Letter to the Editors

No evidence of MERS-CoV in Ghanaian Hajj pilgrims: cautious interpretation is needed

The study by Annan et al. recently published in the Tropical Medicine and International Health is, to our knowledge, the first attempt to describe the epidemiology of respiratory infections including Middle East respiratory syndrome coronavirus (MERS-CoV) among African Hajj pilgrims [1]. The study sample was representative of the Ghanaian Muslim population. However, there are limitations to the interpretation of their findings.

Intense crowding, close contact and shared accommodation amplify the risk of transmission of respiratory infections among Hajj pilgrims [2]. Emergence of MERS-CoV during 2012 in Saudi Arabia and neighbouring countries has raised concern about the risk of global spread of MERS-CoV from Hajj [3]. In 2013, the virus spread to a number of countries, including by Umrah performers/returnees [4, 5]. There were several surveillance studies performed at Hajj 2013, referenced by Annan et al., but others not been cited even though they add to our understanding [6, 7] (Table 1). Studies conducted at Hajj 2013 varied in their methods, study population and sample size, perhaps influencing outcomes. Memish et al. [8] and Annan et al. [1] recruited, respectively, 5235 and 839 people but provided only airport-based surveillance data. In contrast, studies by Barasheed et al. [7] and Benkouiten et al. [6] were conducted at the main Hajj locations (Makkah and Mina) during the peak period of Hajj with daily follow-up. Benkouiten et al. followed one Hajj travel group (n = 129) from Marseille, France, and studied an array of microorganisms including bacteria and uncommon viruses, whereas Barasheed et al. selected participants from several travel groups who developed respiratory symptoms; they were closely followed up in a large trial (n = 1038) involving Saudi Arabian, Australian and Qatari pilgrims.

All these 2013 studies involved testing nasopharyngeal or nasal samples for MERS-CoV (Benkouiten et al. additionally obtained throat swabs), which are less sensitive in detecting MERS-CoV (Table 1); lower respiratory tract samples such as bronchoalveolar lavage and tracheal aspirates result in higher yields [9]; therefore, Annan et al.’s notion that there is ‘no evidence of MERS-CoV in Hajj pilgrims returning to Ghana, 2013’ sounds overenthusiastic [1].

Most studies reported participants’ respiratory symptoms; the most commonly reported symptoms were cough, sore throat and fever. Barasheed et al. [7] and Benkouiten et al. [6] reported the prevalence of influenza-like illness (ILI) among their participants to be 11% and 47%, respectively, but Annan et al. [1] did not provide the prevalence of ILI. One caveat is that the definition of ILI differed between the studies (Table 1). The attack rate of laboratory-proven influenza in Annan et al.’s study was lower than in other studies (Benkouiten et al. and Barasheed et al.) (Table 1). This could be influenced by differences in influenza vaccine uptake. For instance, none of the French recruits received the 2013 influenza vaccine, while 69% of the participants in Barasheed et al.’s study did. The rate of influenza A was 7% and 4%, respectively [6, 7]. Annan et al. [1] reported an attack rate for influenza of 1.1%, but did not provide influenza vaccination data. Of interest, influenza was circulating in tropical Africa during the Hajj 2013 [10]. Thirdly, Annan et al. reported that the prevalence of RSV among returned Ghanaian pilgrims was 5.1% (attack rate 1.1) and contrasted that with Benkouiten’s prevalence of 0.8% among French pilgrims. However, the higher rate of RSV reported by Annan et al. is not unexpected; a higher attack rate of 9% was reported among returned symptomatic UK pilgrims after the Hajj 2005 [11]. Rashid et al. also showed that during the same year the attack rate of RSV among UK pilgrims in Makkah was 4% [12]. By contrast, during the subsequent Hajj season, the attack rate of RSV was very low (0.7%) among UK pilgrims and zero among Saudi pilgrims [13] indicating that the circulation of RSV is dependent on various factors such as seasonality, geographical original of the pilgrims and their close association with children.

Absence of MERS-CoV in nasal or nasopharyngeal samples of pilgrims does not rule out risk of the disease at Hajj. A recent estimate suggests that MERS-CoV has a basic reproduction number (R0) similar to that of SARS, that is 2–6.7 [14], but mathematical modelling studies indicate that the risk of an outbreak is low [15]. Considering the increasing number of Umrah pilgrims in the forthcoming months when the likelihood of a MERS-CoV upsurge is high due to the seasonal pattern of the
disease [16], surveillance must continue. Accordingly, we continued our study in 2014 and recruited over 2000 pilgrims from Gulf countries and Australia. Preliminary findings suggest that of 298 Australian pilgrims, only two (0.7%) had symptoms of severe respiratory infection, but none had pneumonia. Virological testing will provide

| Table 1 | Comparison between respiratory infection studies conducted among Hajj pilgrims in 2013 |
|---------|-----------------------------------------------------------------------------------|
| 2013 Hajj studies | Annan et al. [1] | Barasheed et al. [7] | Benkouiten et al. [6] | Memish et al. [8] |
| Study design | Cross-sectional study (post-Hajj) (prevalence and attack rate) | Randomised controlled trial (attack rate) | Prospective cohort before and at the end of Hajj (prevalence) | Two cross-sectional studies (pre- and post-Hajj) (prevalence of MERS-CoV) |
| Sample size | 839 | 1038 | 129 | 5235 |
| Place of recruitment | Kotoka International Airport, Ghana | Mina, Greater Makkah | Marseille, France, Makkah City and Mina | Jeddah Airport |
| Participants’ country of origin | Ghana | Australia, Saudi Arabia and Qatar | France | International (from 22 countries) |
| Age range (mean) in years | 21–85 (52) | 18–75 (35) | 34–85 (62) | 18–93 (52) |
| Influenza vaccine uptake | Not reported | 69% | None received the 2013 influenza vaccine, but 44% received it in the previous season | 22% |
| ILI | ILI not reported (77.6% [651/839] had respiratory symptoms) | 11% (112/1038) | ILI was defined as subjective (or proven) fever and at least one respiratory symptom such as cough, sore throat and rhinorrhea | Not reported |
| Swabs type | Nasopharyngeal | Nasopharyngeal | Paired nasal and pharyngeal | Nasopharyngeal |
| Laboratory findings | No MERS-CoV Prevalence 16.8% (141/839) Attack rate 17.5% (114/651) | No MERS-CoV Prevalence 25% (28/112) | No MERS-CoV Prevalence 14.7% (19/129) | No MERS-CoV Prevalence 2.7% (3/112) |
| Human rhinovirus (HRV) | 5.1% (43/839) Attack rate 1.1% (7/651) | 0% | 0.8% (1/129) | Not recorded |
| Influenza A | 1.3% (11/839) Attack rate 4% (5/112) | Prevalence 7% (9/129) | Not recorded | Not recorded |
| Influenza B | Not studied | Attack rate 0% | Prevalence 0.8% (1/129) | Not recorded |
| RSV | Prevalence 20.9% (27/129) (16 229E, 5 OC43, 5 HKU1 and 1 NL63) Attack rate 2% (2/112) (OC43 and 229E) | Prevalence 0.8% (1/129) | Not recorded | Not relevant |
| Non-MERS corona | Not studied | Attack rate 2% (2/112) (OC43 and 229E) | Prevalence 20.9% (27/129) (16 229E, 5 OC43, 5 HKU1 and 1 NL63) | Not recorded |
| Parainfluenza | Not studied | Attack rate 2.7% (3/112) | Prevalence 0.8% (1/129) | Not recorded |
| Dual viral infection | Prevalence 1.9% (16/839) (14 RSV/HRV and 2 Flu A/HRV) Attack rate 2% (2/112) (HRV/adenovirus and HRV/coronavirus) | Prevalence 0.8% (1/129) | Not recorded | Not relevant |

MERS-CoV, Middle East respiratory syndrome coronavirus.
further data on the epidemiology of respiratory viruses among Hajj pilgrims. Ongoing active surveillance is mandatory to better understand transmission dynamics of MERS-CoV.

Acknowledgement

The study conducted by our team [7] was made possible by a National Priorities Research Program grant from the Qatar National Research Fund (a member of Qatar Foundation).

Osamah Barasheed1, Mohammad Alfelali1, Mohamed Tashani1, Mohammad Azeem1, Hamid Bokhary2, Haitham El Bashir3, Harunor Rashid1 and Robert Booy1

1National Centre for Immunisation Research and Surveillance, University of Sydney, Sydney, NSW, Australia
2The Custodian of the two Holy Mosques Institute for Hajj and Umrah Research, Umm Al-Qura University, Makkah, Saudi Arabia
3Al Maha Children Unit, Hamad Medical Corporation, Doha, Qatar
E-mail: osamah.barasheed@health.nsw.gov.au

References

1. Annan A, Owusu M, Marfo KS 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: DOI: 10.1111/tmi.12482.
2. Haworth E, Barasheed O, Memish ZA, Rashid H, Booy R. Prevention of influenza at Hajj: applications for mass gatherings. J R Soc Med 2013: 106: 215–223.
3. Al-Tawfiq JA, Memish ZA. Emerging respiratory viral infections: MERS-CoV and influenza. Lancet Respir Med 2014: 2: 23–25.
4. Rashid H, Azeem MI, Heron L, Haworth E, Booy R, Memish ZA. Has Hajj-associated Middle East Respiratory Syndrome Coronavirus transmission occurred? The case for effective post-Hajj surveillance for infection. Clin Microbiol Infect 2014: 20: 273–276.
5. Pavli A, Tsiodras S, Maltezou HC. Middle East respiratory syndrome coronavirus (MERS-CoV); prevention in travelers. Travel Med Infect Dis 2014: 12: 602–8.
6. Benkouiten S, Charrel R, Belhouchat K et al. Respiratory viruses and bacteria among pilgrims during the 2013 Hajj. Emerg Infect Dis 2014: 20: 1821–1827.
7. Barasheed O, Rashid H, Alfelali M et al. Viral respiratory infections among Hajj pilgrims in 2013. Virol Sin 2014: 29: 364–371.
8. Memish ZA, Assiri A, Almasri M 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: 1067–1072.
9. Memish ZA, Al-Tawfiq JA, Makhdoom HQ et al. Respiratory tract samples, viral load, and genome fraction yield in patients with Middle East respiratory syndrome. J Infect Dis 2014: 210: 1590–1594.
10. Raoult D, Charrel R, Gautret P, Parola P. From the Hajj: it’s the flu, idiot. Clin Microbiol Infect 2014: 20: O1.
11. Rashid H, Shafi S, Haworth E, el Bashir H, Booy R. Influenza and RSV among returning travellers. Br J Infect Control 2008: 9: 17–18.
12. Rashid H, Shafi S, Booy R et al. Influenza and respiratory syncytial virus infections in British Hajj pilgrims. Emerg Health Threats J 2008: 1: e2.
13. Rashid H, Shafi S, Haworth E et al. Viral respiratory infections at the Hajj: comparison between UK and Saudi pilgrims. Clin Microbiol Infect 2008: 14: 569–574.
14. Majumder MS, Rivers C, Lofgren E, Fisman D. Estimation of MERS-coronavirus reproductive number and case fatality rate for the Spring 2014 Saudi Arabia outbreak: insights from publicly available data. PLoS Curr 2014: 6; doi: 10.1371/currents.outbreaks.98d2f8f3382d84f390736cd5f5f133c.
15. Lessler J, Rodriguez-Barraquer I, Cummings DA et al. Estimating potential incidence of MERS-CoV associated with Hajj Pilgrims to Saudi Arabia, 2014. PLoS Carr 2014: 6; doi: 10.1371/currents.outbreaks.c5c9c9abd636164a9b6f6d4dbda974369.
16. Alghamdi IG, Hussain I, Almalki SS, Alghamdi MS, Alghamdi MM, El-Sheemy MA. 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 2014: 7: 417–423.