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Evaluation of the Immune Response to Influenza Vaccine in the Staff of Sina Hospital in Hamadan-Iran

Abstract

The medical staff is recognized as a major target group for influenza vaccination by the Ministry of Health and Medical Education every year, according to the global guidelines for influenza treatment and control. The present study was designed and performed due to the importance of evaluating vaccine immunogenicity. This cross-sectional study was performed on 47 male and female healthcare workers of Sina Hospital in Hamadan, Iran, in 2020. The participants were selected from different occupational groups and hospital wards, using stratified and multi-stage quota sampling methods. The staff was compared in two stages (before and after influenza vaccination), based on positive antibody titers with respect to age and sex. Data were analyzed in SPSS version 16 at a 95% confidence level. The mean age of the participants was 36.04±8.80 years (male, 42.6%; female, 57.4%). Out of 47 individuals, 7 (14.9%) showed a positive immune response before vaccination, while after vaccination, this number increased to 36 (76.6%). The frequency of immune response was 72.5% after vaccination. There was no significant relationship between the immune response to the influenza vaccine and the patient's age or sex. Based on the present results, nearly one-third of the hospital staff did not show an immune response to the seasonal flu vaccine. Therefore, it is necessary to evaluate their immune responses following vaccination every year. Revaccination is also essential, besides determining the reasons for the lack of immunity.

Keywords: *Influenza, Vaccination, Immune response, Medical Staff*

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Introduction

Influenza is an acute respiratory disease, which is common among humans and animals (1). Mammals, birds, and bats are the most important reservoirs for influenza viruses. This disease is responsible for 3-5 million cases of severe illness and over 300,000 deaths worldwide each year (2). Evidence shows that people become infected with an influenza virus at intervals of 10 to 20 years on average. Influenza viruses, which belong to the family *Orthomyxoviridae,* are classified into three distinct types: influenza A, influenza B, and influenza C.

Generally, influenza viruses are enveloped, negative-sense, single-stranded RNA viruses. After each infection with an influenza virus, innate and adaptive immune responses are produced (3). Given the importance of influenza in terms of morbidity and mortality, especially in high-risk individuals, such as hospitalized patients with chronic diseases and healthcare workers, influenza vaccination must be seriously considered, and if there is no appropriate immune response, corrective measures are essential.

There are several vaccines available to prevent influenza, including Fluzone, Sanofi Pasteur, attenuated live and trivalent vaccines (FluMist and MedImmune), and tetravalent vaccines (attenuated live vaccines containing influenza B antigens) (4-6). The rate of immune response varies, depending on the type of vaccine, adjuvant use, injection dose, number of injections, age, sex, underlying disease, and other variables, ranging from 20% to 80% in various studies. Evidence shows that influenza vaccination, besides reducing the incidence, hospitalization, and mortality of this disease, especially in the elderly and high-risk individuals, is also effective in reducing cardiac mortality during flu epidemics (2, 7) due to its effects.

Considering the role of vaccination against influenza, especially in high-risk groups, such as healthcare personnel, besides the importance of immune responses to vaccines in reducing the incidence of infection, this study aimed to investigate responses to influenza vaccine in the staff of Sina Hospital in Hamadan, Iran, in 2020.

Methods

In this descriptive, cross-sectional study, the participants were selected from all sectors and occupational groups of both sexes, using a stratified sampling method. This study was conducted on 47 healthcare workers of Sina Hospital in Hamadan, Iran, who were candidates for influenza vaccination in 2020.

Before inoculating the vaccine, a 5-cc blood sample was taken from the subjects. After separating the serum, the samples were placed in a freezer at -20°C. The subjects were then vaccinated against seasonal flu with the French tetravalent Sanofi vaccine. Two months after vaccination, samples were collected again, and the number of antibodies against H1N1 flu was measured by an enzyme-linked immunosorbent assay (ELISA). A Hangzhou Eastbiopharm kit (Hangzhou, Zhejiang, China) was

also used to evaluate the vaccine response. All tests were performed in one laboratory by one operator.

The collected data were analyzed in SPSS version 16. Descriptive statistics, including mean and standard deviation (SD) indices, were measured for quantitative variables, while nominal or categorical data are presented as absolute and relative frequencies in tables and graphs. For data analysis, student's t-test and Chi-square test were performed to compare immune responses to the vaccine by age. Also, a Chi-square test was performed to compare the immune responses in terms of sex. All data analyses were performed at a 95% confidence level.

Results

This descriptive, cross-sectional study was performed on 47 hospital staff to determine their immune responses to the influenza vaccine in Sina Hospital, Hamadan, Iran, in 2020. In terms of sex, 20 (42.6%) participants were male, and 27 (57.4%) were female. The mean age of the participants was 36.04±8.80 years (minimum, 24 years; maximum, 55 years). Out of 47 participants, 7 (14.9%) had antibodies against H1N1 before vaccination, while after vaccination, this number increased to 36 (76.6%). By excluding the participants who were immune before vaccination, the frequency of immunity after vaccination was estimated at 72.5%. None of the staff had a history of an underlying disease. These results are listed in Table 1.

There was no significant relationship between age and immunization titer against influenza after vaccination. There was also no significant relationship between the hospital staff's sex and vaccine antibody titers against influenza following vaccination. These changes are listed in Table 2.

Discussion

Serological studies have shown that vaccination against influenza significantly reduces the incidence of this disease (9). Generally, vaccination increases the long-term responses of T cells to influenza A, influenza B, and matrix M1 antigens. However, in individuals with the flu, the immune response decreases shortly after infection. Unlike infected individuals, there are no signs of interleukin-1-dependent inflammation in vaccinated people (10).

Vaccination in the elderly significantly reduces the costs of diagnosis and treatment and also decreases the mortality rate remarkably in this group (11). In a study by Al-Qhahtani in Saudi Arabia, the effectiveness of the influenza vaccine was 42% among the medical staff (12). Moreover, in a study by Flannery et al., the overall effectiveness of a flu vaccine was estimated at 40% (33% against influenza A and 53% against influenza B) (13); overall, moderate vaccine efficacy was observed in preventing the disease. Besides, studies on different age groups have shown that vaccination is less effective against type A influenza compared to type B (13).

In a study by Jackson et al. in 2017, the efficacy of live and inactivated flu vaccines was 48% (14). Moreover, in a study by Monto et al. in 2009, the efficacy of an inactivated vaccine was 68%, while the efficacy of an attenuated live vaccine was 36% (15). It should be noted that Monto et al. examined a larger sample size compared to the present study. In our study, the vaccine was only inactivated, and rather than evaluating its effectiveness in preventing the disease, the level of antibodies against H1N1 was determined after vaccination; this could indicate the level of staff safety in the current study compared to the study by Monto and colleagues.

In 2009, Greenberg et al. conducted a study in the United States to evaluate the efficacy and titer of inactivated influenza vaccine antibodies at doses of 15 µg and 30 µg twice. An antibody titer of 1:40 was reported in 95% of individuals with a dose of 15 µg and 89.1% of individuals receiving a dose of 30 µg. Overall, the immune responses to the first and second rounds of vaccination were similar (16). This might be due to differences in the type of vaccine used or the timing of immune response assessment. Moreover, Zhu et al. conducted a study in 2009 in China to evaluate the effectiveness of a flu vaccine for 2,200 people from different age groups as compared to a placebo group. Their results showed an optimal immune response in the age range of 12-60 years, without adjuvant injections; in younger or older individuals, the immune response was weaker (8).

In the present study, no significant association was observed between the subjects' immune responses and age, because healthcare workers, who were almost homogeneous in terms of age, were examined in this study (age range: 24-55 years), whereas in the study by Zhu et al., people from different age groups (ranging from <2 years to >60 years) were recruited. Regarding other influential variables in the effectiveness of the influenza vaccine in healthcare workers, Dini et al. conducted a review study in 2018 and reported that influenza vaccination is necessary for healthcare personnel; however, its effectiveness depends on several environmental and individual factors. Therefore, achieving maximum vaccine efficacy is essential (17).

In the present study, none of the hospital staff had a history of an underlying disease that could affect vaccine efficacy. There was no significant relationship between vaccine immunogenicity and age or sex. Additionally, in 2012, a meta-analysis by Osterholm et al. in the United States showed that attenuated live (67%) and inactivated (75%) flu vaccines had the same efficacy (18). It should be noted that our study had a cross-sectional design, only evaluating the immunogenicity of an inactivated vaccine. Despite differences in the sample size

of these studies, our findings are consistent with the results of the study by Osterholm and colleagues.

Moreover, in 2018, a meta-analysis by Restivo et al. compared the effectiveness of the flu vaccine in high-risk populations in Italy, including patients with an underlying disease, pregnant women, and healthcare workers. Based on their results, the overall effectiveness of the influenza vaccine was 39% and 57% in preventing mild (outpatient treatment) and severe (need for hospitalization) influenza, respectively (19). In the current study, only healthcare workers and only the immunogenicity of the vaccine were evaluated, and the results showed the efficacy of >70%.

Conclusion

In the present study, the safety of medical staff against seasonal flu was 14.9% before vaccination. However, after vaccination, the safety of the staff without previous immunity was 72.5%, and the overall safety was 76.6%. There was no significant relationship between anti-influenza antibody titers and age or sex. A significant number of the hospital staff did not show an immune response to the seasonal flu vaccine; therefore, it is necessary to evaluate their immune responses every year following flu vaccination.

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Ethical approval number: The present study was performed with the informed consent of the patients and ensured the confidentiality of the participants' names. The research was conducted with the ethical approval of the Vice Chancellor for Research of Hamadan University of Medical Sciences with the ethics code IR.UMSHA.REC.1400.033

Conflict of Interest: There is no conflict of interest in this article.

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Table 1. Frequency of Ab titers to influenza vaccine in the staff of Sina Hospital in Hamadan in 2020

Time of evaluation	Number	Percent
Before vaccination		
Positive	7	14.9
Negative	40	85.1
Total	47	100
After vaccination		
Positive	36	76.6
Negative	11	23.4
Total	47	100

Table 2: Frequency of Ab titers to influenza vaccine in the staff of Sina Hospital in Hamadan in 2020 by sex

Ab titer **Sex**

	Female Number) %(	**Male Number) %(**
Positive	**21)77.8%(**	**15)75%(**
Negative	**6)22.2%(**	**5)25%(**
Total	**27)100%(**	**20)100%(**