Seasonal Influenza Vaccination Effectiveness and Compliance among Hospital Health Care Workers

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ABSTRACT: **Background:** Recent studies show that vaccination of health care workers (HCW) might reduce influenza transmission and mortality among hospitalized patients. No studies have compared the incidence of laboratory-proven influenza in vaccinated versus unvaccinated hospital HCW.

Objectives: To evaluate the effectiveness of influenza vaccination among hospital HCW and to examine the attitudes of this population towards influenza vaccination.

Methods: We performed a prospective cohort study between 1 January and 30 April 2014 of 1641 HCW at our medical center; 733 were vaccinated and 908 were not. A random sample of 199 subjects was obtained: 97 vaccinated and 102 non-vaccinated. Participating individuals were contacted on a weekly basis during the flu season and were asked to report any respiratory or flu symptoms and, if positive, to undergo a polymerase chain reaction (PCR) test for influenza.

Results: In the general HCW population vaccination was more frequent among physicians (298/498, 58%) than among nurses (324/862, 38%) and among males than females. Flu symptoms were reported by 20 of 199 participants, 13 in the non-vaccinated group (12.7%) and 7 in the vaccinated group (7.2%). A positive PCR test for influenza A virus was present in 4 of 20 people tested (20%). All positive cases were from the non-vaccinated group ($P = 0.0953$).

Conclusions: Non-vaccinated HCW showed a higher, although not statistically significant, tendency for contracting laboratory-proven influenza than the vaccinated population. The main reasons for vaccination and non-vaccination were personal beliefs and habits. Education efforts are needed to improve compliance. Larger studies could further clarify this issue.

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KEY WORDS: influenza, influenza vaccination, health care workers (HCW), polymerase chain reaction (PCR), mandatory vaccination

Influenza is a common respiratory illness caused by influenza virus types A, B or C [1]. Influenza type A is considered the most severe type of influenza. H1N1, a type A virus, was the first influenza virus recovered (1933) and was responsible for the recent influenza pandemic. Type B causes a less severe illness and is more frequent in children. Type C influenza causes a flu-like disease and usually has an uncomplicated course [2].

The World Health Organization (WHO) recommends influenza vaccination in five target populations: children 6–59 months of age, persons with underlying chronic diseases, pregnant women, health care workers (HCW), and elderly people ≥ 65 years old [3]. The vaccine is about 60–75% effective in reducing influenza disease in those exposed to strains of virus that are included in the vaccine [4,5]. On the other hand, several studies have shown that seasonal vaccination compliance is low in different population groups [6], including HCW [7]. The foremost reason for the low vaccination rate among HCW is the belief that influenza vaccine is risky.

The main objective of influenza vaccination among HCW is to reduce the spread of infection from HCW to patients or colleagues. There is some evidence that vaccination of HCW decreases nosocomial influenza and mortality among patients receiving long-term care [8]. The other reason is to reduce absenteeism, a situation that would in itself threaten productivity and patient safety.

Despite studies showing that vaccination is effective among medical personnel and reduces influenza transmission and mortality among hospitalized patients, the evidence for drawing definitive conclusions is not unequivocal [9]. Therefore, the primary objective of the present study was to assess prospectively the effectiveness of the influenza vaccine. Secondary objectives were to examine the knowledge, attitude and compliance of HCW at our medical center toward influenza vaccination and to establish the reasons for acceptance or rejection of seasonal influenza vaccination.

SUBJECTS AND METHODS

This was a prospective cohort study performed during four consecutive months, January to April 2014, at Emek Medical Center, in Afula, Israel. The study received institutional review board approval prior to recruitment. Emek Medical Center is the main reference center for the Galilee area and the northeast of Israel, and encompasses ~500,000 habitants. The hospital had about 500 beds and 2094 workers when the study was conducted, including 1641 HCW.

A vaccination campaign is conducted at our medical center annually during the autumn and winter months, September to December. The influenza vaccine is offered

free of charge and is strongly recommended, but vaccination is not mandatory.

STUDY POPULATION

A random sample of 199 workers (97 vaccinated and 102 non-vaccinated) was obtained from the total vaccinated and non-vaccinated HCW cohort. After signing an informed consent form, each participant completed a questionnaire on their knowledge and feelings regarding influenza vaccine. This was followed by a weekly telephone call or email asking about their medical condition and the appearance of new signs or symptoms suggestive of upper respiratory infection or flu-like symptoms.

Clinical criteria for further evaluation to rule out the presence of influenza included: fever > 38ºC and any of the following symptoms: muscle ache, sore throat, cough, rhinorrhea, or dyspnea. Subjects with one or more of these complaints were asked to report to the trial personnel and to undergo a polymerase chain reaction (PCR) test for influenza in order to confirm or rule out the presence of disease.

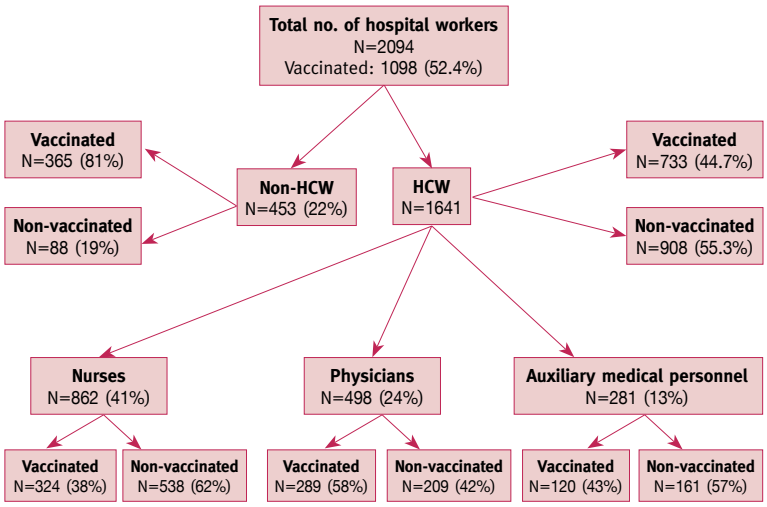
PCR TEST

PCR test was performed in subjects with at least one of the symptoms previously reported, up to 3 days after their appearance. Specimens for PCR test were obtained by swabbing the posterior nasopharynx.

VIRUS DETECTION BY PCR

Nucleic acid extraction was performed with a QiaAMP mini-iElute virus spin kit (QIAGEN, Hilden, Germany) according to the manufacturer's instruction. A total of 200 µl of virus transport medium was extracted into 150 µl of elution solution. Eluted DNA was tested using a multiplex quantitative real-time reverse transcription-PCR (RT-PCR) for respiratory sincytial virus (RSV), influenza A (FLU-A), H1N1, influenza B (FLU-B), and human metapneumovirus (hMPV). Amplification was carried out in a final volume of 20 µl with an RNA AgPath-ID one-step quantitative real-time RT-PCR system (Rotor-Gene Q, QIAGEN, Hilden, Germany) with 5 µl of nucleic acid.

Figure 1. Vaccination rate at Emek Medical Center, 2013–2014



QUESTIONNAIRE

A structured self-administered questionnaire was designed at the beginning of the trial to assess HCW professional characteristics, including gender, age, marital status, occupation, and other questions regarding their attitude towards seasonal vaccination.

STATISTICAL ANALYSIS

Categorical variables were presented by frequencies and percentages. Continuous variables were presented by standard distribution measures (mean, standard deviation, median). The association between influenza immunization and the categorical variables was tested either by chi-square test or Fisher's exact test. The association between influenza immunization and the continuous variables was tested either by *t*-test or the Wilcoxon two-sample test. Odds ratios and their 95% confidence intervals were also presented. Statistical significance was determined when P was < 0.05. Statistical analysis was performed with SAS 9.2 software.

RESULTS

At our hospital, 733 (44.7%) from a total of 1641 HCW were vaccinated. The relative proportion of immunization according to HCW occupation can be seen in Figure 1. Surprisingly, 80.6% of non-HCW underwent vaccination. Among the HCW, the vaccination rate was much higher among physicians than nurses: 289/498 (58%) vs. 324/862 (38%) respectively (P < 0.0001) [Figure 1]. The odds for vaccination were much higher in physicians: 2.3 times higher than in nurses (95% confidence interval 1.83–2.88). Similarly, the odds of vaccination were much higher in physicians than the rest of the population: 1.86 (95%CI 1.38–2.49) (P < 0001).

From a total of 1641 HCW, 199 were randomly selected and enrolled to this study, 97 in the vaccinated group and 102 in the non-vaccinated group. Demographic and clinical variables are presented in Table 1. Vaccinated HCW were older than subjects in the non-vaccinated group: 43.15 vs. 39.32 years, respectively (P = 0.0234). In terms of gender, the study included 78 males and 121 females. In the male population, 45/78 (58%) were vaccinated compared to 52/121 females (43%) (P = 0.0426) [Table 1].

In the vaccinated group, 48 (49.4%) were physicians, 33 (34%) were nurses and 16 (16.5) were auxiliary medical personnel [Table 1]. Of 78 physicians participating in the study, 48 (61.54%) received the vaccine; the respective number of nurses was 33/87 (37.93%) (P = 0.0099).

With regard to ethnicity, Ashkenazi Jews were vaccinated more frequently than Sephardi Jews and Arabs: 52/86 (60.5%), 12/29 (41.38%) and 27/68 (39.7%), respectively [Table 1].

Health workers with chronic diseases underwent vaccination more frequently than the same population without those diseases (67.7% vs. 32.3%, $P = 0.0213$). Among health workers with diabetes mellitus, 8/9 (88.8%) received the vaccine ($P = 0.0164$) [Table 1]. Regarding other associated medical disorders, no differences between the vaccinated and non-vaccinated population were observed. An interesting finding was that HCW taking statins were vaccinated much more frequently than those not on this treatment [Table 1].

People who underwent regular vaccination in the previous 5 years had a higher rate of vaccination in the present year (89.7%). The main reason for vaccination was working in a hospital and the likelihood of acquiring influenza (81.44%). Others stated that vaccination was an annual habit (64.95%). Marital status combined with the presence of young children at home, or advanced age, was a significant reason for vaccination [Table 2A]. In the non-vaccinated group there was no overriding reason for not getting the vaccine [Table 2B].

Influenza or influenza-like episodes were reported by 20 of the participants: 13 in the non-vaccinated group and 7 in the vaccinated group. All of them had fever, 17 had sore throat, and some had muscle pain, cough or other flu-like symptoms.

PCR TEST RESULTS

In the group of 20 participants with symptoms, 7 were vaccinated and 13 were not. A positive PCR test was found in 4 of the 20 people tested (20%). All four health workers with a positive PCR for influenza were from the non-vaccinated group ($P = 0.0953$).

Table 1. Demographic and clinical variables

Variable	Vaccinated N=97 (%)	Non-vaccinated N=102 (%)	*P* value
Age (years)	43.15 ± 12.06 [42]	39.32 ± 10.85 [35]	0.0234
Gender: Males	45 (46.39)	33 (32.35)	0.0426
No. of children	2.15 ± 1.42 [2]	2.13 ± 1.46 [2]	0.7617
BMI (kg/m²)	25.57 ± 3.6 [25.2]	25.21 ± 4.44 [24.5]	0.2557
Occupation			
Physician	48 (49.48)	30 (29.41)	0.0099
Nurse	33 (34.02)	54 (52.94)	
Other medical staff	16 (16.49)	18 (17.65)	
Ethnicity			
Jews (Ashkenazi)	52 (53.61)	34 (33.33)	0.0386
Jews (Sephardi)	12 (12.37)	17 (16.67)	
Arabs	27 (27.84)	41 (40.20)	
Other	6 (6.19)	10 (9.80)	
Background disease			
Medical history	21 (21.65)	10 (9.8)	0.0213
Diabetes	8 (8.25)	1 (0.98)	0.0164
Hypertension	11 (11.34)	6 (5.88)	0.1686
Asthma	3 (3.09)	0 (0)	0.114
Coronary heart disease	3 (3.09)	2 (1.96)	0.6766
Chronic kidney disease	1 (1.03)	0 (0)	0.4874
Malignancy	1 (1.03)	0 (0)	0.4874
Gastrointestinal/Hepatic diseases	1 (1.03)	2 (1.96)	1
Medication			
Concomitant medications	17 (17.53)	10 (9.8)	0.1118
Aspirin	7 (7.22)	4 (3.92)	0.3093
Steroids	1 (1.03)	2 (1.96)	1
Immune suppressive agents	2 (2.06)	0 (0)	0.2363
Statins	8 (8.25)	1 (0.98)	0.0164

Continuous variables are presented with mean ± standard deviation (median)

DISCUSSION

INFLUENZA VACCINE EFFECTIVENESS

In the present clinical study we took advantage of a real-life situation at our hospital, where a large population at risk did or did not receive the vaccine without an external intervention. Previous studies tried to define the effectiveness of vaccination on influenza prevention; some yielded positive results while others were inconclusive. In a retrospective study on the influenza epidemic of 1989–90, Fleming et al. [5] showed that recent immunization had a 75% protective effect against death. Similar results were found in a meta-analysis study from 1995 [10].

A clinical report found that in elderly individuals living in long-term care facilities, but not in the community, the efficacy of influenza vaccination was 23% [11]. For people younger than 65 years, in contrast, the efficacy of the vaccine was 86% and vaccination reduced the number of physician visits but did not show overall economic benefits [2]. The evidence in favor of the effectiveness of influenza vaccine in other studies documented a moderate protection [4].

Although our study could not definitively demonstrate that vaccination prevents the development of influenza, we found that this viral disease occurred in 4/100 non-vaccinated HCW (4%) in contrast to 0/99 of the vaccinated population. In the symptomatic group in our study, 4/13 non-vaccinated subjects with symptoms (31%) had influenza. While this result was not statistically significant, it suggests a protective role for the vaccine.

COMPLIANCE WITH VACCINATION

Compliance with vaccination among hospital workers at our medical center was higher than previously reported around the world as well as in Israel. In our center 53% of general workers and 45% of HCW underwent vaccination [Table 1]. In contrast, compliance with immunization was only 11% in a survey conducted in three main hospitals in northern Israel 15 years ago [12]. Similarly, and more recently, a cross-sectional study of randomly selected Israeli adult subjects showed a low uptake of the A/H1N1 vaccine (17%). Reasons for non-compliance in the mentioned study included passivity, fear and distrust, and assessment of threat versus actual risk [13]. Comparable results were reported during the last H1N1 influenza pandemic in 2009 in the United States [6] and Europe [14]. Compliance with vaccination for general practitioners in the Netherlands increased significantly from 36% during the 2007/2008 season to 63% the next year for

Table 2A. Reason for vaccination, by age group, marital status and occupation

		Age group		Marital status		Occupation		
		24-40	41-66	Married	Unmarried	Physician	Nurse	Other
I tend to vaccinate yearly [a]	No	19 (44.19%)	15 (27.78%)	20 (27.03%)	14 (60.87%)	14 (29.17%)	14 (42.42%)	6 (37.5%)
	Yes	24 (55.81%)	39 (72.22%)	54 (72.97%)	9 (39.13%)	34 (70.83%)	19 (57.58%)	10 (62.5%)
I was not vaccinated last year and got sick	No	41 (97.62%)	50 (92.59%)	71 (97.26%)	20 (86.96%)	44 (93.62%)	31 (93.94%)	16 (100%)
	Yes	1 (2.38%)	4 (7.41%)	2 (2.74%)	3 (13.04%)	3 (6.38%)	2 (6.06%)	0 (0%)
Hospital is a contaminating environment	No	7 (16.28%)	11 (20.37%)	13 (17.57%)	5 (21.74%)	10 (20.83%)	6 (18.18%)	2 (12.5%)
	Yes	36 (83.72%)	43 (79.63%)	61 (82.43%)	18 (78.26%)	38 (79.17%)	27 (81.82%)	14 (87.5%)
I have young children at home [b]	No	22 (51.16%)	30 (55.56%)	33 (44.59%)	19 (82.61%)	24 (50%)	20 (60.61%)	8 (50%)
	Yes	21 (48.84%)	24 (44.44%)	41 (55.41%)	4 (17.39%)	24 (50%)	13 (39.39%)	8 (50%)
I am old [c]	No	38 (88.37%)	38 (70.37%)	55 (74.32%)	21 (91.3%)	35 (72.92%)	29 (87.88%)	12 (75%)
	Yes	5 (11.63%)	16 (29.63%)	19 (25.68%)	2 (8.7%)	13 (27.08%)	4 (12.12%)	4 (25%)
I feel more confident	No	28 (65.12%)	36 (66.67%)	48 (64.86%)	16 (69.57%)	31 (64.58%)	23 (69.7%)	10 (62.5%)
	Yes	15 (34.88%)	18 (33.33%)	26 (35.14%)	7 (30.43%)	17 (35.42%)	10 (30.3%)	6 (37.5%)

[a] A significant difference was found between married and unmarried HCW ($P = 0.003$). [b] A significant difference was found between married and unmarried HCW ($P = 0.0014$). [c] A significant difference was found between age groups ($P = 0.0325$)

Table 2B. Reasons for refusing vaccination, by ethnicity, and age group

		Age group		Marital status		Occupation		
		18-40	41-66	Married	Unmarried	Physician	Nurse	Other
Lack of time [d]	No	52 (77.61%)	28 (82.35%)	62 (77.5%)	18 (85.71%)	18 (60%)	46 (86.79%)	16 (88.89%)
	Yes	15 (22.39%)	6 (17.65%)	18 (22.5%)	3 (14.29%)	12 (40%)	7 (13.21%)	2 (11.11%)
I do not believe in vaccine efficacy	No	48 (71.64%)	23 (67.65%)	57 (71.25%)	14 (66.67%)	25 (83.33%)	37 (69.81%)	9 (50%)
	Yes	19 (28.36%)	11 (32.35%)	23 (28.75%)	7 (33.33%)	5 (16.67%)	16 (30.19%)	9 (50%)
Previous adverse reaction	No	52 (77.61%)	28 (82.35%)	60 (75%)	20 (95.24%)	26 (86.67%)	41 (77.36%)	13 (72.22%)
	Yes	15 (22.39%)	6 (17.65%)	20 (25%)	1 (4.76%)	4 (13.33%)	12 (22.64%)	5 (27.78%)
Illness in the past despite vaccination	No	48 (71.64%)	22 (68.75%)	52 (66.67%)	18 (85.71%)	23 (76.67%)	35 (67.31%)	12 (70.59%)
	Yes	19 (28.36%)	10 (31.25%)	26 (33.33%)	3 (14.29%)	7 (23.33%)	17 (32.69%)	5 (29.41%)
I am healthy [e]	No	51 (76.12%)	19 (55.88%)	61 (76.25%)	9 (42.86%)	24 (80%)	36 (67.92%)	10 (55.56%)
	Yes	16 (23.88%)	15 (44.12%)	19 (23.75%)	12 (57.14%)	6 (20%)	17 (32.08%)	8 (44.44%)

[d] A significant difference was found between physicians and nurses ($P = 0.0053$). [e] A significant difference was found between married and unmarried HCW ($P = 0.0031$)

seasonal influenza and to 85% for pandemic (A/H1N1) influenza, when the Dutch government financed the costs of the vaccine and issued new guidelines for immunization of general practitioners [15].

Among the reasons for the higher compliance with vaccination at our hospital in the 2013–2014 season were higher awareness and the accessibility of influenza immunization. Compliance with vaccination in our study was higher among physicians than among nurses or other clinical personnel. This was also found in other studies [16]. It is possible that the distinctive roles of different HCW influence their knowledge and beliefs regarding vaccination. As for gender and compliance, the present study showed that males underwent vaccination more frequently than females. The same tendency has been described in other countries. Concerns about A/H1N1 vaccine efficacy and safety were more likely expressed by females [17]. Klein and Pekosz [18] argued recently that females develop higher antibody responses, increased inflammatory responses and adverse biological reactions to vaccines as compared to males.

The current study showed differences between the three ethnic groups. Ashkenazi Jews (i.e., of Western origin) were vaccinated more frequently than Sephardi Jews (Middle Eastern or

North African origin), or Arabs. A previous study from Israel demonstrated that the compliance with vaccination was much higher among Jews (19.1%) than among Arabs (6.1%) [13].

Socioeconomic factors play a role in the rate of vaccination. In Israel, being a post-1990 immigrant from the former Soviet Union, living in a densely populated apartment, and being unmarried are important factors in predicting the decision not to be vaccinated. In contrast, chronic illness, previous hospitalizations, older age, and kibbutz membership positively affected the decision to get vaccinated [19]. Similarly, previous studies showed that in the United States, people with different racial and ethnic origin also have different levels of education, marital status, English-language proficiency, insurance status, and a better or worse access to care [20].

Regarding the presence of chronic diseases, our clinical study showed that vaccination was significantly more frequent in individuals with chronic diseases than in the healthy population. People with chronic diseases are at higher risk for more severe disease and death [21].

Some authorities advocate that influenza vaccination should be obligatory and given in a mandatory mode, as conventionally done for other communicable diseases. Comparing mandatory vaccination to other methods believed to improve responsiveness to vaccination, Quan et al. [22] found a significant increase in the vaccination rate when mandatory programs were implemented. This issue has been the subject of recent editorials and perspectives in leading journals [7,22,23]. Caplan [7] concluded that HCW should be vaccinated against influenza and other communicable diseases as a condition of their employment.

Those opposed to coercive or mandatory vaccination claim that the vaccine is not efficient in a significant number of cases and constitutes an infringement of the autonomy of the worker [24]. Others, on the other hand, consider that the greatest benefits are derived from mandatory influenza immunization.

CONCLUSIONS

This study on influenza vaccine effectiveness is unique since the participating subjects were randomly selected after they did or did not receive the vaccine based on their own choice. Furthermore, they were prospectively followed and the diagnosis of influenza was based on clinical parameters confirmed by PCR, the best method available today for the diagnosis of this disease. It will be crucial in the future to evaluate and address the knowledge, concerns and misbeliefs of candidates to immunization in order to improve their compliance and increase the rate of vaccination.

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