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Short communication

Acute respiratory infections among returning Hajj pilgrims—Jordan, 2014

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ABSTRACT

Background: The emergence of Middle East Respiratory Syndrome coronavirus (MERS-CoV) has prompted enhanced surveillance for respiratory infections among pilgrims returning from the Hajj, one of the largest annual mass gatherings in the world.
Objectives: To describe the epidemiology and etiologies of respiratory illnesses among pilgrims returning to Jordan after the 2014 Hajj.
Study design: Surveillance for respiratory illness among pilgrims returning to Jordan after the 2014 Hajj was conducted at sentinel health care facilities using epidemiologic surveys and molecular diagnostic testing of upper respiratory specimens for multiple respiratory pathogens, including MERS-CoV.
Results: Among the 125 subjects, 58% tested positive for at least one virus; 47% tested positive for rhino/enterovirus. No cases of MERS-CoV were detected.
Conclusions: The majority of pilgrims returning to Jordan from the 2014 Hajj with respiratory illness were determined to have a viral etiology, but none were due to MERS-CoV. A greater understanding of the epidemiology of acute respiratory infections among returning travelers to other countries after Hajj should help optimize surveillance systems and inform public health response practices.
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1. Background

Each year, 2–3 million pilgrims from over 180 countries travel to the Hajj in the Kingdom of Saudi Arabia (KSA), where crowded conditions pose potential risks for transmission of respiratory tract infections, the most common infections acquired by Hajj pilgrims [1–3]. The emergence of Middle East Respiratory Syndrome coronavirus (MERS-CoV) prompted additional travel guidance and enhanced surveillance following Hajj, including in Jordan, which has reported cases of MERS-CoV and shares its eastern and southern borders with KSA [1,4]. Based upon the number of Hajj visas issued, approximately 5600 pilgrims from Jordan traveled to KSA for the 2014 Hajj. In October 2014, Jordan established targeted surveillance of acute respiratory illnesses in Hajj pilgrims returning to Jordan.

2. Objectives

In this report, we present the results of a surveillance initiative to describe cases of acute respiratory illnesses in Hajj pilgrims returning to Jordan and detect etiologies of disease, which included

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Table 1
Characteristics of Hajj Pilgrims, Jordan, 2014.

Characteristic	All patients (n = 125)	
	n/total	%
Demographics		
Age groups (years)		
18–64	88/118	75
65+	30/118	25
Sex		
Male	76/123	62
Female	47/123	38
Clinical characteristics		
Symptoms		
Fever	51/125	41
Cough	95/125	76
Sore throat	62/125	50
Nasal discharge	46/125	37
Difficulty breathing	20/125	16
Comorbid conditions		
Diabetes	17/125	14
Hypertension	28/125	22
Heart disease	10/125	8
Kidney disease	1/125	1
Cancer	1/125	1
Bronchial asthma	2/125	2
Current smoker	24/107	22
Currently pregnant	3/42	7
Travel history		
Exposures		
Contact with sick person during Hajj	31/119	26
Contact with animal during Hajj	3/115	3
Visited market	20/22	91
Visited slaughterhouse	2/22	9
Visited health care facility prior to enrollment	36/99	36
Visited Hospital	5/24	21
Visited Center	19/24	79
Healthcare facility in KSA	13/31	42
Healthcare facility in Jordan	18/31	58
Mode of transportation		
Bus	93/125	74
Car	15/125	12
Plane	17/125	14

testing for MERS-CoV and other pathogens known to cause acute respiratory illnesses.

3. Study design

During October 8–23, 2014, a two-week period immediately following the conclusion of Hajj, 12 hospitals and outpatient clinical sentinel surveillance sites in the south, north, and central regions of Jordan conducted surveillance for respiratory illness among returning pilgrims. Pilgrims returning to Jordan with symptoms of respiratory infection were instructed to present to sentinel health facilities via health information cards at points of reentry, and through posted notices and healthcare workers at the sentinel health facilities. Persons were considered for enrollment in surveillance if they (1) traveled to the 2014 Hajj, and (2) presented with respiratory illness. Institutional Review Board approval was obtained in Jordan for this public health response, and verbal consent was obtained prior to enrollment. Targeted demographic and clinical information were collected (listed in Table 1) by in-person interview using a brief, standardized questionnaire.

Nasopharyngeal and oropharyngeal (NP/OP) swabs were sought from all enrolled subjects using flocked swabs. Swab specimens were combined in 2–3 mL of viral transport media, stored at 4 °C, and transported to the Central Public Health Laboratory in Amman, Jordan, within 48 h of collection and divided into aliquots. Total nucleic acid extraction was performed on 140 μL of sample from one aliquot per subject using a QIAamp Viral RNA Mini Kit (QIAGEN), and then tested using Centers for Disease Control and Prevention (CDC) real-time reverse transcription PCR (rRT-PCR) assays for influenza A, B (procedures available upon request at https://www.cdc.gov/flu/clsis/), and MERS-CoV [5].

Table 2
Respiratory pathogens detected among Hajj Pilgrims, Jordan, 2014.

Respiratory pathogen	All patients (n = 125)	
	n/total	%
Virus		
MERS coronavirus	0/125	0
Human coronavirus 229E	8/125	6
Human coronavirus NL63	4/125	3
Human coronavirus OC43	4/125	3
Human coronavirus HKU1	0/125	0
Influenza A[a]	4/125	3
Influenza B	2/125	2
Influenza C	0/125	0
Respiratory syncytial virus	1/125	1
Parainfluenza virus 1[b]	1/125	1
Parainfluenza virus 2	0/125	0
Parainfluenza virus 3	2/125	2
Parainfluenza virus 4	0/125	0
Human metapneumovirus	0/125	0
Rhino/enterovirus	59/125	47
Parechovirus	0/125	0
Adenovirus	1/125	1
≥2 viruses[c]	13/125	10
Bacteria		
Bordetella pertussis	0/125	0
Chlamydophila pneumoniae	0/125	0
Mycoplasma pneumoniae	0/125	0
Legionella pneumophila	0/125	0

[a] All influenza A-positive specimens were subtype H3N2.
[b] One specimen tested positive for parainfluenza virus 1 by panviral PCR.
[c] Specimens testing positive for two viruses included those with co-detection of rhino/enterovirus with human coronavirus 229E (n = 3), NL63 (n = 2), or OC43 (n = 2), influenza A (n = 2), parainfluenza virus 3 (n = 2), or adenovirus (n = 1). In addition, one specimen tested positive for three viruses: rhino/enterovirus, human coronavirus 229E, and influenza B (n = 1).

Frozen specimen aliquots were sent to CDC in Atlanta, Georgia, USA, for additional testing of non-MERS-CoV respiratory pathogens (listed in Table 2). Total nucleic acids were extracted from 300 μL of each specimen aliquot using the NucliSENS easyMAG system (bioMerieux) and tested on a multi-pathogen TaqMan Array card (ThermoFischer Scientific) using CDC-developed singleplex rRT-PCR assays [6–8].

Influenza-positive samples were further confirmed and influenza A-positive samples were sub-typed as human seasonal A(H3) or A(H1)pdm09 using CDC influenza rRT-PCR assays (procedures available upon request at https://www.cdc.gov/flu/clsis/), while influenza-negative samples were additionally tested with broadly reactive panviral family/genus PCRs that were designed to amplify genomic sequences from both known and potentially novel members of the viral families/genera, including those known to be associated with respiratory diseases: Adenoviridae [9], Coronavirinae [10], Orthomyxoviridae [11], Paramyxovirinae [12], Parvovirinae (unpublished in-house PCR), Polyomaviridae [13], and Reoviridae (orthoreovirus) [14].

Differences among subjects were assessed for significance (α = 0.05) using χ^2, Fisher's exact, and Wilcoxon rank sum tests, where appropriate. All data were analyzed using SAS version 9.3 (SAS Institute, Cary, NC).

4. Results

Epidemiologic data and respiratory specimens were collected from 125 subjects (Table 1) with a median age of 51.5 years (range 25–86). Common underlying medical conditions reported included hypertension (22%), diabetes (14%), and heart disease (8%); 22% of those responding reported current smoking. Onset of symptoms

Table 3
Comparison of patient characteristics by rhino/enterovirus (RV/EV) detection ($n = 125$).

Characteristic	RV/EV-negative ($n = 66$) No. (%)	RV/EV-positive ($n = 59$) No. (%)	p value[a]
Demographics			
Age years, median[b] [range]	55 [32–77]	50 [25–86]	0.2865
Gender – male	35 (54)	41 (71)	0.0550
Symptoms			
Fever	26 (40)	25 (42)	0.7351
Cough	49 (74)	46 (78)	0.6265
Sore throat	33 (50)	29 (49)	0.9246
Nasal discharge	21 (32)	25 (42)	0.2219
Difficulty breathing	6 (9)	14 (24)	0.0258
Comorbid conditions			
Diabetes	7 (11)	10 (17)	0.3017
Hypertension	16 (24)	12 (20)	0.6013
Heart disease[c]	5 (8)	5 (8)	0.2523
Kidney disease[c]	0	1 (2)	0.4720
Cancer[c]	0	1 (2)	0.4720
Bronchial asthma[c]	1 (1)	1 (2)	0.5025
Current smoker[d]	9 (16)	15 (29)	0.1218
Currently pregnant[c]	1 (5)	2 (9)	0.9999

[a] χ^2 test p-value unless otherwise indicated.
[b] Wilcoxon rank sum test p-value.
[c] Fisher's exact test p-value.
[d] Current smoker vs. previous smoker or never smoked.

ranged from September 20 to October 20, occurring prior to departure to KSA in five subjects. Most participants (89%) reported at least one of the following symptoms captured by the questionnaire: cough, sore throat, fever, nasal discharge, or difficulty breathing. Of those subjects responding, 31 (26% of 119) reported a history of contact with an ill person during the Hajj, and 36 (36% of 99) reported visiting a healthcare facility prior to enrollment, including 13 who reported having visited a healthcare facility in KSA. NP/OP swabs were obtained from 99 (79%) subjects; 26 (21%) subjects refused NP swabs and provided only OP swab specimens.

Considering all specimen types, at least one virus was detected in 73 (58%) specimens, with 59 (47%) testing positive for rhino/enterovirus (Table 2). Rhino/enterovirus-positive subjects were more likely to present with difficulty breathing than subjects that tested negative for rhino/enterovirus (24% vs. 9%; $p = 0.0258$) (Table 3). Other viruses detected included common human coronavirus species ($n = 16$; 13%), influenza A ($n = 4$, all H3N2; 3%) or B ($n = 2$; 2%), parainfluenza viruses types 3 ($n = 2$; 2%) and 1 ($n = 1$; 1%), RSV ($n = 1$; 1%), and adenovirus ($n = 1$; 1%) (Table 2). MERS-CoV was not detected in any subject, and none of the bacterial pathogens tested (*Bordetella pertussis, Chlamydophila pneumoniae, Mycoplasma pneumoniae, Legionella pneumophila*) were detected. Viral co-detections were observed in 13 (10%) of participants, all of which were rhino/enterovirus-positive. Except for one specimen in which parainfluenza type 1 was identified, panviral family/genus PCR did not add additional clinically relevant results beyond what was already detected by multi-pathogen array cards. There were no significant differences in detection of any single pathogen between NP/OP and OP-only specimens (data not shown).

Among the 28 (22%) participants enrolled at hospitals, three were admitted, one requiring ICU admission. The subject that required ICU admission was positive for rhino/enterovirus and parainfluenza type 3; the other two admitted cases were rhino/enterovirus-positive and influenza A/H3N2-positive, respectively. No deaths were reported.

5. Discussion

Of the 125 pilgrims who presented for respiratory illness upon return to Jordan after attending the 2014 Hajj, 58% tested positive for a viral etiology, of which rhino/enterovirus was most common. Subjects tested included those who reported specific opportunities for exposures to viral illnesses during the Hajj, such as contact with other ill persons, and previous visits to healthcare facilities, including those in KSA. Transmission of MERS has been shown to be associated with healthcare facilities [15], yet despite this potential increased exposure risk, no subjects tested positive for MERS-CoV.

To date, MERS-CoV infection has not been detected among Hajj pilgrims [3,16–20]. In previous studies, the range of rhinovirus positivity among individuals returning from the Hajj with respiratory symptoms has been 5.9–48.8%; our investigation detected rhino/enterovirus positivity at the higher end of this range (47%) [3,17,19,20]. Although the contribution of rhino/enteroviruses to clinical illness may be difficult to ascertain due to the lack of asymptomatic controls, among our subjects, rhino/enterovirus-positive patients were more likely to have difficulty breathing. Less commonly, other respiratory viruses were detected among these individuals, which could reflect seasonality of these viruses during the time of the Hajj or closeness among individuals from other countries where these viruses were circulating.

Our surveillance collected only limited clinical information regarding course of illness and outcomes, and the cross-sectional nature of the study limited our ability to confirm timing of acquisition of infection. However, given that symptomatic pilgrims presented in the two-week surveillance window immediately following Hajj suggests that the large majority of infections would have been acquired during the Hajj pilgrimage. Our surveillance employed geographically diverse sentinel sites and comprehensive targeted health messaging, but it is possible that symptomatic cases were incompletely captured, particularly in pilgrims with milder illness who may have been less likely to present to medical care after their return. Finally, although a minority of subjects refused NP swabs, lower rates of pathogen detection were not observed in these subjects. Despite these limitations, our findings are consistent with previous surveillance studies which suggest they are representative of the epidemiology of post-Hajj respiratory infections.

Understanding the epidemiology and clinical features of acute respiratory infections among returning travelers to other countries after Hajj is important for designing optimal surveillance systems to detect MERS-CoV. Surveillance of returning travelers at risk for MERS-CoV infection should not only help further such understanding, but would also help optimize public health response practices.

Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

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Competing interests

The authors declare no conflicts of interest.

Ethical approval

Institutional Review Board approval was obtained in Jordan for this public health response.

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