VIROLOGICA SINICA 2014, 29 (6): 364-371
DOI 10.1007/s12250-014-3507-x

RESEARCH ARTICLE

Viral respiratory infections among Hajj pilgrims in 2013

Osamah Barasheed[1]✉, Harunor Rashid[1], Mohammad Alfelali[1,2], Mohamed Tashani[1], Mohammad Azeem[1], Hamid Bokhary[3], Nadeen Kalantan[4], Jamil Samkari[2], Leon Heron[1], Jen Kok[5], Janette Taylor[5], Haitham El Bashir[6], Ziad A. Memish[7], Elizabeth Haworth[8], Edward C. Holmes[9,10], Dominic E Dwyer[5, 9], Atif Asghar[3], Robert Booy[1, 9,10] on behalf of the Hajj Research Team**

1. National Centre for Immunisation Research and Surveillance (NCIRS), The Children's Hospital at Westmead, NSW, Australia
2. Department of Family and Community Medicine, Faculty of Medicine, King Abdulaziz University, Rabigh, Saudi Arabia
3. The Custodian of the two Holy Mosques Institute for Hajj and Umrah Research, Umm Al-Qura University, Makkah, Saudi Arabia
4. King Abdulaziz Medical City, Jeddah, Saudi Arabia
5. Centre for Infectious Diseases and Microbiology Laboratory Services, Westmead Hospital, NSW, Australia
6. Hamad Medical Corporation, Doha, Qatar
7. Ministry of Health, Riyadh, Saudi Arabia
8. Menzies Research Institute Tasmania, Hobart, Tasmania, Australia
9. Sydney Medical School, The University of Sydney, NSW, Australia
10. Marie Bashir Institute for Infectious Diseases and Biosecurity, The University of Sydney, NSW, Australia

Middle East respiratory syndrome coronavirus (MERS-CoV) has emerged in the Arabian Gulf region, with its epicentre in Saudi Arabia, the host of the 'Hajj' which is the world's the largest mass gathering. Transmission of MERS-CoV at such an event could lead to its rapid worldwide dissemination. Therefore, we studied the frequency of viruses causing influenza-like illnesses (ILI) among participants in a randomised controlled trial at the Hajj 2013. We recruited 1038 pilgrims from Saudi Arabia, Australia and Qatar during the first day of Hajj and followed them closely for four days. A nasal swab was collected from each pilgrim who developed ILI. Respiratory viruses were detected using multiplex RT-PCR. ILI occurred in 112/1038 (11%) pilgrims. Their mean age was 35 years, 49 (44%) were male and 35 (31%) had received the influenza vaccine pre-Hajj. Forty two (38%) pilgrims had laboratory-confirmed viral infections; 28 (25%) rhinovirus, 5 (4%) influenza A, 2 (2%) adenovirus, 2 (2%) human coronavirus OC43/229E, 2 (2%) parainfluenza virus 3, 1 (1%) parainfluenza virus 1, and 2 (2%) dual infections. No MERS-CoV was detected in any sample. Rhinovirus was the commonest cause of ILI among Hajj pilgrims in 2013. Infection control and appropriate vaccination are necessary to prevent transmission of respiratory viruses at Hajj and other mass gatherings.

KEYWORDS Hajj; influenza-like illness; mass gathering; MERS-CoV; pilgrim; respiratory infections

INTRODUCTION

Respiratory tract infections (RTIs) including influenza are important health hazards among travellers with the incidence of influenza in returning febrile travellers from subtropical and tropical regions being between 5 and 15% (Askling H H, et al., 2010; Belderok S M, et al., 2013, Davis X M, et al., 2013). GeoSentinel data for the 2009 pandemic influenza showed that detection of travel-related cases could be a reliable indicator of sustained influenza transmission within the exposure coun-

Received: 26 September 2014, Accepted: 3 November 2014
Published online: 14 November 2014
✉ Correspondence:
Phone: +61-98451433; Fax: +61-2-98451418,
Email: osamah.barasheed@health.nsw.gov.au

© WIV, CAS and Springer-Verlag Berlin Heidelberg 2014

try and may aid planning for control measures (Davis X M, et al., 2013). Mass gathering events such as the Hajj pilgrimage, the Olympic Games or the Football World Cup are known to amplify the risk of transmission of respiratory viruses including escalating pandemic influenza (Blyth C C, et al., 2010; Haworth E, et al., 2013; Zepeda-Lopez H M, et al., 2010). For instance, it is postulated that a mass event that took place in Iztapalapa, Mexico sparked the rapid global dissemination of H1N1/09 influenza (Zepeda-Lopez H M, et al., 2010).

During Hajj, up to 3 million pilgrims assemble in Mecca city before moving in a body to Mina (a small valley at the outskirts of Mecca), where they live in tents shared by, depending on size, between 30 and 150 persons. The interplay of multitude of factors including severe crowding, limited facilities and time for personal hygiene, and particulate and microbiological air pollution at Hajj increases the risk of acquisition of respiratory viruses by up to 8 fold (Benkouiten S, et al., 2013; Hameed A A, et al., 2013; Haworth E, et al., 2013; Rashid H, et al., 2008). The emergence of the Middle East respiratory syndrome coronavirus (MERS-CoV) in the Gulf region with its epicentre in Saudi Arabia has raised major concern over the possibility of home-bound pilgrims' spreading of MERS-CoV globally (Al-Tawfiq J A, et al., 2014; Rashid H, et al., 2014). Limited virological and syndromic surveillance data during the Hajj 2012 did not show Hajj-associated transmission of MERS-CoV (Gautret P, et al., 2014, Rashid H, et al., 2014), but the virus was detected in pilgrims who visited Mecca and Medina on Umrah pilgrimage 2012 and 2013 (Devi J P, et al., 2014; Health Protection Agency (HPA) UK Novel Coronavirus Investigation team, 2013).

Two studies attempted to assess the prevalence of MERS-CoV and influenza among pilgrims during the Hajj 2013 (Memish Z A, et al., 2014, Benkouiten S, et al., 2014). These studies provided timely and valuable data, but had some methodological limitations: one provided airport-based surveillance data and therefore did not reflect the true Hajj epidemiology (Memish Z A, et al., 2014), while the other, although conducted at the Hajj site and studied an array of bacterial and viral pathogens, involved only one travel group of pilgrims from Marseille and therefore may not be generalisable to other pilgrims (Benkouiten S, et al., 2014). In the current report we present the data on the attack rate of common respiratory viruses among symptomatic pilgrims from Saudi Arabia, Australia and Qatar who participated in a large trial assessing the efficacy of facemasks against respiratory infections including MERS-CoV during the Hajj 2013.

MATERIALS AND METHODS

Study protocol

The protocol of this study is published in detail elsewhere (Wang M, et al., 2014). Breifly, pilgrims from Saudi Arabia, Australia and Qatar were recruited in a large-scale cluster-randomised controlled trial to assess the efficacy of facemasks in the prevention of respiratory viruses including influenza and MERS-CoV among Hajj pilgrims. This report analyses data from symptomatic pilgrims only.

At the Hajj 2103, conveniently placed individual tents accommodating Hajj pilgrims from Saudi Arabia, Australia or Qatar were randomly assigned to 'supervised use of facemasks' versus 'standard infection control measures' recommended by Saudi Ministry of Health (MoH). Every member of each participating tent was eligible to participate in the study. During the morning and afternoon of the first day of Hajj (13th October, 2013), research team members consisting of physicians and trained medical students explained the study to the pilgrims in each tent, and invited those aged 18 years or older to participate in the study voluntarily.

Participants who consented were asked to complete a baseline questionnaire on 13th October, 2013 that included contact details, relevant demographics, vaccination history and clinical information including current respiratory symptoms with duration and pre-existing medical conditions. Participants were provided with diaries that had a unique barcode number for identification. The pilgrims recorded on the dairies the severity and outcome of new or continuing influenza-like illness (ILI). Diaries were collected on the conclusion of Hajj on 16th October 2013.

Pilgrims aged ≥ 65 years, and/or with pre-existing medical illnesses such as chronic lung, heart, kidney, liver, neuromuscular, metabolic or immunocompromising conditions were defined as 'at risk' individuals since they were at higher risk of developing severe complications from influenza infections (Memish Z A, et al. 2014).

Specimen collection and testing

Each day, the research team members visited the tents and actively searched for pilgrims who had developed ILI, defined as subjective (or proven) fever and at least one respiratory symptom such as cough, sore throat and rhinorrhoea. Nasopharyngeal (NP) swabs (or a throat swab if NP swab was not possible) were taken from pilgrims with an ILI by a trained team member using Copan Nylon® Flocked swabs placed in Universal Transport Medium (UTM™ [Copan Italia, Brescia, Italy]). Swabs were frozen at -80°C within the same day of collection and stored at the same temperature until tested at Westmead

Hospital, New South Wales, Australia. The shipping process took about 2 months because the swabs could not be moved until after the Jeddah airport's cold storage facilities had been repaired and certified effective.

Nucleic acid extraction was performed using the Qiagen bioROBOT EZ instrument (Qiagen, Valencia, CA), and amplification carried out using the Roche LC 480 (Roche Diagnostics GmbH, Mannheim, Germany) real-time instrument. Respiratory viruses were detected using a real-time, multiplex RT-PCR assay targeting human coronaviruses (OC43, 229E and NL63), influenza A, influenza B, respiratory syncytial virus, parainfluenza viruses 1 –3, human metapneumovirus, rhinovirus, enterovirus and adenoviruses as described in detail elsewhere (Ratnamohan V M, et al., 2014; Gaunt E R, et al., 2010). A MERS-CoV assay targeting regions upstream of the E gene (upE) was also performed as described previously (Corman V M, et al., 2012).

This study was approved by the Hunter New England Human Research Ethics, Australia (Ref: 13/07/17/3/04), Hamad Medical Corporation/Weill Cornell Medical College in Qatar Joint Institutional Review Board, Qatar (Ref: 13-00039) and by the Saudi Ministry of Health.

RESULTS

A total of 1038 pilgrims were recruited from 47 tents and followed during the peak period of Hajj in 2013 (Figure 1). Of the recruited pilgrims, 443 (43%) were male, 923 (89%) were from Saudi Arabia, 90 (9%) from Australia and 25 (2%) from Qatar.

The prevalence of ILI among the recruited pilgrims was 11% (112/1038). NP swabs were collected from all symptomatic pilgrims; initially throat swabs were collected from two participants but from them too eventually NP swabs were collected (Figure 1). They were aged between 18 and 75 (mean 35) years. The participants' demographic characteristics are described in Table 1 according to their country of origin.

Twenty two (20%) of those reporting ILI were considered 'at risk' of acquiring respiratory infections due to their age ≥ 65 years (2 [9%]), or coexisting of chronic medical conditions such as chronic respiratory diseases (15 [68%]), diabetes (9 [41%]), cardiac diseases (1 [4%]) or renal disorders (1 [4%]). Only 35 (31%) of these symptomatic pilgrims reported receiving influenza vaccine before Hajj. The uptake of influenza vaccine among Australian, Qatari and Saudi pilgrims was 87%, 80% and 20% respectively.

Sixty (54%) pilgrims fulfilled ILI definition at the time of recruitment. On D1–Sunday 13th of October 2013–20 (18%) fresh new cases of ILI were reported; 7 (6%) new cases on D2, Monday the 14th; 14 (12%) on D3, Tuesday the 15th, and 11 (10%) on D4, Wednesday the 16th (Figure 2). The most common respiratory symptom was sore throat 66 (59%), followed by cough 45 (40%) and runny nose 38 (34%). Of the 112 symptomatic pilgrims, only 11 (10%) visited clinics or health care centres in Mecca for ILI or RTI symptoms. Forty two (38%) pilgrims had laboratory-confirmed viral infections: 28 (25%) rhinovirus, 5 (4%) influenza A (4 H3N1 and 1 H1N1/09), 2 (2%) adenovirus, 2 (2%) human coronavirus OC43/229E, 2 (2%) parainfluenza virus 3, 1 (1%) parainfluenza virus 1, and 2 (2%) dual infections (rhinovirus/adenovirus and rhinovirus/human coronavirus OC43/229E) (Table 1). The rate of influenza in vaccinated pilgrims was similar to that in unvaccinated pilgrims (5.2% [4/77] versus 2.9% [1/35]), P = 0.58). MERS-CoV was not detected in any sample.

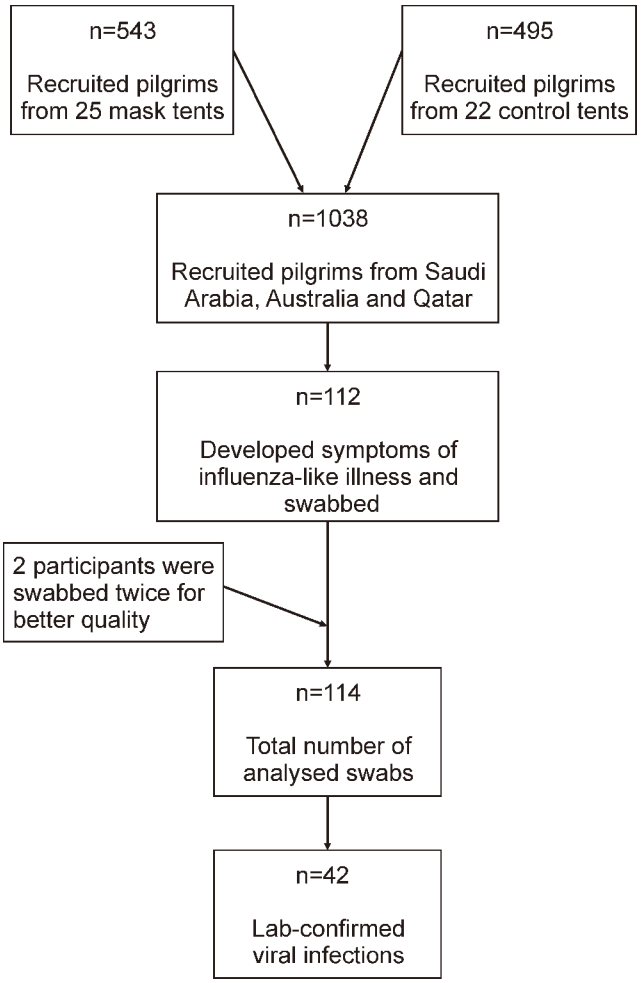

Figure 1. Flow diagram showing recruitment of participants during Hajj in 2013

DISCUSSION

This study showed that the point-prevalence of ILI among pilgrims from Saudi Arabia, Australia and Qatar

Table 1. Demography and virology of 112 Hajj pilgrims with respiratory symptoms in 2013 by country of origin

Pilgrims' country of origin	Saudi Arabia n (%)	Australia n (%)	Qatar n (%)
Number of symptomatic participants	92	15	5
Median age in years (range)	34 (18 – 62)	40 (25 – 61)	56 (31 – 75)
Gender	38 (41%) male	6 (40%) male	5 (100%) male
'At risk'*	17 (19%)	3 (20%)	2 (40%)
Received influenza vaccine in 2013	18 (20%)	13 (87%)	4 (80%)
Visit medical centres during Hajj	9 (10%)	2 (13%)	0
Lab-confirmed infection	33 (36%)	7 (47%)	2 (40%)
Viruses			
Rhinovirus	21 (22.8%)	6 (40%)	1 (20%)
Influenza	5 (5.4%)	--	--
Parainfluenza 3	2 (2.2%)	--	--
Adenovirus	2 (2.2%)	--	--
Coronavirus (OC43/229E)	2 (2.2%)	--	--
Parainfluenza 1	--	--	1 (20%)
Rhino + coronavirus	--	1 (6.7%)	--
Rhino + adenovirus	1 (1.1%)	--	--

*Pilgrims aged ≥65 years, and/or with pre-existing medical illnesses such as chronic lung, heart, kidney, liver, neuromuscular, metabolic or immunocompromising conditions were considered 'at risk'.

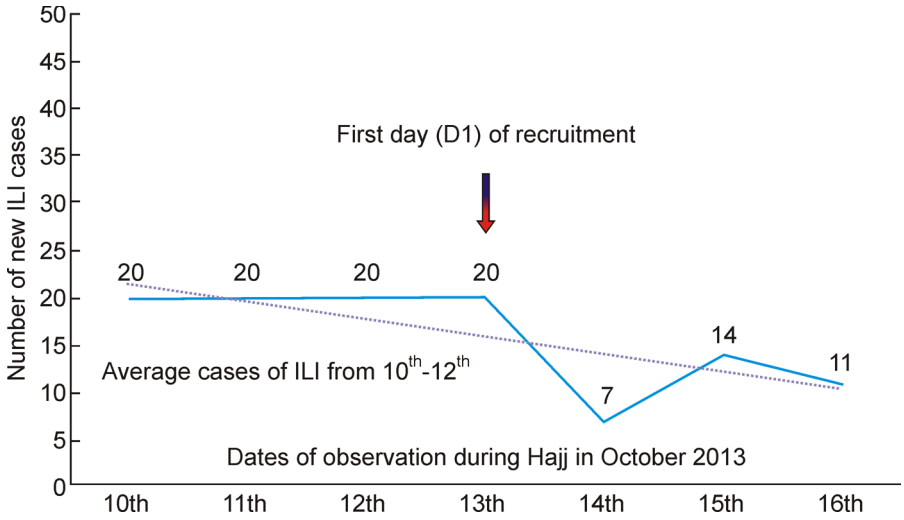

Figure 2. New ILI cases according to the date of onset during the peak period of Hajj

who volunteered to participate in this study during the Hajj 2013 was 11%, and that 38% (42/112) of symptomatic pilgrims had laboratory-confirmed viral infections which is comparable to a virus detection rate of 38.6% among French pilgrims during the Hajj 2012 (Benkouiten S, et al., 2013). This rate of ILI was lower than that was seen in French pilgrims (47%) during the same year, however in the latter, 91% subjects had at least one respiratory symptom (Benkouiten S, et al., 2014); an unpublished report involving Malaysian pilgrims showed that 86% suffered from ILI during the Hajj 2013, with prevalence varying according to the geographic locations within Mecca (Dr Habsah Hasan, Kelantan, Malaysia, personal communication). A decline in ILI rates over the next few days of stay in Mina is interesting and unexpected (Figure 2), but its significance is unexplained at this stage. It is possibly because of the effect of facemask use in many pilgrims, but these data are insufficient to support or refute this notion.

Studies conducted over the past few years have shown that the prevalence of ILI among Hajj pilgrims varies by country of origin and by year. For instance, in 2012,

approximately 9% of Australian pilgrims compared to 41% of French pilgrims had respiratory symptoms, which was consistent with the findings for 2013 Hajj (Gautret P, et al., 2014; Rashid H, et al., 2013). However, in a pilot study conducted by our team we observed that 44% of Australian pilgrims had ILI during the Hajj 2011 (Barasheed O, et al., 2014), however only 8% of French Hajj pilgrims reported having ILI in 2009 (Gautret P, et al., 2011). During the Hajj 2007, 40% Malaysian pilgrims developed ILI (Deris Z Z, et al. 2010). Such disparity can be explained by factors such as differences in age and prevalence of underlying chronic diseases, as well as seasonal and geographic variations in respiratory virus circulation. The average age among our participants was 35 years and only 20% had an underlying chronic disease. This contrasts to the situation seen in French pilgrims whose mean age was 62 years and where 53% had chronic underlying medical conditions (Benkouiten S, et al., 2014). Also, it is noteworthy that the definition of ILI deferred across the studies. No MERS-CoV was detected in any of the pilgrims in this study; this corroborates the findings of both the French study and Saudi airport-based surveillance for MERS-CoV, neither of which identified this virus among pilgrims who attended Hajj 2013 (Memish Z A, et al., 2014; Benkouiten S, et al., 2014).

Despite this absence of laboratory confirmed MERS-CoV among Hajj pilgrims, a spike in MERS cases occurred in April 2014 in Saudi Arabia, importantly in the port city of Jeddah through which most pilgrims enter and leave Mecca (Alghamdi I G, et al., 2014). In addition, the Malaysian Ministry of Health reported a fatal case of laboratory-confirmed MERS-CoV infection in a 54 year old man returning from Umrah pilgrimage at the end of March 2014; the patient visited a camel farm and drank camel milk (Devi J P, et al., 2014). Another laboratory-confirmed case of MERS-CoV was reported in a 69 year old Greek man who returned from Jeddah; this individual did not report any contact with camels, but regularly visited his wife who was hospitalised in Jeddah for enteric fever (Tsiodras S, et al., 2014). Similarly, the first two confirmed cases of MERS-CoV infection in North America was reported in US healthcare workers, aged ≥60 and ≥40 years respectively, who lived and worked in hospitals in Saudi Arabia where patients with MERS had received care (Bialek S R, et al., 2014). These updates indicate that enhanced surveillance is urgently required to tease out the modality of transmission, and explore effective preventive measures and potential therapeutic interventions.

The commonest cause of ILI in our study was rhinovirus which was detected in 25% of symptomatic pilgrims. Similarly, rhinovirus was the most common cause of ILI among British pilgrims in 2006 (14%), international pilgrims (arriving from the Middle East, Asia and Africa) in 2009 (13%) and French pilgrims in 2012 (27%) (Benkouiten S, et al., 2013; Memish Z A, et al., 2012; Rashid H, et al., 2008). In addition, rhinovirus infections were reported among Iranian pilgrims in 2006 and subsequently among non-Hajj travellers during the onset of the pandemic A (H1N1) influenza in 2009 (Alborzi A, et al., 2009; Jaureguiberry S, et al., 2012). Although rhinovirus infection is usually relatively mild, it can lead to hospitalisation of the patients with chronic medical condition (Walker E, et al., 2014).

The attack rate of influenza virus in our symptomatic pilgrims was only 4% (5/112) during the Hajj 2013, whereas the prevalence of influenza virus among the French pilgrims in the same year was 7.8% (Benkouiten S, et al., 2014). Observing the global influenza activity at the time of Hajj, experts opined that pilgrims from tropical Africa might have introduced the virus at the Hajj 2013 and thus facilitated its spread among European pilgrims (Raoult D, et al., 2014). Only 3.2% of returning French Hajj pilgrims had influenza in the year 2012 (Benkouiten et al., 2013). During the 2009 influenza pandemic, the prevalence of influenza virus infection (including H1N1/09) among international Hajj pilgrims was 0.2% (Memish Z A, et al., 2012). In 2006, the influenza attack rate was reported to be 10% in Saudi Arabian, British and Iranian Hajj pilgrims (Alborzi A, et al., 2009; Rashid H, et al., 2008), while in 2005, the attack rate among UK pilgrims was 14% (Rashid H, et al., 2008). These differences may be due to varying methodology, sample size, influenza vaccine uptake or seasonal variations of influenza in pilgrims' countries of origin or change of season of the Hajj that happens with Hajj moving 10-12 days forward in the Gregorian calendar.

The strength of this study is that these data originate from a large sample size (1038), and the pilgrims were closely followed for the 4 peak days of Hajj. Furthermore, the timing, site of recruitment and follow-up of this study was conducted at the main Hajj spot (Mina) during the most intense Hajj activities, so that it presents more representative Hajj epidemiology. In our study throat swabs were obtained from only two participants, but from them too ultimately NP swabs were obtained, a recent study has confirmed that nasal swabs are superior in detecting common respiratory viruses among Hajj pilgrims (Benkouiten S, et al., 2014). However, nasal or nasopharyngeal swabs have been shown to be poor in detecting MERS-CoV in people with pneumonia; lower respiratory tract samples such as sputum or preferably bronchoalveolar lavage samples produce better yields (Memish Z A, et al., 2014). Also, it should be noted that these data derive from symptomatic patients recruited in a randomised controlled trial, asymptomatic individuals were not swabbed, and the effect of facemask has not

been explored. The trial continues (Wang M, et al., 2014), and the full results will be published once the required number of participants is obtained.

In summary, MERS-CoV was not detected in a target population of 1038 pilgrims from Saudi Arabia, Australia and Qatar during the peak period of Hajj in 2013. Amongst 112 pilgrims with respiratory symptoms, rhinoviruses were the most common respiratory viruses identified, and several other respiratory viruses including influenza, adenovirus, coronaviruses and parainfluenza viruses were also detected. Infection control measures to minimise the risk of transmission of respiratory viruses and relevant vaccination, particularly for influenza, should continue as methods to prevent transmission of respiratory viruses at Hajj and other mass gatherings.

ACKNOWLEDGMENTS

This report was made possible by a National Priorities Research Program grant (NPRP 6-1505-3-358) from the Qatar National Research Fund (a member of Qatar Foundation). ECH is supported by an NHMRC Australia Fellowship.The authors acknowledge the help and support of: the Royal Embassy of Saudi Arabia, Canberra; Saudi Arabian Cultural Mission, Canberra; Ministry of Higher Education, Riyadh; Ministry of Health, Riyadh; Ministry of Hajj (Deputy Minister's Office), Mecca; the Custodian of the two Holy Mosques Institute for Hajj and Umrah Research (Dr. Abdulaziz Seroji and Dr. Turki Habeebullah), Mecca.

COMPLIANCE WITH ETHICS GUIDELINES

Professor Robert Booy and Dr Leon Heron have received funding from Baxter, CSL, GSK, Merck, Novartis, Pfizer, Roche, Romark and Sanofi Pasteur for the conduct of sponsored research, travel to present at conferences or consultancy work; all funding received is directed to research accounts at The Children's Hospital at Westmead. The other authors have declared no conflict of interest in relation to this work.

AUTHOR CONTRIBUTIONS

OB executed the trial, analysed data and prepared the first draft of the manuscript; HR is the guarantor of the study, and oversaw implementation of the study, contributed to data analysis and manuscript preparation; MAF, MT, MA, HB, NK and JS participated in data collected and contributed to the manuscript; LH supervised preparation of the research protocol and research tools; JK and JT were responsible for conducting molecular diagnostic tests; HEB contributed to data interpretation; ZAM contributed to study design; EH contributed to the study design and supervised data analysis and interpretation; ECH and DED contributed to the design and interpreted molecular diagnostic tests; AA contributed to the collection, analysis and interpretation of data; RB supervised data interpretation and overseen manuscript revision; Hajj Research Team participated in data collection and sorting logistics.

**Hajj Research Team:

[Ibtihal Malawi, Ebtehal Matar, Abrar Tawakoul, Abrar ALnami, Atheer Alshareif, Israa Kalantan, Asal Arbaeen, Eatimad Alalawi, Afnan AlGhamdi, Amani Koshak, Ameerah Alkhaldi, Enasm Al-Nami, Anwar Howsawi, Bashaier Fairaq, Bushra Maghrabi, Tafaol Murad, Hanan Alzahrani, Kholood Almehmadi, Doaa Milibari, Rehab Hafiz, Rawdhah Kalantan, Shahad Al-Ansari, Aeshah Rajab, Anood Alfahmy, Ghaida Ali, Fatimah Abu naji, Lujin Hassan, Lulwah Althumali, Layla Farhat, Najlaa Baddour, Hibh Alandanusi, Waad Alqurashi, Sumayyah Fallata, Azhar Alharbi, Joud Bahakeem, Abrar Alshareef, Badr Rawa, Daniah Alnemari, Mawadah Hariri, Samah Alhadramy, Ahmed Alghamdi, Ahmed Muqadimi, Ahmad Bimah, Osama Alamri, Jehad Qutub, Abdulrahman Al-Ghamdi, Abdurrahman Mirza, Abdulghafur Alandijani, Omar Qoqandi, Faisal Mandourah, Muhammad Alghamdi, Mohammed Mahboob, Mohannad Alsulami, Moayyd Hinnawi, Naif Hawsawi, Mousab Alsudais, Nawaf Dhabab, Ahmed Balamash, Mohammed Bawazir, Raif Nassir, Mohammed AlAsmari, Faisal Alzahrani, Abdulrahman Alomari and Ahmad Makeen]

REFERENCES

Al-Tawfiq J A, Memish Z A. 2014. Emerging respiratory viral infections: MERS-CoV and influenza. Lancet Respir Med, 2: 23–25.

Alborzi A, Aelami M H, Ziyaeyan M, Jamalidoust M, Moeini M, Pourabbas B, Abbasian A. 2009. Viral etiology of acute respiratory infections among Iranian Hajj pilgrims, 2006. J Travel Med, 16: 239–242.

Alghamdi I G, Hussain, II, Almalki S S, Alghamdi M S, Alghamdi M M, El-Sheemy M A. 2014. The pattern of Middle East respiratory syndrome coronavirus in Saudi Arabia: a descriptive epidemiological analysis of data from the Saudi Ministry of Health. Int J Gen Med, 7: 417–423.

Askling H H, Rombo L. 2010. Influenza in travellers. Curr Opin Infect Dis, 23: 421–425.

Barasheed O, Badahdah A-M, Heron L, Taylor J, McPhee K, Ridda I, Haworth E, Dwyer D E, Rashid H, Booy R, On behalf of the Hajj Research T. 2014. Pilot randomised controlled trial to test effectiveness of facemasks in preventing influenza-like illness transmission among Australian Hajj pilgrims in 2011. Infect Disord Drug Targets, 14: 110–116.

Belderok S M, Rimmelzwaan G F, van den Hoek A, Sonder G J. 2013. Effect of travel on influenza epidemiology. Emerg Infect Dis, 20: 1821–1827.

Benkouiten S, Charrel R, Belhouchat K, Drali T, Nougairede A, Salez N, Memish Z A, A L Masri M, Fournier P-E, Raoult D,

Brouqui P, Parola P, Gautret P. 2014. Respiratory Viruses and Bacteria among Pilgrims during the 2013 Hajj. Emerg Infect Dis, Epub ahead of print.

Benkouiten S, Gautret P, Belhouchat K, Drali T, Nougairede A, Salez N, Memish Z A, Al Masri M, Raoult D, Brouqui P, Parola P, Charrel R N. 2014. Comparison of nasal swabs with throat swabs for the detection of respiratory viruses by real-time reverse transcriptase PCR in adult Hajj pilgrims. J Infect, 20: 1821–1827.

Benkouiten S, Charrel R, Belhouchat K, Drali T, Salez N, Nougairede A, Zandotti C, Memish Z A, Al Masri M, Gaillard C, Parola P, Brouqui P, Gautret P. 2013. Circulation of respiratory viruses among pilgrims during the 2012 Hajj pilgrimage. Clin Infect Dis, 57: 992–1000.

Bialek S R, Allen D, Alvarado-Ramy F, Arthur R, Balajee A, Bell D, Best S, Blackmore C, Breakwell L, Cannons A, Brown C, Cetron M, Chea N, Chommanard C, Cohen N, Conover C, Crespo A, Creviston J, Curns A T, Dahl R, Dearth S, DeMaria A, Echols F, Erdman D D, Feikin D, Frias M, Gerber SI, Gulati R, Hale C, Haynes L M, Heberlein-Larson L, Holton K, Ijaz K, Kapoor M, Kohl K, Kuhar D T, Kumar A M, Kundich M, Lippold S, Liu L, Lovchik J C, Madoff L, Martell S, Matthews S, Moore J, Murray L R, Onofrey S, Pallansch M A, Pesik N, Pham H, Pillai S, Pontones P, Pringle K, Pritchard S, Rasmussen S, Richards S, Sandoval M, Schneider E, Schuchat A, Sheedy K, Sherin K, Swerdlow D L, Tappero J W, Vernon M O, Watkins S, Watson J, Centers for Disease Control and Prevention (CDC). 2014. First confirmed cases of Middle East respiratory syndrome coronavirus (MERS-CoV) infection in the United States, updated information on the epidemiology of MERS-CoV infection, and guidance for the public, clinicians, and public health authorities-May 2014. MMWR Morb Mortal Wkly Rep, 63, 431–436.

Blyth C C, Foo H, van Hal S J, Hurt A C, Barr I G, McPhie K, Armstrong P K, Rawlinson W D, Sheppeard V, Conaty S, Staff M, Dwyer D E. 2010. Influenza outbreaks during World Youth Day 2008 mass gathering. Emerg Infect Dis, 16: 809–815.

Corman V M, Muller M A, Costabel U, Timm J, Binger T, Meyer B, Kreher P, Lattwein E, Eschbach-Bludau M, Nitsche A, Bleicker T, Landt O, Schweiger B, Drexler J F, Osterhaus A D, Haagmans B L, Dittmer U, Bonin F, Wolff T, Drosten C. 2012. Assays for laboratory confirmation of novel human coronavirus (hCoV-EMC) infections. Euro Surveill, 17.

Davis X M, Hay K A, Plier D A, Chaves S S, Lim P L, Caumes E, Castelli F, Kozarsky P E, Cetron M S, Freedman D O. 2013. International travelers as sentinels for sustained influenza transmission during the 2009 influenza A (H1N1) pdm09 pandemic. J Travel Med, 20: 177–184.

Deris Z Z, Hasan H, Sulaiman S A, Wahab M S, Naing N N, Othman N H. 2010. The prevalence of acute respiratory symptoms and role of protective measures among Malaysian hajj pilgrims. J Travel Med, 17:82–88.

Devi J P, Noraini W, Norhayati R, Kheong C C, Badrul A, Zainah S, Fadzilah K, Hirman I, Hakim S L, Hisham A N. 2014. Laboratory-confirmed case of Middle East respiratory syndrome coronavirus (MERS-CoV) infection in Malaysia: preparedness and response, April 2014. Euro Surveill, 19. pii: 20797.

Gaunt E R, Hardie A, Claas E C, Simmonds P, Templeton K E. 2010. Epidemiology and clinical presentations of the four human coronaviruses 229E, HKU1, NL63, and OC43 detected over 3 years using a novel multiplex real-time PCR method. J Clin Microbiol, 48: 2940–2947.

Gautret P, Vu Hai V, Sani S, Doutchi M, Parola P, Brouqui P. 2011. Protective measures against acute respiratory symptoms in French pilgrims participating in the Hajj of 2009. J Travel Med, 18: 53–55.

Gautret P, Charrel R, Benkouiten S, Belhouchat K, Nougairede A, Drali T, Salez N, Memish Z A, Al Masri M, Lagier J C, Million M, Raoult D, Brouqui P, Parola P. 2014. Lack of MERS coronavirus but prevalence of influenza virus in French pilgrims after 2013 Hajj. Emerg Infect Dis, 20: 728–730.

Hameed A A, Habeeballah T. 2013. Air Microbial Contamination at the Holly Mosque, Makkah, Saudi Arabia. Curr World Environ, 8.

Haworth E, Barasheed O, Memish Z A, Rashid H, Booy R. 2013. Prevention of influenza at Hajj: applications for mass gatherings. J R Soc Med, 106: 215–223.

Health Protection Agency (HPA) UK Novel Coronavirus Investigation team. 2013. Evidence of person-to-person transmission within a family cluster of novel coronavirus infections, United Kingdom, 2013. Euro Surveill, 18: 20427.

Jaureguiberry S, Boutolleau D, Grandsire E, Kofman T, Deback C, Ait-Arkoub Z, Bricaire F, Agut H, Caumes E. 2012. Clinical and microbiological evaluation of travel-associated respiratory tract infections in travelers returning from countries affected by pandemic A(H1N1) 2009 influenza. J Travel Med, 19: 22–27.

Memish Z A, Assiri A M, Hussain R, Alomar I, Stephens G. 2012. Detection of respiratory viruses among pilgrims in Saudi Arabia during the time of a declared influenza A(H1N1) pandemic. J Travel Med, 19: 15–21.

Memish Z A, Al Rabeeah A A. 2014. Health conditions for travellers to Saudi Arabia for the Umra and pilgrimage to Mecca (Hajj) - 2014. J Epidemiol Glob Health, 4:73–75.

Memish Z A, Assiri A, Almasri M, Alhakeem R F, Turkestani A, Al Rabeeah A A, Al-Tawfiq J A, Alzahrani A, Azhar E, Makhdoom H Q. 2014. Prevalence of MERS-CoV nasal carriage and compliance with the Saudi health recommendations among pilgrims attending the 2013 Hajj. J Infect Dis, 210:1067–1072.

Memish Z A, Al-Tawfiq J A, Makhdoom H Q, Assiri A, Alhakeem R F, Albarrak A, Alsubaie S, Al-Rabeeah A A, Hajomar W H, Hussain R, Kheyami A M, Almutairi A, Azhar E I, Drosten C, Watson S J, Kellam P, Cotten M, Zumla A. 2014. Respiratory tract samples, viral load, and genome fraction yield in patients with Middle East respiratory syndrome. J Infect Dis, 210: 1590–1594.

Raoult D, Charrel R, Gautret P, Parola P. 2014. From the Hajj: it's the flu, idiot. Clin Microbiol Infect, 20:O1.

Rashid H, Barasheed O, Booy R. 2013. Acute febrile respiratory infection symptoms in Australian Hajjis at risk of exposure to Middle East respiratory syndrome coronavirus. Med J Aust, 199: 453.

Rashid H, Azeem M I, Heron L, Haworth E, Booy R, Memish Z A. 2014. Has Hajj-associated Middle East Respiratory Syndrome Coronavirus transmission occurred? The case for effective post-Hajj surveillance for infection. Clin Microbiol Infect, 20:273–276.

Rashid H, Shafi S, Haworth E, El Bashir H, Memish Z A, Sudhanva M, Smith M, Auburn H, Booy R. 2008. Viral respiratory infections at the Hajj: comparison between UK and Saudi pilgrims. Clin Microbiol Infect,14:569–574.

Rashid H, Shafi S, Booy R, El Bashir H, Ali K, Zambon M, Memish Z, Ellis J, Coen P, Haworth E. 2008. Influenza and respiratory syncytial virus infections in British Hajj pilgrims. Emerg Health Threats J, 1: e2.

Ratnamohan V M, Taylor J, Zeng F, McPhie K, Blyth C C, Adamson S, Kok J, Dwyer D E. 2014. Pandemic clinical case definitions are non-specific: multiple respiratory viruses circulating in the early phases of the 2009 influenza pandemic in New South Wales, Australia. Virol J, 11: 113.

Tsiodras S, Baka A, Mentis A, Iliopoulos D, Dedoukou X, Papamavrou G, Karadima S, Emmanouil M, Kossyvakis A, Spanakis

N, Pavli A, Maltezou H, Karageorgou A, Spala G, Pitiriga V, Kosmas E, Tsiagklis S, Gkatzias S, Koulouris N, Koutsoukou A, Bakakos P, Markozanhs E, Dionellis G, Pontikis K, Rovina N, Kyriakopoulou M, Efstathiou P, Papadimitriou T, Kremastinou J, Tsakris A, Saroglou G. 2014. A case of imported Middle East Respiratory Syndrome coronavirus infection and public health response, Greece, April 2014. Euro Surveill, 19:20782.

Walker E, Ison M G. 2014. Respiratory viral infections among hospitalized adults: experience of a single tertiary healthcare hospital. Influenza Other Respir Viruses, 8:282–292.

Wang M, Barasheed O, Rashid H, Booy R, El Bashir H, Haworth E, Ridda I, Holmes E C, Dwyer D E, Nguyen-Van-Tam J, Memish Z A, Heron L. 2014. A cluster-randomised controlled trial to test the effectiveness of facemasks in preventing respiratory virus infection among Hajj pilgrims. J Epidemiol Glob Health, Epub ahead of print.

Zepeda-Lopez H M, Perea-Araujo L, Miliar-Garcia A, Dominguez-Lopez A, Xoconostle-Cazarez B, Lara-Padilla E, Ramirez Hernandez J A, Sevilla-Reyes E, Orozco M E, Ahued-Ortega A, Villasenor-Ruiz I, Garcia-Cavazos R J, Teran L M. 2010. Inside the outbreak of the 2009 influenza A (H1N1)v virus in Mexico. PLoS One, 5: e13256.