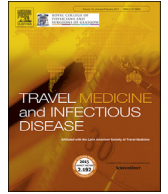




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## Original article

# Influenza not MERS CoV among returning Hajj and Umrah pilgrims with respiratory illness, Kashmir, north India, 2014–15



Parvaiz A. Koul<sup>a, \*</sup>, Hyder Mir<sup>a</sup>, Siddhartha Saha<sup>b</sup>, Mandeep S. Chadha<sup>c</sup>, Varsha Potdar<sup>c</sup>, Marc-Alain Widdowson<sup>d</sup>, Renu B. Lal<sup>b</sup>, Anand Krishnan<sup>e</sup>

<sup>a</sup> Department of Internal & Pulmonary Medicine, Sheri Kashmir Institute of Medical Sciences (SKIMS), Srinagar, J&K, India

<sup>b</sup> Influenza Division, US Centers for Disease Control & Prevention (CDC), India Office, New Delhi, India

<sup>c</sup> National Institute of Virology, Pune, India

<sup>d</sup> Influenza Division, US Centers for Disease Control & Prevention (CDC), Atlanta, GA, USA

<sup>e</sup> Center for Community Medicine, All India Institute of Medical Sciences, (AIIMS), New Delhi, India

## ARTICLE INFO

## Article history:

Received 22 June 2016

Received in revised form

3 December 2016

Accepted 3 December 2016

Available online 6 December 2016

## Keywords:

Middle East Respiratory Virus syndrome

Pilgrimage

Hajj

Acute respiratory infection

## ABSTRACT

**Background:** The increasing reports of Middle East Respiratory Syndrome (MERS) caused by MERS coronavirus (MERS-CoV) from many countries emphasize its importance for international travel. Muslim pilgrimages of Hajj and Umrah involve mass gatherings of international travellers. We set out to assess the presence of influenza and MERS-CoV in Hajj/Umrah returnees with acute respiratory infection.

**Methods:** Disembarking passengers (n = 8753) from Saudi Arabia (October 2014 to April 2015) were interviewed for the presence of respiratory symptoms; 977 (11%) reported symptoms and 300 (age 26–90, median 60 years; 140 male) consented to participate in the study. After recording clinical and demographic data, twin swabs (nasopharyngeal and throat) were collected from each participant, pooled in viral transport media and tested by real-time RT PCR for MERS-CoV and influenza A and B viruses and their subtypes.

**Results:** The participants had symptoms of 1–15 days (median 5d); cough (90%) and nasal discharge (86%) being the commonest. None of the 300 participants tested positive for MERS-CoV; however, 33 (11%) tested positive for influenza viruses (A/H3N2 = 13, A/H1N1pdm09 = 9 and B/Yamagata = 11). Eighteen patients received oseltamivir. No hospitalizations were needed and all had uneventful recovery.

**Conclusion:** Despite a high prevalence of acute respiratory symptoms, MERS CoV was not seen in returning pilgrims from Hajj and Umrah. However detection of flu emphasises preventive strategies like vaccination.

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## 1. Introduction

Middle East Respiratory Syndrome (MERS) is a highly lethal viral respiratory illness that is caused by a novel, single-stranded beta-coronavirus (MERS-CoV), first reported in Saudi Arabia during 2012 in a patient with acute pneumonia and renal failure [1]. As of April 2016, the WHO reported 1728 laboratory-confirmed cases of MERS-CoV, and at least 624 deaths [2]. All known reported cases have been associated with nine affected countries in or near the Arabian Peninsula. Twenty-seven countries in Europe, USA, Africa and Asia

have also reported cases, among people who travelled from the Middle East or their contacts [2,3]; but none have been reported from India. In 2015, the largest outbreak of MERS-CoV outside of the Middle East (186 infections and 36 deaths) was reported in the Republic of Korea that was traced to a single person returning from Saudi Arabia [4].

Although the reservoir and method of transmission remain incompletely characterized, MERS-CoV appears to be transmitted through respiratory droplets and in all probability has zoonotic repositories in dromedary camels with possible origin in bats [1,3]. Human to human transmission requires close contact with infected persons [1,4]. Muslim pilgrimages of Hajj and Umrah, draw millions of people (>2.0 and > 5.0 million, respectively in 2014) to Mecca annually. Hajj is performed in the 12th month of the lunar calendar and Umrah throughout the year. A high risk of acquisition of

\* Corresponding author. Department of Internal & Pulmonary Medicine, Sheri Kashmir Institute of Medical Sciences, Soura, Srinagar, 190011, J&K, India.

E-mail address: [parvaizk@gmail.com](mailto:parvaizk@gmail.com) (P.A. Koul).

respiratory tract infections has been reported during these pilgrimages [5] which has implications of subsequent international transmission to other countries [6,7]. Kashmir valley in the northern Indian state of Jammu and Kashmir receives 6–7 thousand Hajj and 25–30 thousand Umrah returnees every year. We report our findings of screening the returning pilgrims with acute respiratory tract infection for MERS-CoV and influenza viruses.

## 2. Methods

We screened Hajj and Umrah returnees from October 2014 to April 2015 for MERS-CoV and influenza virus infections; during this period Hajj occurred from October 1–6, 2014. In-flight announcements for all airlines arriving from Mecca and landing at Srinagar airport were arranged for disembarking passengers, and advised pilgrims with current respiratory symptoms or fever to report to the medical team stationed in the arrival hall. Disembarking passengers were also questioned about the symptoms and enrolment in the study was offered to symptomatic passengers after their informed verbal consent. Data on demographics, symptoms, and history of prior influenza vaccination were recorded in a predefined case report form. Two swabs (nasopharyngeal and throat) were collected from each participant and pooled in viral transport media; and then transported to the laboratory in Sheri Kashmir Institute of Medical Sciences (SKIMS) within 3–4 h of collection. Samples were tested by real-time reverse transcriptase polymerase chain reaction (PCR) for MERS-CoV using a WHO recommended protocol (targeting region upstream of E protein gene (upE) of MERS-CoV [8]) and influenza viruses. Patients with positive results for influenza viruses were contacted for assessment for therapy by the medical clinic at SKIMS or by respective physicians and treated if indicated. Descriptive statistics was used to assess various prevalence rates. Comparison of proportions was performed by SPSS (Statistical Package for Social Sciences) Version 17 software, IBM Limited, USA. Values have been expressed as percentages and a *p*-value of <0.05 was considered significant. The study was approved by the Institute Ethics Committee of SKIMS.

## 3. Results

Of the 8753 pilgrims, 977 (11.2%) reported symptoms of fever and/or respiratory symptoms and 300 (31%) consented to participate in the study. Participants' median age was 60 years (range 26–90 years) and 140 (47%) were male. Participants had been in Saudi Arabia for 21–42 days (median 40 days) and reported symptoms of 1–15 days duration (median 5 days) (Table 1). Cough (89.7%) and nasal discharge (86.3%) were the most commonly reported symptoms. None of the 300 participants tested positive for

MERS-CoV; however, 33 (11%) participants aged 37–86 years tested positive for influenza viruses (A/H3N2 = 13), A/H1N1pdm09 = 9 and B/Yamagata = 11). Influenza positive cases had a significantly higher frequency of fever, rigors, and chills than influenza test-negatives (Table 1). All influenza positive cases were asked to follow-up at the study-hospital based-clinic and advised about infection control. Sixteen (48%) patients reported back to the study clinic and were prescribed oral oseltamivir. Seventeen (52%) patients who did not reach the hospital clinic were advised to seek medical help locally and the reports were conveyed to their physicians; two were prescribed oseltamivir. There is no state policy for use of influenza antivirals, however the common practice is to prescribe oseltamivir during an influenza season for suspected influenza cases who appear sick and febrile without waiting for laboratory confirmation. No hospitalizations were needed and all had uneventful recovery over a period of 2–5 days (median 5 d).

Of the 300 participants, 216 (72%) reported receiving inactivated influenza vaccine (comprising of A/California/7/2009 (H1N1) pdm09-like virus; A/Texas/50/2012 (H3N2)-like virus and B/Massachusetts/2/2012 (Yamagata)-like virus) approximately 2 weeks (median 16 days, range 14–21 days) prior to the pilgrimage. About 10% (*n* = 21) of these tested positive for influenza in comparison to 14.3% (*n* = 12) of those not vaccinated prior to the pilgrimage (*p* = 0.26). No differences in age, gender, onset or frequency of symptoms were seen between vaccinees who tested positive and those who tested negative for influenza. Some of the participants also gave a history of spontaneous recovery from their respiratory illness that they had developed while in Saudi Arabia. However there was no record of any laboratory confirmation for any bacterial or a viral pathogen having caused the illness.

## 4. Discussion

Peak travel periods to Saudi Arabia (e.g., Ramadan, Umrah, or the Hajj) are of concern for the spread of respiratory viruses, including influenza and MERS-CoV, and the Saudi Government recommends pre-travel influenza vaccination [9,10]. The normal influenza season in Kashmir occurs during January–April [11]; thus, even before Hajj, many of the pilgrims, especially the elderly are at high-risk for influenza illness and its complications. The Hajj in 2014 drew more than 2 million travelers at a time when Saudi Arabia's capital was battling a large hospital-linked MERS-CoV outbreak with smaller clusters recently detected elsewhere, including the holy city of Medina [2,3].

In the current study, vaccination against influenza had no significant effect on confirmed influenza. Additionally no differences in age, gender, onset or frequency of symptoms were seen between vaccinees who tested positive and those who tested negative for

**Table 1**  
Comparative symptoms in Influenza positive and influenza negative participants.

Symptoms & Signs	Influenza positive N = 33	Influenza negative N = 267	<i>p</i> -value
Fever	24 (72.7)	133 (49.8)	0.015
Chills and Rigors	18 (54.5)	96 (35.9)	0.04
Nasal discharge	30 (90.9)	229 (85.7)	0.41
Ear discharge	1 (3.0)	4 (1.5)	0.53
Cough	29 (87.8)	240 (89.8)	0.72
Sore throat	19 (57.5)	177 (66.2)	0.32
Breathlessness	11 (33.3)	69 (25.8)	0.36
Expectoration	10 (30.3)	65 (24.3)	0.45
Headache	19 (57.5)	137 (51.3)	0.50
Bodyache	20 (60.6)	145 (54.3)	0.49
Fatigue	16 (48.4)	132 (49.4)	0.91
Vomiting	2 (6.1)	10 (3.7)	0.50
Diarrhea	2 (6.1)	8 (3.0)	0.35
Seizures	1 (3.0)	2 (0.8)	0.24

influenza. Assuming self-report correctly characterized vaccination status, the occurrence of influenza cases among those vaccinated especially the elderly needs to be studied further.

Despite a high prevalence of acute respiratory illness (ARI) among returning pilgrims from Saudi Arabia, none of the 300 (one-sided 97.5% CI 1.2) study participants with ARI tested positive for MERS-CoV. Although we only screened one-third of ill travelers, our data is compatible with earlier reports in which no MERS-CoV cases were identified in Hajj returnees [12,13] in other countries outside of India. In another large study involving 5235 adult Hajj pilgrims from 22 countries, including 3 with reports of MERS Co–V and those with geographic proximity to Saudi Arabia, there was no evidence of MERS-CoV nasal carriage among Hajj pilgrims (3210 pre-Hajj, 2025 post-Hajj) which could supporting poor or moderate interhuman transmission, despite the pilgrims having stayed in close contact with persons with respiratory symptoms [14]. Our findings demonstrated the risk of influenza among travellers returning from such mass gatherings which therefore requires continued health awareness on vaccination and other preventive measures.

#### Disclaimer

The conclusions, findings, and opinions expressed by authors contributing to this journal do not necessarily reflect the official position of the U.S. Centers for Disease Control and Prevention.

#### Funding

This study was supported in part by cooperative agreements U01IP000206 from the Centers for Disease Control and Prevention, Atlanta, USA

#### Conflict of Interest statement

The authors declare no conflict of interest in connection with the manuscript.

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