Impact of influenza vaccine in reduction of incidence and severity of influenza-like illness

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Abstract

Background: Vaccination is useful for protection against seasonal influenza but has a low uptake. Evidence of a protective effect of influenza vaccine among Arab populations would be a useful tool for advocacy.

Aims: To evaluate the impact of vaccine in reducing the incidence and severity of influenza-like illness among health staff of a tertiary care eye hospital in Saudi Arabia.

Methods: This retrospective cohort study was conducted in 2018–2019. Hospital staff were divided into vaccinated and unvaccinated groups. Influenza-like illness episodes and their severity were compared between the groups and influenza-like illness rate before and after vaccination was reviewed in the vaccinated group.

Results: The uptake of flu vaccine among 1180 health staff was 41%. There were 28 (9.3%) and 51 (17%) persons with influenza-like illness in the vaccinated (n = 300) and nonvaccinated (n = 300) groups, respectively. The nonvaccinated group had a significantly higher rate of influenza-like illness than the vaccinated group had. Vaccination, young age and absence of comorbidity were independent protectors against influenza-like illness.

Conclusions: Influenza vaccine confers significant protection and reduces the incidence and severity of influenza-like illness. However, this was a retrospective review of health data; therefore, the association of vaccine with outcomes should be considered as a weak form of evidence. The low uptake of influenza vaccine in hospital staff and their dependents is a matter of concern and should be addressed by greater awareness and education. This evidence can be used to improve overall vaccine coverage.

Keywords: influenza vaccine, influenza-like illness, airborne communicable diseases, respiratory infections, health workers

Conclusion

Influenza is a contagious viral illness that can cause severe morbidity and mortality. Each year up to 650,000 deaths due to influenza are reported by the World Health Organization (WHO) (1). There are yearly epidemics of influenza due to changes in circulating virus undergoing mutations, emergence of multiple variants and lack of specific immunity in susceptible hosts (2). Hence, timely vaccination is crucial to prevent severe complications and mortality in communities.

Influenza-related complications include otitis media, pneumonia, exacerbation of chronic respiratory disease, neurological complications, and myocarditis (3). Adults with chronic illnesses are more vulnerable to influenza-related complications (3). Many viruses can cause respiratory illnesses similar to influenza, called influenza-like illness (ILI). The symptoms of ILI include fever, cough, sore throat and myalgia. Therefore, differentiating influenza from ILI without a laboratory-confirmed test is challenging (4). According to WHO, ILI is the most predictive factor for influenza infection and seasonal variation of influenza activity.

Vaccination against influenza virus is used to decrease the severity and complications of respiratory illness and mitigate the risk of hospitalization (5,6). Unfortunately, changes in the circulating influenza virus strains every year require new vaccines to provide virus-specific immunity (7). Influenza vaccination of health workers is a cost-effective approach that provides protection to frontline medical staff involved in the care and management of patients (8). In spite of educational programmes and public health initiatives in many countries, the vaccination rate continues to be less than desired (33.2%) (9,10).

The annual Hajj pilgrimage in Saudi Arabia presents a unique challenge for controlling the spread of influenza. During the Hajj, pilgrims from many countries gather in a single region, posing a major risk for virus transmission and an influenza outbreak (11). While large mass gathering of many nationalities may be linked to influenza in the community, this study was undertaken after the completion of the 2018 Hajj season and did not overlap with the annual event. The Ministry of Health in Saudi Arabia therefore provides free vaccination to Saudi citizens and residents to protect against influenza virus circulating in the community, as well possible spread of disease emanating from influx of pilgrims. The uptake of these vaccinations is low in Saudi Arabia due to a...
negative attitude to immunization and possible lack of understanding of its benefits in the community (12).

In Saudi Arabia, the epidemiology of influenza during the 2018–2019 season included both influenza A and B viruses (13). While influenza A (H1N1) pdm09 strain was predominant, other influenza A viruses (not subtyped) were also circulating earlier in the season. In contrast to the first half of 2018 when many cases of influenza B were noted, the number of infections due to influenza B declined later in the year, with the virus lineage undetermined. This coincided with an increase in the incidence of influenza A during the influenza season. In 2019, the type of influenza viruses circulating in Saudi Arabia was similar to 2018, with influenza A (H1N1) pdm09 being predominant compared to influenza B in earlier months. Other influenza A strains (not subtyped) were also circulating in the same period in 2019. This pattern was noted to be similar later in the season with increasing numbers of cases during October to December 2019. The vaccine provided by the Saudi Ministry of Health for the same season was a trivalent inactivated influenza virus vaccine with the following strains: Influenza A/ Michigan/45/2015(H1N1) pdm-09 virus, Influenza A/ Singapore/INFIMH-16-0019/2016(H3N2)-like virus, and Influenza B/Colorado/06/2017-like virus (B/Victoria/2/87 lineage). Unfortunately, there are no national data in Saudi Arabia available to evaluate the extent of vaccine match with circulating viruses in the community.

The King Khaled Eye Specialist Hospital (KKESH) is a specialized tertiary eye hospital in Riyadh, Saudi Arabia. Hospital staff and their dependents are offered free vaccines before the influenza season. Influenza vaccination records are maintained electronically for each staff member and their dependents. To the best of our knowledge, there are no currently available studies evaluating the impact of influenza vaccination on the burden and severity of influenza in a healthcare setting in Saudi Arabia. Since influenza infection in hospital staff can have profound consequences for patients, we present the profile of ILI and its determinants among hospital staff and their dependents who were vaccinated against influenza compared to those who were not vaccinated during the 2018–2019 season.

Methods

The study was performed in compliance with the local health authority ethical regulations and requirements and was approved by the Institutional Review Board of KKESH (R-19100923).

The study population comprised all staff at KKESH and their dependents enrolled with the Employee Health Department during the influenza season from October 2018 to March 2019. Only those who were or were not vaccinated in 2018 were included in the study. The study population was divided into vaccinated and unvaccinated groups and subjects were randomly selected for each group.

For the calculation of sample size, we estimated the number of health staff with ILI that would need active intervention. In the vaccinated group, it was assumed to be 20% of the total vaccinated and in the unvaccinated group, it was 41% of the total unvaccinated (14). To achieve 95% confidence interval (CI), 80% power of a historical cohort study with a 1:1 ratio of vaccinated and unvaccinated individuals, we required a random selection of at least 268 vaccinated and 268 unvaccinated individuals. For logistic ease, we included 300 individuals in each group.

ILI was defined as fever ≥ 38°C and cough, with onset within the last 10 days (15). In addition to the aforementioned signs and symptoms, we also included cases with myalgia, dyspnea or pharyngitis, in the absence of another diagnosis (16). The severity of ILI was based on: (i) presence of tachycardia, abnormal oxygen saturation, and laboured breathing and adventitious breath sounds; (ii) recommendation for further care at another referral hospital with specialized facilities; (iii) provision of respiratory assistance therapy within KKESH and; (iv) sick leave endorsed by a consultant physician for rest, time off work and to avoid the spread of ILI.

The retrospective chart (electronic medical record) review was performed to gather data on clinical and demographic variables including, age, gender, medical comorbidity (e.g., cardiac, pulmonary, neuromuscular, vascular or endocrine disease, or cancer), documented history of ILI during the current influenza season, severity of ILI, number of follow-up visits related to ILI, and sick leave.

The data were documented on a pretested data collection form and then transferred to an Access spreadsheet (Microsoft Corp., Redmond, WA, USA). Univariate analysis was performed using SPSS version 25 (IBM Corp., Armonk, NY, USA). Frequencies and percentage proportions were reported for qualitative data. Mean and standard deviations were reported for quantitative data. If the data were not normally distributed, the median and interquartile range were estimated. To compare the outcomes of vaccinated and unvaccinated groups, we calculated the difference of the means, the 95% CI and the two-sided P values. For outcomes of qualitative variables, the relative risk, 95% CI and two-sided P value were reported. If > 2 subgroups were compared, \( \chi^2 \) value was estimated, along with degrees of freedom and P value. Binominal regression analysis was performed to study the effect of age, gender and comorbidity on the association of vaccination to rate of ILI. The adjusted odds ratio (OR) was estimated, 95% CI and two-sided P value using OpenEpi stat calculator (17). \( P < 0.05 \) was considered statistically significant.

Results

Among the study population of 1180 individuals in the Employee Health Department, KKESH, 489 (41%) were vaccinated in 2018–2019. We randomly selected 300 people each from the vaccinated and unvaccinated groups.
Their demographic characteristics and systemic comorbidities are compared in Table 1. There were significantly more women in the vaccinated group compared to unvaccinated group.

There were 28 (9.3%, 95% CI 6.0–12.6%) people with ILI among the vaccinated group compared with 51 (17%, 95% CI 12.7–21.3%) in the unvaccinated group (Table 2). The vaccinated group had a significantly lower rate of ILI than the vaccinated group had (relative risk 0.7, 95% CI 0.5–0.9, \( P = 0.006 \)). The rate of ILI according to different determinants is shown in Table 2. The incidence of ILI was significantly lower in the vaccinated group (\( P = 0.005 \)) and in people of young age (\( P < 0.001 \)).

In the vaccinated group, 9 (3%) people had symptoms only before vaccination, 15 (5%) had symptoms only after vaccination, and 4 (1.3%) had symptoms before as well as after vaccination. In the vaccinated group, 6 (2%) people were given nebulization treatment. In the unvaccinated group, 12 (4%) people underwent nebulization treatment in hospital and 2 at home. None of the cases (vaccinated and unvaccinated) had abnormal oxygen saturation. In the vaccinated group, the number of follow-up visits after initial presentation was 10 (3.3%) compared with 21 (7%) in the unvaccinated group. In the vaccinated group, 21 (7%) were given sick leave compared with 44 (14.7%) in the unvaccinated group.

We compared the impact of influenza vaccine in our study to that reported in literature (Table 3). Influenza vaccine reduces the risk of ILI, hospitalization and mortality related to influenza illness.

**Discussion**

In our study, the vaccine uptake was 48% among health staff of a tertiary care eye hospital in Saudi Arabia. We noted that influenza vaccination provided good protection against ILI in all age groups, and reduced the number of episodes and severity of ILI. The number of follow-up visits and absenteeism decreased considerably among vaccinated compared to unvaccinated individuals. Vaccination status, age and systemic comorbidity were independent risk factors for ILI. The ILI episodes before vaccination suggested that scheduling the vaccination in the earlier part of an epidemic season in our institute would be justified in future programmes.

The low uptake of vaccination among our study population is not a novel finding and has been shown in other reports. It was < 20% in an underprivileged community in the United States of America (18). Uptake of influenza vaccination ranging from 6% to 45% has been reported among the global adult population at low risk (19). This low uptake is of concern, and aggressive efforts are required to identify the responsible factors to improve vaccination rates. The clinical outcomes used to determine the impact of vaccination in protecting humans against ILI is a unique feature of this study. These clinical parameters can be applied to most developing countries with limited laboratories resources for confirming the diagnosis of influenza. The low uptake of vaccine among health staff has also been reported in other Arab populations (20). The impact of vaccination in reducing infectious diseases and their severity is not new and our study confirmed this universal observation. There are many published reports that favour vaccination to protect populations against severe complications of influenza and other infectious diseases (21).

The benefits of influenza vaccine in reducing mortality, morbidity, hospitalization and disease burden and costs for countries are undisputed, and it has been shown to be beneficial for elderly people and children (22–24). In a study from Taiwan, mortality in people aged > 65 years was lower in the group who received influenza vaccine. This was after adjusting for confounding factors (22). In another study, the efficacy of influenza vaccine in children was reviewed based on a meta-analysis of effectiveness of influenza vaccine in reducing the incidence of ILI or laboratory-confirmed influenza. It was found that live influenza vaccines had higher efficacy in children (24). A German

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**Table 1: Profile of participants in influenza-like illness study**

| Age, yr | Vaccinated group (\( n = 300 \)) | Nonvaccinated group (\( n = 300 \)) | Validation |
|---------|----------------------------------|-------------------------------------|------------|
|         | Number | Percentage | Number | Percentage | Difference in mean 6.2 |
|         |        |           |        |           | 95% CI: 4.5–8.0, \( P < 0.001 \) |
| Gender  |        |           |        |           | OR = 1.9, 95% CI: 1.35–2.6, \( P < 0.001 \) |
| Male    | 95     | 31.7      | 140    | 46.7      | \( \chi^2 = 25 \) |
| Female  | 205    | 68.3      | 160    | 53.3      | \( df = 8 \) |
| Systemic comorbidity |        |           |        |           | \( P < 0.001 \) |
| None    | 236    | 78.7      | 274    | 91.3      | \( \chi^2 = 25 \) |
| Cardiac | 0      | 0.0       | 3      | 1.0       | \( df = 8 \) |
| Pulmonary | 23   | 7.7       | 13     | 4.3       | \( P < 0.001 \) |
| Vascular | 3     | 1.0       | 2      | 0.7       | \( \chi^2 = 25 \) |
| Endocrine | 2     | 0.7       | 1      | 0.3       | \( df = 8 \) |
| Combination | 31   | 10.3      | 7      | 2.3       | \( P < 0.001 \) |
|          | 5      | 1.7       | 0      | 0.0       | \( \chi^2 = 25 \) |

CI = confidence interval; df = degrees of freedom; OR = odds ratio; SD = standard deviation.
study reported that prior influenza vaccination was associated with less severe clinical course and improved overall long-term survival in patients with community acquired pneumonia during influenza seasons. (25). A surveillance data review confirmed the health benefits of vaccination in preventing influenza, related clinical visits and hospitalization (26). In European countries, gaps between vaccination coverage and recommendations resulted in higher influenza-related morbidity (27). Our findings are comparable with these studies; although the target population and methods used varied, the findings similarly suggest a gap between vaccination rates and public health recommendations.

In the current study, the health staff in the vaccinated group were older than in the unvaccinated group. Knowledge of the higher risk of complications of influenza in old age with greater systemic comorbidity among health staff could also occur in older individuals. The presence of comorbidity in a higher proportion of participants among the vaccinated group compared to

### Table 2 ILI and its determinants among health staff of an eye hospital in Saudi Arabia

|                      | ILI present (n = 79) | ILI not present (n = 521) | Validation          |
|----------------------|----------------------|---------------------------|---------------------|
| **Age, yr**          |                      |                           |                     |
| Mean                 | 30.4                 | 35.8                      | Difference in mean = 5.4 |
| SD                   | 10.7                 | 11.4                      | (95% CI: 2.7–8.0) P < 0.001 |
| **Vaccination status** |                      |                           |                     |
| Yes                  | 28                   | 272                       | RR = 0.7 (95% CI: 0.5–0.9) P = 0.005 |
| No                   | 51                   | 249                       | RR = 1.1 (95% CI: 0.8–1.5) P = 0.5 |
| **Gender**           |                      |                           |                     |
| Male                 | 34                   | 201                       | RR = 0.96 (95% CI: 0.86–1.1) P = 0.6 |
| Female               | 45                   | 320                       |                     |
| **Comorbidity**      |                      |                           |                     |
| Present              | 63                   | 446                       |                     |
| Absent               | 16                   | 95                        |                     |
| **Type of principal comorbidity** |              |                           |                     |
| None                 | 63                   | 446                       | \( \chi^2 = 0.02 \) |
| Cardiac              | 1                    | 3                         | df = 5              |
| Pulmonary            | 11                   | 28                        | \( P = 0.9 \)       |
| Neuromuscular        | 0                    | 6                         |                     |
| Vascular             | 1                    | 2                         |                     |
| Endocrine            | 3                    | 35                        |                     |

CI = confidence interval; df = degrees of freedom; ILI = influenza-like illness; OR = odds ratio; RR = relative risk; SD = standard deviation.

### Table 3 Comparison of impact of influenza vaccine reported in different studies

| Study no. | Authors          | Location       | Sample                        | Main findings                                                                 | Refs |
|-----------|------------------|----------------|-------------------------------|-------------------------------------------------------------------------------|------|
| 1         | Wang et al.      | Taiwan         | 35 637 (age > 65 yr)          | Influenza vaccination reduces risk of major cause-specific mortality in elderly population. | 22   |
| 2         | Groenwold et al. | Netherlands    | 50 906 periods of observation | Influenza vaccination reduced mortality risk in 65 years and older in epidemic period compared to summer in Netherlands | 23   |
| 3         | Rhorer et al.    | USA            | 27 000 children               | Live attenuated influenza vaccine resulted in 46% fewer cases of influenza illness in children | 24   |
| 4         | Tessmer          | Germany        | 2368 patients                | Prior influenza vaccination was associated with less severe clinical course and improved survival in patients with community-acquired pneumonia in influenza seasons. | 25   |
| 5         | Kostova et al.   | USA            | Influenza illnesses in 6 yr   | Influenza vaccination programs in the US averted cases, clinic visits and hospitalizations. | 26   |
| 6         | Ryan et al.      | 25 EU countries| Population at risk of 25 EU countries | Low influenza vaccination coverage in 25 European countries increased morbidity, hospitalizations and mortality associated with influenza-related complications. | 27   |
| 7         | Bresee et al.    | USA            | Data of FluSurv-NET           | Influenza vaccination prevented 6.6 million influenza illnesses and 3.2 million medically attended illnesses in 2012–2013 influenza season | 32   |
| 8         | Reed et al.      | USA            | Laboratory-confirmed ILI FluSurv-NET | Influenza vaccination prevented approximately 7.2 million illnesses, 3.1 million medically attended illnesses, and 90 000 hospitalizations associated with influenza in 2013–2014 | 33   |
| 9         | Present study    | Saudi Arabia   | 600 Saudi patients attending clinic | Influenza vaccinated group had reduced the number of episodes and the severity of ILI. | —    |
Impact du vaccin antigrippal sur la réduction de l'incidence et de la gravité du syndrome de type grippal

Résumé

Contexte : La vaccination est utile pour se protéger contre la grippe saisonnière, mais son taux d’utilisation est faible. Démontrer l’effet protecteur du vaccin contre la grippe dans les populations arabes permettrait de mener des actions de sensibilisation.

Objectifs : Évaluer l’impact du vaccin sur la réduction de l’incidence et de la gravité du syndrome de type grippal (STG) parmi le personnel de santé d’un hôpital ophtalmologique de soins tertiaires en Arabie saoudite.

Méthodes : La présente étude de cohorte rétrospective a été menée en 2018-2019. Le personnel hospitalier a été divisé en groupes vaccinés et non vaccinés. Les épisodes de syndromes de type grippal et leur gravité ont été comparés entre les groupes avant et après la vaccination.

Résultats : Le taux d’utilisation du vaccin contre la grippe parmi les 1180 membres du personnel de santé était de 41 %. Les groupes vaccinés (n = 300) et non vaccinés (n = 300) comptaient respectivement 28 (9,3 %) et 51 (17 %) personnes atteintes de STG. Le groupe non vacciné présentait un taux de STG significativement plus...
**Conclusions:** The vaccine antigrrippal confere a protection importante and réduit l’incidence et la gravité des STG.

Cependant, il s’agit d’une étude rétrospective sur des données sanitaires ; par conséquent, l’association du vaccin au résultats devrait être considérée comme une preuve peu solide. La faible utilisation du vaccin contre la grippe par le personnel hospitalier et les personnes à leur charge est préoccupante et devrait être traitée par une sensibilisation et une éducation accrues. Ces données peuvent être utilisées pour améliorer la couverture vaccinale globale.

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