seventy-nine patients, 67.1% of whom were women, did not consider getting vaccinated. When the reasons for vaccine rejection were examined, 39.2% did not want to get vaccinated because of fear of vaccine side effects, 39.2% had allergy concerns, 17.7% did not trust the effectiveness of the vaccine, and 3.8% would get the vaccine from a different vaccine company if possible. The reasons why patients did not consider getting vaccinated significantly varied according to gender. While the majority of women (47.2%) who did not want to get vaccinated were concerned about vaccine side effects, the majority of men (34.6%) did not want to get vaccinated because they did not trust the efficacy of the vaccine (Figure 1) (**p=0.001**).

One-hundred and eight people considered getting vaccinated and 104 (96.3%) of them were vaccinated. One-hundred and ninety-six people filled the anti-vaccination scale, 4 people did not. There was no statistically significant difference between males and females in terms of the mean of the anti-vaccination score. The mean of the anti-vaccination score was found 27.93 (± 6.93) in females and 28.14 (± 7.29) in males ($p>0.05$). It was determined that the anti-vaccination score did not change according to features such as marital status, comorbidity, known allergy, the history of anaphylaxis or allergy history with any vaccine. The mean of the anti-vaccine score was significantly found to be lower in patients who were considering getting vaccinated and had been vaccinated (**p=0.002**, **p=0.047** respectively) (Table 2).

Was the education effective?

Vaccination rates have been increased with the information we provided to our patients who did not consider getting the COVID-19 vaccine. Out of 79 people who did not consider getting vaccinated before the information, 76 could be reached by phone. Of 76 patients, 81.6% were vaccinated, and 18.4% were not. When we examined the patients who did not consider getting vaccinated according to their demographic characteristics, the vaccination rates were significantly different according to their marital status and educational level with the information provided. After the information given to the patients by our team, married patients (88.7%) were vaccinated at a significantly higher rate than singles (65.2%) (**p=0.024**). After the information, university graduates (69%) had the lowest vaccination rate compared to primary (86.1%) and high school (100%) graduates (**p=0.049**). No statistically significant difference was found in the examination of vaccination rates after information according to gender, comorbidity, known allergy, the history of anaphylaxis, and the history of allergy with any vaccine ($p>0.05$) (Table 3).

There was a significant difference in vaccination rates after education between patients with a history of anaphylaxis and those with known allergies or allergy to any vaccine. In patients who did not consider vaccination, 88.2% of those with known allergies were vaccinated after education, while 64.7% of those with a history of anaphylaxis were vaccinated (**p=0.0001**). Similarly, in patients who did not consider vaccination, 87.5% of those with an allergy to any vaccine were vaccinated after education, while 64.7% of those with a history of anaphylaxis were vaccinated (**p=0.01**).

DISCUSSION

A discussion about the potential increased risk of severe anaphylactic or allergic reactions following COVID-19 vaccination among individuals with a history of allergy has been raised in the scientific community. Firstly, no evidence of an increased risk of anaphylaxis in patients with prior severe but unrelated allergic reactions was found in the enhanced surveillance of more than one million doses of the

vaccine in North America and the U.K. (12). Then, two women developed immediate anaphylaxis within 24 hours in the UK on December 8, 2020. The Medicines and Healthcare products Regulatory Agency (MHRA) included a contraindication of use in people with previous allergic reaction history to the ingredients of the vaccine, except those with any other allergies, after the review of additional data, on December 30, 2020. (13)

After several cases of severe allergic reactions, in particular with mRNA vaccines, a history of hypersensitivity (e.g. anaphylaxis) to any component of these vaccines was introduced as a contraindication to the use of mRNA vaccines by the United States (U.S.) Food and Drug Administration (FDA) and European Medicines Agency (EMA) following the extended use of COVID-19 vaccines worldwide. A second COVID-19 vaccine dose should not be applied to those who have experienced severe allergic reactions or anaphylaxis to the first dose. According to the recent multicenter observational study conducted by Krantz et al., the safety of the second dose of mRNA COVID-19 vaccines was confirmed in individuals who reported immediate suspected allergic reactions after the first dose (except for individuals with evidence of IgE-mediated allergy and/or severe allergic reactions), based on a previous allergist assessment. (14)

To the best of our knowledge, this is the first study investigating the vaccination rates of patients in the immunology and allergy outpatient clinic, by questioning their perspectives on COVID-19 vaccines and their vaccination status before and after giving accurate information. The percentage of patients participating in the study who were considering getting vaccinated was 60.5 %. Perceptions of patients about COVID-19 vaccines, as measured by the questionnaire in which we asked if they consider getting vaccination, were significantly more unfavorable among females. Seventy-nine patients, 67.1% of whom were women, did not consider getting vaccinated. Vaccination rates of primary school graduates were lower than the high school and upper graduates (Table 2). When the reasons for vaccine rejection were examined, 39.2% did not consider getting vaccinated because of fear of vaccine side effects, 39.2% had allergy concerns, 17.7% did not trust the effectiveness of the vaccine, and 3.8% would get the vaccine from a different vaccine company if possible. The reasons why patients did not consider getting vaccinated significantly vary according to gender. While the majority of women (47.2%) who did not consider getting vaccinated were concerned about vaccine side effects, the majority of men (34.6%) did not consider getting vaccinated because they did not trust the efficacy of the vaccine (Figure 1). One hundred and ninety-six people filled out the anti-vaccination scale, 4 people did not. The mean of the anti-vaccination score was significantly found to be lower in patients who were considering getting vaccinated and had been vaccinated (Table 2).

Vaccination rates have been increased with the information we provided to our patients who did not consider getting the COVID-19 vaccine. Out of 79 people who did not consider getting vaccinated before the information, 76 could be reached by phone. Of 76 patients, 81.6% were vaccinated, and 18.4% were not. When we examined the patients who did not consider getting vaccinated according to their demographic characteristics, the vaccination rates were significantly different according to their marital status and educational level with the information provided. After the information given to the patients by our team, married patients (88.7%) were vaccinated at significantly a higher rate than singles (65.2%). After the information, university graduates (69%) had the lowest vaccination rate compared to primary (86.1%) and high school (100%) graduates (Table 3).

In the present study, similar to the literature, 60.5% of 200 participants were considering getting vaccinated against COVID-19. The highest COVID-19 vaccine acceptance rates (>70%) were reported in six studies from U.K. (71.7%), France (77.6%) China (91.3%), Indonesia (93.3%), Malaysia (94.3%), Ecuador (97.0%), and and lower acceptance rates were reported (<60%) in eight studies from France (58.9%), US (56.9%), Poland (56.3%), Saudi Arabia (55.1 %), Russia (54.9%), Italy (53.7), Jordan (28.4%) and Kuwait (23.6%).(15,16,17)

The rate of considering vaccination in the US was found to be 56.9-75% in three studies. (15,18,19) The rate of considering vaccination in the France was 58.9-77.6 in two different studies.(15,16) There is a need for clinical studies with higher participant rates in our country.

Based on our findings, the participants' perceptions were significantly more favorable among males (Table 1). Sixty-nine percent of males and 54.3% of females were considering getting vaccinated. Similarly, males were more COVID-19 vaccine acceptors in France. (16) And also in the U.S. the females were less likely to be willing to get a COVID-19 vaccine than males. (19). There was a positive association between male sex and acceptance of COVID-19 vaccination in the literature. (17,20-22) The reasons why males were more likely to get vaccinated may be associated with that, they were more likely to perceive the disease as very dangerous than women, and they had a lesser tendency to believe in conspiracies from vaccines and virus origin, as they mostly trusted medical doctors, scientists, and scientific journals, compared to women who relied more on social media platforms. (23,24)

Also, in a systematic review investigating factors associated with acceptance of vaccination against pandemic influenza, men were more likely to intend to be vaccinated than women in the general population in France, Greece and the Netherlands. The explanation of women's non-compliance may be fears about the efficacy and safety of the vaccines.(25,26) Interestingly, females have better ranking scores for the perception about COVID-19 vaccination in Saudi Arabia. The possible reasons identified are differences in the education and socioeconomic factors. Also number of males were nearly four times of females. (27) However, while the vaccination acceptance rate is significantly different according to gender in many studies, this does not translate into a different score on the vaccine hesitancy scale. There should be gender distribution on the scale for accurate results of vaccination hesitancy.

When the patients' approaches to getting vaccinated according to their educational status were examined, it was found that the vaccination request rate of high school and higher education graduates was higher than the vaccination request rate of primary school graduates. While 52.4% of primary school graduates considered getting vaccinated, 75% of high school graduates and 60.8% of higher education graduates were considering getting vaccinated. Similarly, university and/or upper graduate degree holders (75%) compared to people with less than a university degree were more likely to accept the vaccine in the U.S. (28). Lower education level was associated with vaccine hesitation in the literature. (29). However, individuals with the lowest education levels were more likely to believe the disease was very dangerous in another study. (23)

Because anaphylaxis is a life-threatening condition, patients with a history of anaphylaxis (55.3%) were less likely to consider getting the COVID-19 vaccine than those without (61.7%), but this difference was not statistically significant. Similarly, the majority of the patients (61.8%) without a history of allergy to any vaccine were considered to have the COVID-19 vaccine more than those with a history of allergy to any vaccine (57.1%). However, this difference was not statistically significant because of the insufficient number of participants (Table 2).

When the reasons for vaccine rejection were examined through the questionnaire, 39.2% did not want to get vaccinated because of fear of vaccine side effects, 39.2% had allergy concerns, 17.7% did not trust the effectiveness of the vaccine, and 3.8% would get the vaccine from a different vaccine company if possible (Table 2). Major reasons were fear of vaccine side effects and allergy concern. Similar to our study, in a survey study conducted by Metin Yiğit et al. at Ankara City Hospital, the highest anti-vaccination reason was the concern about vaccine side effects including allergy (40.4%) while the second rank was distrust in the efficacy of vaccines (38.3%). (10) Also, in Saudi Arabia, about 60.8% of the population were concerned about the side effects, and 48.2% were worried about the allergic reaction to the COVID-19 vaccine. (27) It's known that individuals who consider themselves to have a higher risk of disease, demonstrated higher vaccine acceptance. A personal risk-benefit perception that is influenced by misinformation regarding vaccine safety implies the necessity of information by

health institutions. (22). For this reason, the information we provide to patients about the side effects and efficacy of vaccines has been extremely valuable.

Vaccine hesitancy was associated with lower acceptance of a COVID-19 vaccine. (16). There was no statistically significant difference between men and women in terms of anti-vaccination scores in the present study. While the mean of anti-vaccination score was 27.93 (± 6.93) in females, it was 28.14 (± 7.29) in males. It was determined that the anti-vaccination score did not change according to the characteristics such as gender, marital status, comorbidity, known allergy, the history of allergy with any vaccine, or the history of anaphylaxis. Vaccine hesitancy was associated with a decrease in COVID-19 vaccine acceptance. As expected, patients with a lower anti-vaccination score were those who consider vaccination and who were vaccinated at a higher rate (Table 2).

Increasing the vaccination rate is one of the most important steps to be taken to demonstrate the effectiveness of the COVID-19 vaccine in the clinic. As a matter of fact, in the early stages of the H1N1 pandemic, a trend also emerged against influenza vaccines in 2009. However, vaccination rates have been increased with accurate information, and it has been observed that the influenza vaccine significantly reduced pneumonia and influenza-related hospitalizations. The effectiveness of the influenza vaccine has been reported to be 25-53%. (28).

Vaccination rates have been increased with the information we had provided to our patients who did not want to get the COVID-19 vaccine. Out of 79 people who did not think of getting vaccinated before the information, 76 could be reached by phone. It was noted that 81.6 % of them were vaccinated, and 18.4% were not vaccinated. This marks a great success in increasing vaccination rates. Although it is known that some of the unvaccinated population delayed getting vaccinated because they were infected with COVID-19 probably, we believe that this population can be vaccinated with repeating information. After the information given to the patients by our team, married patients (88.7%) were vaccinated at a higher rate than singles (65.2%). Because married people were at higher risk of infecting their wives or husbands, and perhaps children when they have been infected.

When the patients who did not plan to get vaccinated were examined according to their education levels, there was a difference between the rates of vaccination after the information given by our team. All of the high school graduates, 69% of higher education graduates, and 86.1% of primary school graduates were vaccinated after the information (Table 3). While the highest increase in vaccination rates was seen in high school graduates, the least increase was seen in higher education graduates. This shows us that we need to make the most effort to persuade the populations with the highest and lowest education levels to increase the vaccination rates.

In patients who did not consider vaccination, 88.2% of those with known allergies, 87.5 % of those with an allergy to any vaccine were vaccinated after education, while 64.7% of those with a history of anaphylaxis were vaccinated. Patients with a history of anaphylaxis were more worried about getting COVID-19 vaccines than patients with known allergies or allergies to any vaccine. Even with the education given, their concerns could not be sufficiently reduced. This might be due to the life-threatening anaphylaxis they experienced.

The main limitations of our study include the limited number of patients participated in the study, difficulty to contact the patients after vaccination by phone, lack of confirmatory medical documents for history of allergies and anaphylaxis in many patients, unavailability of in vivo allergy tests for all patients, and organizational difficulties due to the pandemic. Despite these limitations, this study describes useful and related practical approaches related to increasing the rate of COVID-19 vaccination from the allergist perspective based on real-life experiences in a tertiary clinic hospital in Turkey.

CONCLUSION

It has been shown that the vaccination rates have been increased with the information given by allergists to the patients who did not consider getting the COVID-19 vaccine in this study. It is one of our most important duties as physicians to inform our patients correctly and decrease

the rates of vaccine hesitancy. As our study shows, we can increase the vaccination rates of our patients by providing accurate information, even between the patient population in the allergy immunology outpatient clinics that are difficult to persuade.

Declaration:

I have not submitted my manuscript to a preprint server before submitting it to *Revue Française d'Allergologie*.

This manuscript has not been published and is not under consideration for publication elsewhere. We have no conflicts of interest to disclose.

Ethical Approval: Written informed consent forms were signed by the participants before the study, and the study was approved by Manisa Celal Bayar University Ethics Committee (Decision number: 2021/721).

Authors Contributions:

Nurhan SAYACA: Conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, resources, software, supervision, validation, visualization, writing – original draft preparation, and writing - review and editing. Kübra AŞIK CANSIZ: Conceptualization, methodology, project administration, resources, supervision, validation. Beyhan CENGİZ ÖZYURT: Conceptualization, data curation, formal analysis, statistical analysis, investigation, methodology, validation. Eylem YILDIRIM: Visualization Cengiz KIRMAZ : Conceptualization, visualization, writing - original draft, and writing - review and editing

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Figure 1: The reasons for rejection of the COVID-19 vaccine