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Infection Diseases Section *Review Article*

Time to Revisit Presumptions on the Essentiality of Influenza Vaccination for Hajj Pilgrims: A Prospective Cohort Study

Reza Imani[1*], Masoud Hafizi Esfahani[2], Maryam Ale Rasul[2], Saeed Taheri[3]

Abstract

Introduction: Although health authorities encourage pilgrims to vaccinate themselves against influenza virus; no data exist on how much this vaccination is effective in the Iranian Hajj pilgrims. In the current study, we aimed to evaluate potential effects of influenza vaccination on preventing symptoms of upper respiratory tract infections in Iranian Hajj pilgrims.

Methods : Three hundred eighty prospective Hajj pilgrims in 2006 were randomly included into this study. The study was performed after communications with Hajj and Pilgrimage Institution of Iran. Two hundred (52.6%) of the study participants have gotten influenza vaccine, 2 weeks before entering Saudi Arabia, and 185 entered to the study as controls.

Results: Vaccinated pilgrims in the case group were significantly more likely to develop some of upper respiratory tract infection symptoms than the control group: coryza (p=0.01), voice hoarseness (p=0.003), and wheezing (p<0.001). Other signs and symptoms were comparably seen between the two groups and for none of them a statistically significant predominance was detected in the control group.

Conclusion: We recommend stopping routine vaccination against influenza in ordinary Hajj pilgrims, and save it for the people of high-risk health condition, like children, elderly and immunocompromised individuals. We also emphasize on the relevance of education for preventing virus transmission; and to alert pilgrims on the relevance of implementing hygienic precautions and its superiority over vaccination.

Keywords: Influenza Virus, Vaccination, Haj Pilgrims

1. Cellular and Molecular Research Center, Shahre-Kord University of Medical Sciences, Shahre-Kord, Iran
2. Department of Medicine, Shahre-Kord University of Medical Sciences, Shahre-Kord, Iran
3. Dr. Taheri Medical Research Group, Tehran, Iran

*** Corresponding Author**
Reza Imani, Cellular and Molecular Research Center, Shahre-Kord University of Medical Sciences, Shahre-Kord, Iran
Dr. Reza Imani (M.D.)
Tel: +98-913 381 5531;
Fax: +98-3813334588;
Email:.Dr.reza.imani@gmail.com

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Introduction

Hajj pilgrimage is one of the most blessed rituals in Islamic culture which brings over two million pilgrims, every year, from all over the world to Mecca. This huge population congregation inevitably endangers pilgrims to develop several types of infections due to microbial transmission which is facilitated in this condition [1]. Respiratory tract infections, especially viral ones are the most important pathogens in this category because of its high transmission rate and health burden gravity. Respiratory illnesses are responsible for most hospital admissions at Hajj with pneumonia being the leading cause [2]. Among respiratory infective pathogens, influenza virus is one of the most frequent and relevant infections reported in mass gatherings; due to its potential to cause serious respiratory failure or bacterial superinfections which might complicate them, especially in immunocompromised people. Estimations suggest influenza virus is responsible for 6% of upper respiratory tract infections in Hajj pilgrims [3]. On the other hand, Hajj pilgrims are considered a source of infection at their home return, which can cause serious influenza outbreaks in local and/or global perspectives.

Several investigators have addressed the protective value of vaccination against different pathogens in travelers of different populations. In several cases, they found some beneficial effects for vaccination [4]. Influenza vaccination, although it has not been recommended for use in

all populations; immunocompromised patients as well as people of high or low age groups are among targets recommended for influenza immunization [5]. Most previous studies have focused on the power of vaccines on inducing antibodies against pathogens, and very few prospective studies have been performed to evaluate whether vaccination has practical significance. In Hajj a large number of people gather together which results in endangering pilgrims to transmissible infections. Influenza virus is one of these pathogens that can result in infection outbreaks in large scales. Nowadays, health authorities encourage pilgrims to vaccinate themselves against influenza virus; however, no data exist on how much this vaccination was able to prevent influenza infection in Iranian Hajj pilgrims. In the current study, we aimed to evaluate potential effects of influenza vaccination on preventing symptoms of upper respiratory tract infections in Iranian Hajj pilgrims.

Material and Method

Study participants: Three hundred and eighty people who were admitted to participate in Hajj ritual in 2006 and accepted to go under this study were randomly included into this study. The study was performed after communications with Hajj and Pilgrimage Institution of Iran. 200 (52.6%) of the study participants have gotten influenza vaccine (Influvac ® wholevirus vaccine, Influvac subunit vaccine; SolvayDuphar BV, Weesp, The Netherlands), 2 weeks before entering Saudi Arabia.

Inclusion and Exclusion Criteria

Inclusion criteria for the study participants included: adult age (over 25 years of age), and being in general health (as evaluated by their physician). Exclusion criteria included: diabetes mellitus, chronic obstructive pulmonary disease (COPD), chronic kidney disease, chronic liver disease, history of any acute or chronic heart disease, and having respiratory system symptoms or infections at the time of evaluation (cough, nasal discharge, sputum purulence, sore throat, dyspnea, wheezing, fever).

Method of Study

After sample size calculation, we contacted Iran's Hajj and Pilgrimage Institution of Charmahal & Bakhtiari Province for the list of people who were admitted to attend Hajj ritual of 2006 with their demographic data. 380 people with the mentioned criteria were asked to participate and went under medical evaluations. Wherever one of them was excluded from analysis due to any of the mentioned criteria, another person from the list was added, so the overall number of the study does not fall down. After completing the study sample, 200 of the participants were entered into the case group and got the vaccine while the remaining 185 were entered as controls. All the participants including the cases and controls also participated in a mandatory educational session in which a physician has teach them how they can protect themselves against transmissible respiratory infections. Patients were evaluated during their attendance to pilgrims' outpatient clinic due to any complaints or check up during Hajj. Physicians have filled standard forms after careful evaluations, and signs and symptoms of the patients were stated.

Statistical Analyses

Software used for data analyses was SPSS v.17.0 (SPSS Corp., Chicago, Il, USA). Statistical differences between patients' subgroups were performed by using $\chi 2$ and fishers' exact tests for proportions and the students t test for continuous data. All statistical tests were performed at the 0.05 significance level.

Results

Overall 380 Hajj pilgrims from Charmahal & Bakhtiari Province of Iran entered into the study. Mean ± SD age of the case group was 62.5±12.9 years of age and for the control group was 60.9±12.3 years of age (p=0.222). 202 (53.2%) number of participants was male and 178 (46.8%) were female.

338 (88.9%) of the study participants attended our outpatient clinic during the Hajj pilgrims. Figure 1 shows the overall frequencies of upper respiratory tract signs and symptoms in the study population. Coughing was the most frequent symptom of the pilgrims with 70% frequency rate for the admitted pilgrims. Hoarseness (53.6%), sore throat (49.7%), coryza (43.8%), wheezing (43.5%), headache (35.2%), myalgia (30.8%), and dyspnea (17.8%) were other major complaints or detected signs.

Then, frequency of the study variables were compared between the vaccinated (case) and non-vaccinated (control) people. As can be seen in table 1, vaccinated pilgrims in the case group were significantly more likely to develop some of upper respiratory tract infection symptoms than the control group: coryza (p=0.01), voice hoarseness (p=0.003), and wheezing (p<0.001). Other signs and symptoms were comparably seen between the two groups and for none of them a statistically significant predominance was detected in the control group.

Discussion

The burden of symptomatic influenza infection in different international samples of pilgrims from different parts of the world has been reportedly between 4 to 14% defined by molecular analyses and virus culture [3], [6]. For Iranian pilgrims, a previous study from Fars Province, Influenza has been condemned as the main cause of upper respiratory tract infection comprising 30.1% of all causes, followed by parainfluenza virus and rhinovirus [7]. This high rate of infection in accordance with few possibility of intensive care for infected patients in the large crowd of Hajj rings the bells to alert us to find effective methods which can prevent symptomatic disease in pilgrims.

There are studies in the current literature proposing routine surveillance and vaccination for Hajj pilgrims against influenza infection.

In a study from Saudi Arabia, Balkhy et al. [3], have reported a 75% rate of influenza infection among pilgrims representing viral respiratory infections. According to this finding, they concluded that influenza vaccination should be a routine practice in Hajj pilgrims.

However, in the current study, our findings suggest quite an adverse message; we found that people who had gotten influenza vaccines were significantly more likely to develop symptoms of upper respiratory tract infection. Our study result is confirmatory to some previous studies which found no beneficial effect for influenza vaccination; but also it is in contrast to some others which recommend vaccination. In some previous studies, in concordance to our results, authors have reported no beneficial effect for vaccination against influenza. Razavi et al. [8], in their study on Iranian pilgrims to Hajj in 2003, reported no advantage for influenza vaccination.

Table 1. Comparison between Vaccinated and Non-vaccinated Iranian Hajj Pilgrims Regarding Symptoms of Upper Respiratory Tract Infections

Symptoms	Vaccinated	Non-vaccinated	Sig.
Fever (%)	62 (32.6)	26 (32.9)	0.536
Cough (%)	160 (84.2)	62 (78.5)	0.291
Coryza (%)	111 (58.4)	32 (40.5)	0.011
Headache (%)	81 (42.6)	33 (41.8)	0.503
Hoarseness (%)	133 (70)	40 (50.6)	0.003
Wheezing (%)	117 (61.6)	27 (34.2)	<0.001
Nausea (%)	17 (8.9)	3 (3.8)	0.202
Diarrhea (%)	9 (4.7)	4 (5.1)	0.563
Sore throat (%)	117 (61.6)	42 (53.2)	0.222
Dyspnea (%)	45 (23.7)	14 (17.7)	0.333
Myalgia	75 (39.5)	24 (30.4)	0.168
Vomiting (%)	4 (2.1)	1 (1.3)	0.541
Conjunctivitis (%)	0	1 (2)	0.294
Pharyngitis as sign (%)	15 (7.8)	12 (15.2)	0.08
Sinus tenderness (%)	2 (1.1)	1 (1.3)	0.649
Ronchy (%)	6 (3.2)	6 (7.6)	0.117
Rhales (%)	4 (2.1)	2 (2.5)	0.568

The same finding was reported by Alborzi et al. [7], which reported no effect for influenza vaccination in preventing respiratory infections In Iranian Hajj pilgrims of 2006 (similar to ours). On the other hand, in a study on Pakistani Hajj pilgrims, Qureishi et al. [9], have reported a positive effect for influenza vaccination in preventing influenza-like syndrome. There are some differences in their practice compared to that of ours which might be able to describe the observed differences. First of all, the vaccine material which was used in the mentioned study was Vaxigrip (Influenza vaccine manufactured by Aventis-Pasteur (formerly Pasteur MeÂrieux Connaught; Lyon, France) and ours was Influvac (Influvac)® Influvac subunit vaccine; SolvayDuphar BV, Weesp, The Netherlands). It is possible that this difference in the vaccine material could make this difference. Moreover, in their study the vaccine was administered just before departure to Saudi Arabia which makes a difference in timing to ours which was 2 weeks before departure. However, the more likely rationale behind the observed discrepancy could be the year of study. Their study was performed in 1999 while ours was done in 2006. The changeable nature of influenza virus and modifications in its genome which could result in its surface antigens transform and appearance of new drift variants empowers the virus to escape the immune system defense, even after vaccination. On the other hand, Hajj pilgrims are performed in different times in different years due to the lunar calendar of Saudi Arabia. The Hajj pilgrimage time in 2006 was in late December while in 1999 it was in March. Moreover, due to a lack of PCR analysis or viral culture neither in the study by Qureishi et al. [9], nor in ours, we cannot conclude that how much vaccination was successful in preventing symptomatic influenza infection. It is quite possible that the epidemiologies of pathogens responsible for infections are different in the two studies, although due to the overwhelming data on the high frequency of influenza virus in almost all previous studies, it is not a highly likely reason.

Although the abovementioned reasons may satisfy the question why vaccination was not effective in our study population, it cannot explain why vaccinated people among our pilgrims were more likely to develop respiratory symptoms. As one reason, one may think that vaccinated people may presume that vaccination has immunized them against the disease and less carefully watch themselves to prevent virus transmission. As mentioned in the methods section, both of the two groups received equal education regarding transmission routs of the virus. However, non-vaccinated people probably were more aware of implementing preventive endeavors for protecting themselves against vaccination. Our findings, besides suggesting zero or minimal effect for vaccination against influenza, suggests another important issue: implementation of preventive strategies against influenza transmission including behavioral modifications can be highly more effective than immunization via vaccination.

Nowadays, influenza vaccination is routinely recommended to most Iranian people who want to participate in Hajj pilgrimage. This is not in accordance to the findings of our study as well as several previous reports indicating no protective value for influenza vaccination in Hajj pilgrims, and can make a big financial burden to the society which is not necessary. We recommend stopping routine vaccination against influenza in ordinary Hajj pilgrims, and save it for the people of high-risk health condition, like children, elderly and immunocompromised individuals. On the other hand, we emphasize on the relevance of educational endeavors for preventing virus transmission, and to sound an alert to pilgrims on the relevance of implementing this methods and its high superiority over vaccination.

Acknowledgements

None Declared.

Conflict of Interests

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