

Prevalence and Determinants of Influenza-like illness among Pilgrims in Makkah, during Hajj Season 1439 H

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معدل انتشار متلازمة الاعراض التنفسية الشبيهة بالانفلونزا والعوامل المرتبطة بها بين الحجاج بمكة المكرمة خلال موسم الحج ١٤٣٩ هـ

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ملخص البحث (Abstract):

خلفية الدراسة: تعد الأمراض المعدية خلال موسم الحج قضية بالغة الأهمية بسبب الازدحام الشديد. وتمثل عدوى الجهاز التنفسي السبب الأكثر شيوعاً للتنويم بالمستشفيات. تعتبر متلازمة الأعراض المشابهة للانفلونزا تشخيصاً طبياً محتملاً لمرض الإنفلونزا أو غيرها من الأمراض التي تتشارك في مجموعة من الأعراض الشائعة.

أهداف الدراسة: التعرف على معدل انتشار متلازمة الاعراض التنفسية الشبيهة بالانفلونزا بين الحجاج بمكة المكرمة خلال موسم الحج ١٤٣٩ هـ، ومدى ارتباطها بمجموعة من عوامل الخطورة، ودور لقاح الأنفلونزا في الحماية.

منهجية الدراسة: هي دراسة مقطعية مسحية تم إجراؤها على عينة من الحجاج البالغين القادمين لمكة المكرمة موسم حج عام ١٤٣٩ هـ. نتائج الدراسة: تم إجراء ٥٩٩ مقابلة ناجحة، منها ٥٤١ للقادمين من خارج المملكة بنسبة ٩٠,٣%، كان متوسط عمر المشاركين 40.7±8.37 عاماً، وشكلت الإناث (٢٣١) ٣٨,٦٪. بلغ عدد من أفادوا بالإصابة بأعراض متلازمة الأعراض الشبيهة بالانفلونزا ١٠١ مصاباً بنسبة ١٧,٦%، وكانت نسبة الإصابة بين المطعمين بلقاح الأنفلونزا منهم حوالي ٣,٢٪ مقارنة بنسبة ٨٦% بين غير المطعمين، وتبين وجود ارتباطاً قوياً بين الإصابة وعدم تلقي لقاح الأنفلونزا (الاختطار النسبي (RR=9.04; 95% CI 6.89-11.89): وفرق اختطار (RD%=80.55; 95% CI 72.26-88.83). ووجد أن الذكور، والعمر أقل من ٣٠ عاماً، وذوي التعليم المنخفض، وكثرة أداء العمرة، والحجاج القادمين من خارج المملكة بصفة عامة، وحجاج جنوب آسيا وأفريقيا بصفة خاصة، وضعف المعرفة بمرض الإنفلونزا ولقاحه، عوامل اختطار أخرى مرتبطة بالإصابة بالأعراض الشبيهة بالإنفلونزا. وبين تحليل الانحدار اللوجستي متعدد المتغيرات وجود ارتباط مستقل بين الإصابة بمتلازمة الأعراض الشبيهة بالانفلونزا وبين الذكور من الحجاج، والأصغر سناً ممن تقل أعمارهم عن ٣٠ عاماً، والأقل تعليماً، والحجاج القادمين من خارج المملكة العربية السعودية.

الخلاصة: كانت نسبة المصابين بمتلازمة الأعراض الشبيهة بالإنفلونزا بين الحجاج غير المطعمين بلقاح الأنفلونزا عالية، وتبين أن تلقي اللقاح كان إجراءً وقائياً فعالاً خلال موسم الحج ١٤٣٩ هـ.

الكلمات الدالة: متلازمة الأعراض الشبيهة بالإنفلونزا، لقاح الأنفلونزا، الحج، عوامل الخطورة،

Background: Infectious diseases during the Hajj are critical issue due to the extreme congestion of people. Respiratory infections are the most common cause of hospital admissions. Influenza-like illness (ILI), also known as acute respiratory infection (ARI) and flu-like syndrome/symptoms, is a medical diagnosis of possible influenza or other illness causing a set of common symptoms.

Objectives: To assess prevalence and risk factors of Influenza-like illness among adult pilgrims in Makkah and the role of influenza vaccine in prevention.

Methods: This work was a cross-sectional survey carried out on a conventional sample of adult pilgrims during Hajj season 1439 H.

Results: Overall, 599 successful interviews were completed, of them 541 (90.3%) were coming from outside Saudi Arabia. The mean age (SD) of the participants was 40.7 (8.37). Females (231) constituted 38.6%. Overall, 101 (17.6%) of participants self-reported having Influenza-like illness. About 3.2% of the vaccinated and 86.0% of the unvaccinated reported having the Influenza like illness during their stay for Hajj 1439 H. A strong association between getting Influenza-like illness and not receiving influenza vaccine ((Relative risk (RR)=9.04; [95% CI: 6.89-11.89]; Risk Difference (RD%)=80.55; 95% CI: 72.26- 88.83)). Other factors associated with getting influenza-like illness were: younger age, male gender, low education, frequently done Umrah, pilgrims from outside KSA, pilgrims coming from south Asia and Africa and participants with poor knowledgeable about influenza disease and vaccine. Multivariate logistic regression analysis revealed that, male gender, younger pilgrims under 30 years, less educated (illiterates or primary school graduated), pilgrims coming from outside KSA, were independently associated with self-reporting sustaining Influenza-like illness among pilgrims.

Conclusion: Self-reported influenza-like illness was high among influenza unvaccinated. Influenza vaccine appears to be an effective preventive measure during 1439 Hajj season.

Key Words: Influenza-like illness (ILI); influenza Vaccine; Hajj; Risk Factors

Introduction

Infectious diseases during the Hajj are critical issue due to the extreme congestion of people. Crowding in tents, sharing domestic facilities, moving and staying in buses for long period, fatigue and the extreme climatic conditions are important factors for transmitting air- and droplet-borne infections. It has been estimated that 1 in 3 pilgrims experience respiratory symptoms. [1] Respiratory tract infections (RTIs) are the most common cause of hospital admissions. [2,3] Several transmissible pathogens are responsible for respiratory infections; viral infections been reported to cause the majority [4] and by far influenza viruses are the most common. [1,5] Influenza-like illness (ILI), also known as flu-like syndrome/symptoms, is a medical diagnosis of possible influenza or other illness causing a set of common symptoms. This clinical syndrome not easily distinguished influenza from other respiratory infections. WHO defined ILI as an acute respiratory infection with: measured fever of $\geq 38\text{ C}^\circ$; and cough; with onset within the last 10 days. [6,7] Preventive strategies, e.g., vaccination and respiratory hygiene, need to be enhanced, and antiviral influenza prophylaxis should be considered. The role of the influenza vaccine has been established in reducing mortality and morbidity of influenza. [8] Both inactivated and live attenuated vaccine prevented about 70% of cases of laboratory-confirmed symptomatic

influenza in healthy adults. [9] Studies showed a low rate of influenza among vaccinated pilgrims compared to an unvaccinated. [10-14]

Epidemiologic studies in Hajj seasons targeting respiratory infections are crucial for monitoring trends, evaluation of preventive measures and planning for next seasons.

Research aims

The present study aimed to:

- (1) Assess prevalence of Influenza-like illness among pilgrims;
- (2) Explore risk factors of getting infection and to
- (3) Evaluate the role of influenza vaccine in prevention.

Research methodology

Study design and participants

This work was a cross-sectional interview survey carried out on a conventional sample of adult pilgrims during Hajj season 1439 H. Pilgrims, during their stay in Makkah, after embarking on the religious pilgrimage during the period 1-20/12/1439 H., were asked to participate in the study. Those who agreed to participate were interviewed after explanation of the study objective and taking a verbal consent. Participants were recruited randomly from those who were available at hotel lobbies around and near Haram after prayers in the day time, with inclusion criteria of being adult man or woman from any nationality and present for Hajj.

Data collection tool

Upon inclusion, the participants were interviewed by two investigators (male and female) using a standardized questionnaire that collected information on demographics, influenza vaccination status, history of current or past attack with influenza-like illness during their stay in Makkah. Operationally, ILI was defined for participants as having been sick with fever and cough during Hajj period. Those who reported receiving the seasonal influenza vaccine before coming to Hajj by at least two weeks were considered as having valid vaccination. Statistical analysis Differences in the proportions were tested by Pearson's chi-square, or Fisher's exact tests when appropriate. All statistical tests were two-sided. Percentages and odds ratio (OR) with 95% confidence interval (CI) estimations and comparisons were carried out. Associations between variables, Relative risk (RR), Risk Difference (RD%) and its 95% CI were done. Univariate followed by multivariate logistic regression analysis were carried out to capture independent predictor factors associated with the outcome variable of interest. Statistical analysis was undertaken using Epi Info 7.1.3 (CDC, Atlanta, GA, USA). A p value of ≤ 0.05 was considered significant.

Ethical consideration

The study was done under collaborative umbrella of Saudi Community Board of Postgraduate studies, the Custodian of the Two Holy Mosques Institute for Hajj and Umrah Research, Umm Al-Qura University, and Directorate of Health Affairs, Ministry of Health, Makkah. The study was performed in accordance with the Declaration of Helsinki and its amendments. All participants provided oral informed consent.

Results and discussion

Results

Overall, 599 successful interviews were completed, of them 541 (90.3%) were coming from outside Saudi Arabia. The mean age (SD) of the participants in our sample was 40.7 (8.37) distributed as 6.5, 36.6, 29.2 and 14.7 percentages for the age groups <30, 30-39, 40-49 and ≥50 years respectively. Females (231) constituted 38.6%. More than sixty percent (61.4%) of the participants were university educated. Participants belongs to Arab countries, southeast Asia, south Asia, Africa and western countries were 10.5, 60.8, 9.9, 3.2 and 16.5% respectively. Thirty-six percent of the participants frequently attended Umrah during their stay in Makkah. Overall, 101 (17.6%) of participants self-reported having Influenza-like illness. About eighty percent (79.3%) of the participants reported a valid influenza vaccination before coming to Hajj (Table 1). Among adult pilgrims (Table 2), the highest prevalence of ILI was reported by younger age <30 years (40.1%) compared to older age groups (28.8%, 8.7% and 6.8% for age groups 30-39 years, 40-49 years and ≥50 years respectively); male gender (21.8%) compared to female (10.5%); lower education than secondary school (82.9%) compared to highly educated pilgrims (12.8% and 5.9% for secondary school and university educated respectively); those who frequently attended Umrah more than once (30.0%) compared to others (11.5%); pilgrims coming from south Asia (90.7%) and Africa (84.2%) compared to those who were coming from southeast Asia (4.9%), western countries (6.1%) and Arab countries (32.4%); pilgrims assessed as having low knowledge score about influenza disease and vaccine (14.6%) compared to those with better score (6.5%); and among influenza unvaccinated participants (86.0%) compared to vaccinated (3.2%) (Figure 1).

A strong association between sustaining Influenza-like illness and not receiving influenza vaccine ((Relative risk (RR)=9.04; [95% CI: 6.89-11.89]; Risk Difference (RD%)=80.55; 95% CI: 72.26- 88.83)) (not shown in tables). Applying adjusted multivariate logistic regression analysis, controlling for other predictor variables and potential confounders (Table 3), younger age <40 years (OR 2.7, 95% CI=1.14-6.23); male gender (OR 4.3, 95% CI=1.46-12.66), less than secondary education schooling (OR 4.1, 95% CI=1.35-12.50); domestic pilgrims (OR 6.2, 95% CI=1.38-27.69); and influenza unvaccinated (OR 165.9, 95% CI=53.13-518.01) were found to be independently associated with the participants' self-reported influenza like illness. The coefficient of determination R² of linear correlation that measured the strength and the direction of a linear relationship between participants' self-reported influenza-like illness and other predictor variables in the model was 0.70, which means that 70% of the total variation in the self-reported influenza like illness among participants can be explained by these predictor variables in the model (not shown in tables).

Discussion

Acute respiratory infections among pilgrims during Hajj season has a special concern, being the most prevalent infections, with higher rates of hospital admissions and mortalities. Influenza viral infections is by far is the most common and leading to a serious complication especially among vulnerable population like elderly and those with chronic medical conditions and immunocompromised. Influenza-like illness is a proxy for influenza prevalence. Among efforts of contentious monitoring of health condition of pilgrims as well as the effectiveness of the preventive measures in every Hajj season, this study aimed to assess prevalence of influenza-like illness among pilgrims, risk factors for getting infection and the role of influenza vaccine in protection.

An average attack rate 17.6% of self-reported influenza-like illness among study population in Hajj period was estimated and revealed wide variation among pilgrims. The attack rate was at lowest (4.9% and 6.1%) among southeast Asian and western countries respectively; higher than average among Arab countries pilgrims (32.4%) and the highest reported rates were among south Asian (90.7%) and African pilgrims (84.2%). This variation could be explained by disparities in socio-demographic, behavioral factors and influenza vaccine uptake. Engaging in recommended protective behaviors (hand hygiene, wearing a face mask, cough etiquette, social distancing, and contact avoidance) proved effective preventive measures at to reduce the risk of respiratory illness during Hajj. [15] The higher prevalence (84.2%) of ILI reported among African pilgrims in our study was consistent with the outcomes of similar studies like the study carried out by Annan et al. in 2013, who found that 77.6% of pilgrims returning to Ghana suffered from respiratory symptoms. [16] The comparatively lower rates (32.4%) of ILI among Arab pilgrims compared to Africans and south Asians pilgrims in the present study was comparable to others studies. Refaey et al. reported that 30% of Egyptian pilgrims returning from Hajj during 2012-2015 met the case definition for influenza-like illness (ILI). [17]

Our study revealed that the highest rates of ILI were independently associated with younger age, male gender, low education, being a domestic pilgrims and unvaccinated against influenza. This higher rate of ILI in youngest age were also reported in other community-based studies [11,18] This can be explained that youngsters are more active, so that have more contact with crowding and exposure to infections. They are additionally, relies on their natural immunity compared to older age groups who are more compliant to receive influenza vaccination and minimize their exposure to infections.

Male pilgrims in our study, reported a higher rate of ILI. Male pilgrims are more active than females and have the responsibility to care others, and they also tend to frequently perform Umrah than females. This by itself can explain the higher rates of ILI among males. Other studies indicate that in general males develop respiratory tract infections more frequently than females [19], explained by anatomic, lifestyle, behavioral between males and females. The role of sex hormones in the regulation of the immune system may also contribute to the reported sex differences in the incidence and severity of the various types of RTIs, especially in adolescents and adults. [19] Frequent performance of Umrah among pilgrims was an independent factors associated with ILI. This apparently, demands more movement in crowding allowing more chance of exposure to infections in general and RTIs in particular.

The highly educated participant pilgrims among the study participants, independently reported less ILI attacks. The highly educated persons of course, may have better knowledge, more compliant with respiratory etiquettes and practicing other recommended protective measures and tend to minimize their exposure to infections. Domestic pilgrims were independently reported more ILI compared to abroad pilgrims, which can be explained in part by exposure to a variants of imported infections not circulating in their local environment. Domestic pilgrims, like other pilgrims from middle east countries are less likely to use of face masks compared to Hajj pilgrims from other areas. [20] Use of surgical face mask proved effective in reducing ILI. In a randomized controlled trial to assess the effectiveness of facemasks use at Hajj, based on developing syndromic ILI, surgical mask proved effective in intervention group compared to control group incidence 31% versus 53%, $p= 0.04$) in a randomized controlled trial carried out by Barasheed et al. [21]. Our results, strongly suggest, that influenza vaccination gives marked protection against ILI. Not being vaccinated was the greatest independent predictor of reporting an ILI among participant's pilgrims. This result is

consistent with other studies. [10-14] In a systematic review with meta-analysis carried out by Alfelali, 2015, [22] used raw and published data from eleven Hajj seasons between 2005 and 2014, involving pilgrims from multiple countries. The data from both sources were synthesized to estimate the relative risk (RR) of acquisition of ILI in vaccinated versus unvaccinated pilgrims. The prevalence of ILI decreased among Hajj pilgrims as the vaccine coverage increased over the last decade (RR 0.2, $P < 0.01$), suggesting the beneficence of influenza vaccine for Hajj pilgrims. A study conducted on 32370 Iranian pilgrims to determine influenza vaccine's efficacy, the incidence of illness among influenza vaccinated was about 56% and compared to 72% among unvaccinated; the difference was significant ($P < 0.001$), with OR = 0.50 and $(1 - OD) = 0.50$; indicating 50% efficacy and was efficient in reducing the cases of ILI. [13]

Study Limitations

The findings in this report are subject to some limitations. First, all results are based upon self-report, and neither illness nor vaccination status were validated with medical records; not all ILI are influenza, and respondents might not have accurately reported which vaccine(s) they received. Second, selection bias might have resulted from the unbalanced sample participants according their country and demographic criteria compared to characteristics of the actual Hajj population.

Summary and conclusion

Self-reported influenza-like illness was high among influenza unvaccinated patients. The very low attack rate among influenza vaccinated pilgrims, indicates, first, a higher percentage of influenza virus infections among pilgrims compared to other infections causing influenza-like illness. Second, influenza vaccine strains appears to be comparable to the circulating strains among pilgrims in this season.

Recommendations

1. To ensure compliance, the recommended influenza vaccination for pilgrims should be a mandatory requirement.
2. Health education campaigns for prevention of respiratory infections targeting pilgrims emphasizing on the importance of utilization of surgical mask and adherence to respiratory hygiene.

Table 1: Participants' background information (n=599).

Characteristic	% (n) or Mean SD
Age in years	
- <30	6.5 (39)
- 30-39	36.6 (219)
- 40-49	29.2 (253)
- ≥50	14.7 (88)
Mean (SD)	40.7 (8.37)
Gender	
- Male	61.4 (368)
- Female	38.6 (231)
Level of Education	
- Less than higher school	14.5 (87)
- Higher school	22.2 (133)
- University	63.2 (378)
Omra/Hajj Frequency	
- 1-2	64.0 (383)

- 3+	36.0 (215)
Coming from	
- Domestic	9.7 (58)
- Abroad	90.3 (90.3)
Nationalities	
- Arab	10.5 (63)
- Southeast Asia	60.8 (364)
- South Asia	9.0 (54)
- Africa	3.2 (19)
- Western	16.5 (99)
Past History of Flu vaccination	
- Unvaccinated	8.9 (53)
- Vaccinated	91.1 (545)
Influenza vaccine validated	
-Unvaccinated	20.7 (142)
-Vaccinated	79.3 (475)
Attacked with Flu-Like Illness during Hajj (n=598)	
-Yes	17.6 (101)
-No	82.4 (472)
Knowledge score* about influenza disease and vaccine	
-Up to 5 point	41.4 (223)
-6-8	58.6 (315)
Mean Score (SD)	5.7 (1.29)

*Score with maximum 8 points.

Table 2: Factors associated with Flu-Like Illness among Pilgrims in Makkah, 1439 H. (n=599).

Characteristic	% (n) or Mean SD	Flu Like Illness		p-value
		Yes	No	
Age in years				
- <30	6.5 (39)	40.0 (14)	60.0 (21)	$\chi^2= 50.53, df=3$
- 30-39	36.6 (219)	28.8 (60)	71.2 (128)	
- ≥40-49	29.2 (253)	8.7 (21)	91.3 (221)	
- ≥50	14.7 (88)	6.8 (6)	93.2 (82)	
Gender				
- Male	61.4 (368)	21.8 (79)	78.2 (284)	$\chi^2=11.68, df=1$
- Female	38.6 (231)	10.5 (22)	89.5 (188)	
Level of Education				
- Less than secondary school	14.5 (87)	82.9 (63)	17.1 (13)	$\chi^2= 259.59, df=2$
- Secondary school	22.2 (133)	12.8 (16)	87.2 (109)	
- University/higher	63.2 (378)	5.9 (22)	94.1 (349)	
Omra Frequency				
- ≤1	64.0 (383)	11.5 (44)	88.5 (338)	$\chi^2= 29.81, df=1$
- ≥1	36.0 (215)	30.0 (57)	70.0 (133)	
Coming from				
				P=0.516

- Domestic	9.7 (58)	21.9 (7)	78.1 (25)	$\chi^2= 0.42, df=1$
- Abroad	90.3 (90.3)	17.4 (94)	82.6 (447)	
Nationalities				P<0.001
- Arab	10.5 (63)	32.4 (12)	67.6 (25)	$\chi^2= 311.85, df=4$
- Southeast Asia	60.8 (364)	4.9 (18)	95.1 (346)	
- South Asia	9.0 (54)	90.7 (49)	9.3 (5)	
- Africa	3.2 (19)	84.2 (16)	15.8 (3)	
- Western	16.5 (99)	6.1 (6)	93.9 (93)	
Influenza vaccine validated				
- Unvaccinated	20.7 (142)	86.0 (86)	14.0 (14)	$\chi^2= 390.05, df=1$
- Vaccinated	79.3 (475)	3.2 (15)	96.8 (458)	
Knowledge score* about influenza disease and vaccine				P=0.002
- <5 point	41.4 (223)	14.6 (30)	85.4 (175)	$\chi^2=9.20, df=1$
- 6-8 points	58.6 (315)	6.5 (20)	93.5 (287)	

*A score with maximum 8 points

Table 3: Adjusted Multivariate Logistic regression analyses for demographic and other potential factors associated flu-like illness among pilgrims during Hajj season, Makkah, 1439 H.

Term	aOR	95% CI	Coefficient	S. E.	Z-Statistic	P-Value
- Age (<40/1_40+)	2.7	1.14-6.23	0.981	0.43	2.269	0.023
- Gender (Male/Female)	4.3	1.46-12.66	1.459	0.55	2.651	0.008
- Education (< Secondary school/ Higher)	4.1	1.35-12.50	1.411	0.57	2.482	0.013
- Coming From (Domestic/Abroad)	6.2	1.38-27.69	1.822	0.77	2.383	0.017
- Influenza vaccination (No/Yes)	165.9	53.13-518.01	5.111	0.58	8.798	<0.001
CONSTANT	*		-6.394	1.05	-6.104	<0.001

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval;
Final -2*Log-Likelihood: 190.63; Likelihood Ratio: 342.66; Model P-Value: <0.001.

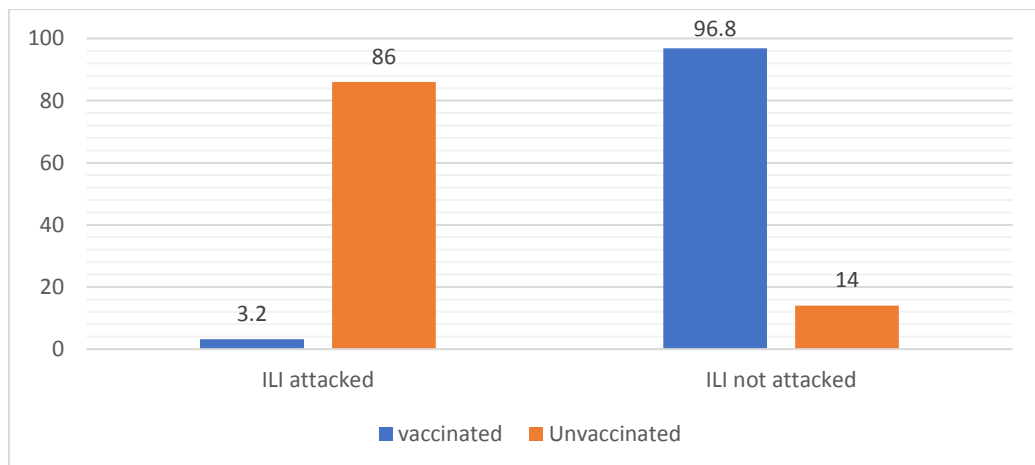


Figure 1: Attack rate of Influenza-Like Illness (ILI) among influenza vaccinated and unvaccinated Pilgrims

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