



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

The spectrum of respiratory pathogens among returning Hajj pilgrims: myths and reality



Phillipe Gautret ^{a,*}, Samir Benkouiten ^b, Jaffar A. Al-Tawfiq ^{c,d}, Ziad A. Memish ^e

^a Aix Marseille Université, URMITE, UM63, CNRS 7278, IRD 198, Inserm 1095, 13005 Marseille, France

^b Institut Hospitalo-Universitaire Méditerranée Infection, Marseille, France

^c Johns Hopkins Aramco Healthcare, Dhahran, Kingdom of Saudi Arabia

^d Indiana University School of Medicine, Indianapolis, USA

^e Ministry of Health, Riyadh, College of Medicine, Al Faisal University, Kingdom of Saudi Arabia

ARTICLE INFO

Article history:

Received 29 November 2015

Received in revised form 23 January 2016

Accepted 25 January 2016

Corresponding Editor: Eskild Petersen, Aarhus, Denmark.

Keywords:

Surveillance

Hajj

Umrah

Coronavirus

Influenza

Rhinovirus

SUMMARY

Enhanced surveillance systems have been implemented recently in many countries in order to rapidly detect and investigate any possible cases of Middle East respiratory syndrome coronavirus (MERS-CoV) infection among travellers returning from the Middle East, including notably Hajj pilgrims. According to the available surveillance data, only a few sporadic travel-associated MERS-CoV cases have been reported outside the Arabian Peninsula so far, mainly in Europe, North Africa, and Asia. These have resulted in no cases, or limited numbers of secondary cases except in Korea. The vast majority of viral respiratory infections in pilgrims returning home have been due to seasonal influenza viruses, rhinoviruses, and other known coronaviruses distinct from the MERS coronavirus. Influenza vaccination should be a priority for all Hajj pilgrims, as recommended by experts.

© 2016 The Authors. Published by Elsevier Ltd on behalf of International Society for Infectious Diseases. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

The emergence of severe acute respiratory syndrome coronavirus (SARS-CoV) in 2003 in China,¹ the H1N1 influenza pandemic in 2009,² and the emergence of Middle East respiratory syndrome coronavirus (MERS-CoV) in the Kingdom of Saudi Arabia (KSA) in 2012³ has aroused widespread fear and concern for their potential threat to global health security.^{4,5} Elaborate surveillance and infection control measures were put in place during the 2009 Hajj. In the event, it was found that there were more cases of seasonal influenza reported than of H1N1.⁶

One thousand six hundred and twenty-four laboratory-confirmed cases of MERS-CoV, including 586 related deaths, had been reported to the World Health Organization as of January 23, 2016 (<http://www.who.int/emergencies/mers-cov/en/>). Millions of Muslims, from over 180 countries worldwide, make the annual pilgrimage to Mecca, Saudi Arabia. Due to the overcrowded conditions, there is the potential for increased person-to-person

spread of infectious diseases and a favourable transmission of respiratory tract infections.⁶ The occurrence of such events spreads fear of a massive outbreak among pilgrims that could spread to their countries of origin.⁷

This situation has prompted health authorities to establish enhanced surveillance systems in many countries in order to rapidly detect and investigate any possible cases of MERS-CoV infection among travellers returning from the Middle East. Fortunately, only a few sporadic travel-associated MERS-CoV cases have been reported outside the Arabian Peninsula, mainly in Europe, North Africa, and Asia.^{8,9} These have resulted in no cases, or some secondary cases, with the notable exception of the Republic of Korea. In the Republic of Korea, 185 cases were epidemiologically linked to a single index case who had visited several countries in the Middle East.¹⁰

A large-scale surveillance study has provided interesting insights into the epidemiology of respiratory tract infections in travellers returning from the Middle East, including Hajj and Umrah pilgrims. During September 2012 to October 2013, 77 travellers from the Middle East who met the possible case

* Corresponding author. Tel.: +33 (0)491 96 35 35/36; fax: +33 (0)491 96 89 38. E-mail address: philippe.gautret@club-internet.fr (P. Gautret).

definition for MERS were tested in England and two of them tested positive for MERS-CoV.¹¹ Also, 22 had positive results for alternative respiratory pathogens, including 10 (13%) cases of influenza A or B and four (5%) cases of rhinovirus.⁹ UK surveillance data focusing on the period of return of Hajj pilgrims during the years 2013–2015 (September–October) evidenced influenza infection in 46% and rhinovirus in 30% of 50 patients suspected of MERS (<https://www.gov.uk/government/publications/health-protection-report-volume-9-2015/hpr-volume-9-issue-36-news-9-october>). Of the first 14 patients returning from the Middle East who were hospitalized for respiratory symptoms and screened for MERS-CoV in Marseille, France in October 2013, nine (64%) were infected with influenza and all samples tested negative for MERS-CoV.¹² In another small survey conducted in 2014 in Austria and investigating seven Hajj pilgrims suspected of MERS, none had MERS-CoV, five had influenza, and two were infected by rhinovirus.¹³ A survey conducted among 177 travellers from the Middle East suspected of MERS on returning to Ontario, Canada in 2012–2014, showed that none tested positive for MERS-CoV, 41 (23%) were positive for influenza, and 35 (20%) for rhinovirus.¹⁴ Finally, in a survey conducted in 2013–2014 in California, USA among 52 patients suspected of MERS, none was positive for MERS, 17 (33%) were positive for influenza, and seven (13%) for rhinovirus.¹⁵ Other pathogens were isolated in smaller proportions, including parainfluenza viruses, human metapneumovirus, respiratory syncytial virus, enterovirus, adenovirus, non-MERS coronaviruses, *Chlamydia pneumoniae*, and *Legionella spp.*^{11–15}

Besides surveillance implemented in returned travellers suspected of MERS, several teams in Egypt, Iran, Saudi Arabia, France, and Ghana have conducted systematic PCR-based screening surveys among cohorts of returning Hajj pilgrims independently of their clinical status. MERS-CoV carriage was investigated in four studies and was not detected.^{12,16–18} Influenza carriage was investigated in six studies and its mean prevalence was 3% (range 1–8%);^{18–23} rhinovirus carriage was investigated in four studies and its mean prevalence was 13% (range 8–17%).^{18,21–23} Carriage of non-MERS coronavirus was investigated in two studies and the prevalence was found to be 1% and 21%, respectively.^{21,23} Finally, the carriage of *Streptococcus pneumoniae* was investigated in two studies, which reported prevalences of 20% (nasal carriage) and 62% (throat carriage).^{22,23} Other viruses were isolated in smaller proportions, including parainfluenza viruses, human metapneumovirus, respiratory syncytial virus, enterovirus, and adenovirus.^{18,21–23} Finally, two PCR-based studies were conducted among returning Iranian pilgrims suffering from upper respiratory tract infections and reported a prevalence of influenza of 10% and 12%, respectively.^{24,25}

Taken together, these results strongly suggest that Mecca may act as a global hub for respiratory pathogens through the Muslim pilgrimage and contribute to their globalization.²⁶

Obviously, the vast majority of viral respiratory infections in Hajj and Umrah pilgrims returning home are due to seasonal influenza viruses, rhinoviruses, and other known coronaviruses distinct from the MERS coronavirus. Bacteria like *S. pneumoniae* may also play a role, as well as *Haemophilus influenzae* and *Klebsiella pneumoniae*, for which a high rate of acquisition following participation in the Hajj has been observed in pilgrims before leaving Saudi Arabia.²⁶ Tuberculosis has also been reported among patients admitted to hospital during the Hajj;⁶ however, given the incubation time of the disease, it is challenging to identify such cases.

Clinicians should be aware that influenza is the most commonly identified pathogen in returning pilgrims with an acute respiratory tract infection. However, a microbial cause is not identified in a significant proportion of patients with a respiratory infection,

which makes the overall incidence of influenza very low. Empirical antiviral treatment for influenza on admission when indicated may be considered pending the results of laboratory investigations, although oseltamivir resistance among influenza strains has been reported. Influenza vaccination should be a priority for all Hajj pilgrims, as recommended by experts.^{27,28} However, since Hajj dates are now moving to the summer season, the lack of availability of the influenza vaccine in many countries during this period will hamper this strategy. Public health measures introduced by Saudi Arabia in 2015, banning the sacrifice of camels for Hajj and discouraging visits by pilgrims to camel barns during Hajj pilgrimage activities, are sensible precautionary measures that should be considered as part of pre-travel advice in the home countries of pilgrims.

Despite the paucity of actual cases of MERS in travellers returning from the Middle East and the virtual absence of Hajj-associated cases in this context, continuous surveillance should be implemented to ensure the timely detection of possible imported cases of MERS and their immediate isolation in order to avoid secondary cases. The recent experience in South Korea, with a single chain of transmission associated with healthcare facilities resulting in many cases, is a reminder that enhanced surveillance at ports of entry is critical. The few pilgrimage-associated cases of MERS in travellers reported so far were in Umrah pilgrims.⁷ An estimated eight million pilgrims perform the Umrah yearly.²⁹ The number of Umrah pilgrims is particularly high during the month of Ramadan, and that period could be considered the second mass gathering in Saudi Arabia, although of a lesser size compared to the Hajj. Studies on respiratory tract infections during Ramadan are scarce; thus continued surveillance of respiratory infections and of the spectrum of associated pathogens among pilgrims returning from the Umrah during Ramadan and from the subsequent Hajj is of critical importance.

Conflict of interest: No conflict of interest to declare.

References

- Lee N, Hui D, Wu A, Chan P, Cameron P, Joynt GM, et al. A major outbreak of severe acute respiratory syndrome in Hong Kong. *N Engl J Med* 2003;**348**: 1986–1994.
- Fraser C, Donnelly CA, Cauchemez S, Hanage WP, Van Kerkhove MD, Hollingsworth TD, et al. Pandemic potential of a strain of influenza A (H1N1): early findings. *Science* 2009;**324**:1557–61.
- Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus AD, Fouchier RA. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. *N Engl J Med* 2012;**367**:1814–20.
- Memish ZA, McNabb SJ, Mahoney F, Alrabiah F, Marano N, Ahmed QA, et al. Establishment of public health security in Saudi Arabia for the 2009 Hajj in response to pandemic influenza A H1N1. *Lancet* 2009;**374**:1786–91.
- Al-Tawfiq JA, Zumla A, Memish ZA. Travel implications of emerging coronaviruses: SARS and MERS-CoV. *Travel Med Infect Dis* 2014;**12**:422–8.
- Al-Tawfiq JA, Zumla A, Memish ZA. Respiratory tract infections during the annual Hajj: potential risks and mitigation strategies. *Curr Opin Pulm Med* 2013;**19**: 192–197.
- Sharif-Yakan A, Kanj SS. Emergence of MERS-CoV in the Middle East: origins, transmission, treatment, and perspectives. *PLoS Pathog* 2014;**10**:e1004457.
- Pavli A, Tsiodras S, Maltezos HC. Middle East respiratory syndrome coronavirus (MERS-CoV): prevention in travelers. *Travel Med Infect Dis* 2014;**12**: 602–608.
- Sridhar S, Brouqui P, Parola P, Gautret P. Imported cases of Middle East respiratory syndrome: an update. *Travel Med Infect Dis* 2015;**13**:106–9.
- Korea Centers for Disease Control and Prevention. Middle East respiratory syndrome coronavirus outbreak in the Republic of Korea, 2015. *Osong Public Health Res Perspect* 2015;**6**:269–78.
- Thomas HL, Zhao H, Green HK, Boddington NL, Carvalho CF, Osman HK, et al. Enhanced MERS coronavirus surveillance of travelers from the Middle East to England. *Emerg Infect Dis* 2014;**20**:1562–4.
- Gautret P, Charrel R, Benkouiten S, Belhouach K, Nougaiyre A, Drali T, et al. Lack of MERS coronavirus but prevalence of influenza virus in French pilgrims after 2013 Hajj. *Emerg Infect Dis* 2014;**20**:728–30.
- Aberle JH, Popow-Kraupp T, Kreidl P, Laferl H, Heinz FX, Aberle SW. Influenza A and B viruses but not MERS-CoV in Hajj Pilgrims, Austria, 2014. *Emerg Infect Dis* 2015;**21**:726–7.

14. German M, Olsha R, Kristjanson E, Marchand-Austin A, Peci A, Winter AL, et al. Acute respiratory infections in travelers returning from MERS-CoV-affected areas. *Emerg Infect Dis* 2015;**21**:1654–6.
15. Shahkarami M, Yen C, Glaser C, Xia D, Watt J, Wadford DA. Laboratory testing for Middle East respiratory syndrome coronavirus, California, USA, 2013–2014. *Emerg Infect Dis* 2015;**21**:1664–6.
16. Gautret P, Charrel R, Belhouchat K, Drali T, Benkouiten S, Nougairede A, et al. Lack of nasal carriage of novel corona virus (HCoV-EMC) in French Hajj pilgrims returning from the Hajj 2012, despite a high rate of respiratory symptoms. *Clin Microbiol Infect* 2013;**19**:E315–7.
17. Memish ZA, Assiri A, Almasri M, Alhakeem RF, Turkestani A, Al Rabeeah AA, et al. Prevalence of MERS-CoV nasal carriage and compliance with the Saudi health recommendations among pilgrims attending the 2013 Hajj. *J Infect Dis* 2014;**210**:1067–72.
18. Annan A, Owusu M, Marfo KS, Larbi R, Sarpong FN, Adu-Sarkodie Y, et al. High prevalence of common respiratory viruses and no evidence of Middle East respiratory syndrome coronavirus in Hajj pilgrims returning to Ghana, 2013. *Trop Med Int Health* 2015;**20**:807–12.
19. Kandeel A, Deming M, Elkreem EA, El-Refay S, Afifi S, Abukela M, et al. Pandemic (H1N1) 2009 and Hajj pilgrims who received predeparture vaccination, Egypt. *Emerg Infect Dis* 2011;**17**:1266–8.
20. Ziyaeyan M, Alborzi A, Jamalidoust M, Moeini M, Pouladfar GR, Pourabbas B, et al. Pandemic 2009 influenza A (H1N1) infection among 2009 Hajj pilgrims from southern Iran: a real-time RT-PCR-based study. *Influenza Other Respir Viruses* 2012;**6**:e80–4.
21. Memish ZA, Assiri AM, Hussain R, Alomar I, Stephens G. Detection of respiratory viruses among pilgrims in Saudi Arabia during the time of a declared influenza A(H1N1) pandemic. *J Travel Med* 2012;**19**:15–21.
22. Benkouiten S, Charrel R, Belhouchat K, Drali T, Salez N, Nougairede A, et al. Circulation of respiratory viruses among pilgrims during the 2012 Hajj pilgrimage. *Clin Infect Dis* 2013;**57**:992–1000.
23. Benkouiten S, Charrel R, Belhouchat K, Drali T, Nougairede A, Salez N, et al. Respiratory viruses and bacteria among pilgrims during the 2013 Hajj. *Emerg Infect Dis* 2014;**20**:1821–7.
24. Alborzi A, Aelami MH, Ziyaeyan M, Jamalidoust M, Moeini M, Pourabbas B, et al. Viral etiology of acute respiratory infections among Iranian Hajj pilgrims, 2006. *J Travel Med* 2009;**16**:239–42.
25. Moattari A, Emami A, Moghadami M, Honarvar B. Influenza viral infections among the Iranian Hajj pilgrims returning to Shiraz, Fars Province, Iran. *Influenza Other Respir Viruses* 2012;**6**:e77–9.
26. Memish ZA, Assiri A, Turkestani A, Yezli S, Al Masri M, Charrel R, et al. Mass gathering and globalization of respiratory pathogens during the 2013 Hajj. *Clin Microbiol Infect* 2015;**21**. 571.e1–571.e8.
27. World Health Organization. Health conditions for travelers to Saudi Arabia for the pilgrimage to Mecca (Hajj), 2015. *Wkly Epidemiol Rec* 2015;**90**:381–4.
28. Alqarni H, Memish ZA, Assiri AM. Health conditions for travellers to Saudi Arabia for the pilgrimage to Mecca (Hajj)—2015. *J Epidemiol Glob Health* 2015 Jul 13 [Epub ahead of print].
29. Memish ZA, Zumla A, Alhakeem RF, Assiri A, Turkestani A, Al Harby KD, et al. Hajj: infectious disease surveillance and control. *Lancet* 2014;**383**:2073–82.