

Editorial

The Hajj pilgrimage and surveillance for Middle East Respiratory syndrome coronavirus in pilgrims from African countries

Alimuddin Zumla^{1,2,3,4}, Peter Mwaba², Matthew Bates^{2,3}, Jaffar A. Al-Tawfiq^{1,5}, Markus Maeurer⁶ and Ziad A. Memish¹

¹ Global Centre for Mass Gatherings Medicine, Ministry of Health, Riyadh, Saudi Arabia

² UNZA-UCLMS Research and Training Programme, University Teaching Hospital, Lusaka, Zambia

³ Division of Infection and Immunity, University College London, London, UK

⁴ UCL Hospitals NHS Foundation Trust, London, UK

⁵ Saudi Aramco Medical Services Organization, Saudi Aramco, Dhahran, Saudi Arabia

⁶ Therapeutic Immunology Division, Department of Laboratory Medicine, Karolinska Institutet, Stockholm, Sweden

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It is well documented that mass gatherings attracting people from all over the world create an ideal environment for rapid transmission and spread of viral and bacterial respiratory infections (Abubakar *et al.* 2012). Africa has a large Muslim population estimated at over 250 million (Government 2011). Every year, more than 1 million pilgrims from African countries travel to Makkah and Madinah, Kingdom of Saudi Arabia (KSA) to join 10 million other pilgrims from around the globe to perform either the annual Hajj pilgrimage (Figure 1) or the Umrah, which can be performed at any time of the year (Memish *et al.* 2014a). One of the major public health concerns related to these journeys is the importation on arrival, or exportation on departure, of a range of

infectious diseases, some of which may have epidemic potential (Al Rabeeah *et al.* 2012; Al-Tawfiq & Memish 2012). For example, Rift Valley fever from East Africa caused outbreaks in KSA and Yemen (Fagbo 2002), and there have been two important meningococcal disease outbreaks in KSA related to the Hajj (al-Gahtani *et al.* 1995; Aguilera *et al.* 2002).

The past 15 years have seen the emergence of several killer respiratory tract infectious diseases with epidemic potential that generated global health alerts from WHO. Notable threats have come from avian influenza viruses, the Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and, more recently, the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and multidrug-resistant tuberculosis (Lee *et al.* 2003; Al-Tawfiq *et al.* 2013; Zumla *et al.* 2013b). The 2012 and 2013 Hajj pilgrimages were of major international concern because of the appearance in September 2012 of a new human pathogen, the Middle East respiratory syndrome coronavirus (MERS-CoV), first isolated from a patient in Jeddah, KSA, who died of a severe respiratory illness (Zaki *et al.* 2012). The appearance of this new, initially rapidly fatal infectious disease of unknown origin, and the uncertainty about its mode of transmission quickly focussed political and scientific attention, especially when MERS cases were detected in the UK, France, Germany and Italy (Zumla 2014). Contact and droplet transmission are the most likely route of human-to-human transmission of MERS-CoV, and people with medical comorbidities are more likely to succumb to the disease (WHO 2014a). MERS-CoV causes disease in all age and gender groups and can present as a spectrum of clinical presentations from the asymptomatic, to mild and more severe, rapidly fatal

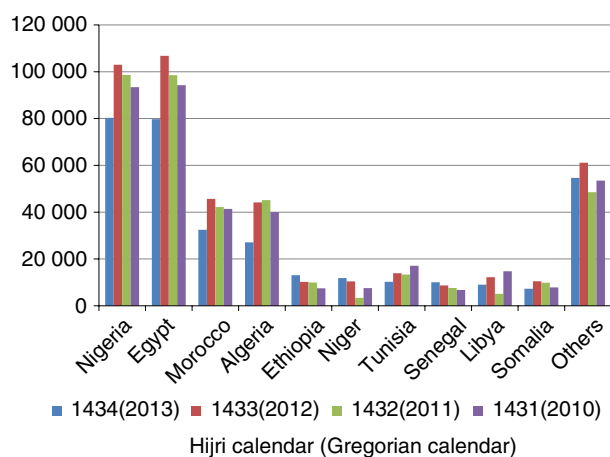


Figure 1 Absolute numbers of pilgrims traveling from different countries in Africa, stratified by year during period from 2010–2013.

illness (Assiri *et al.* 2013; Memish *et al.* 2014b; WHO 2014a).

The crucial missing epidemiological link is the source of MERS-CoV and mode of transmission from the reservoir to humans (Zumla 2014). Apart from KSA, MERS cases have been linked to six other countries in the Middle East: Jordan, Kuwait, Oman, Qatar, Tunisia and the United Arab Emirates, indicating that a widespread reservoir of MERS-CoV must exist in the Arabian Gulf. The search to find an animal source has implicated bats and dromedary camels as possible reservoirs of MERS-CoV. A study from KSA reported detection of a short nucleotide sequence the faeces of the bat *Taphozous perforatus*, which was identical to that of MERS-CoV isolated from the index human MERS case in Jeddah, KSA (Memish *et al.* 2014b). Several betacoronaviruses genetically closely related to MERS-CoV have been isolated from the faeces of South African bats (Memish *et al.* 2013). There is growing evidence from several studies that dromedary camels may be playing an important role in MERS-CoV transmission to humans. Serological studies have found MERS-CoV antibodies in camels in Jordan, Tunisia, Ethiopia, Nigeria, Egypt, Saudi Arabia, Canary Islands and UAE, and MERS-CoV has been detected in camels from Qatar, Saudi Arabia and Egypt (Hemida *et al.* 2013; Reusken *et al.* 2013; Alagaili *et al.* 2014; Alexandersen *et al.* 2014; Haagmans *et al.* 2014), lending strong support to the hypothesis that transmission is likely occurring from camels to humans, infection occurring either directly or indirectly through consumption of contaminated food or contaminated fomites. Several important epidemiological questions regarding the distribution and determinants of MERS-CoV infection in humans arise:

- As of March 1st 2014, nearly 2 years after MERS-CoV was first discovered, there have been a total of 180 cases of MERS-CoV infection with a 46% mortality rate reported worldwide to the WHO. All cases have had links to the Middle East, and the majority of cases (151 with 62 deaths (41% mortality) have been reported from KSA as of March 5, 2014. Does MERS-CoV only affect populations in the Middle East or is it also prevalent in countries in Africa, Asia, Australia and South America where camels are present?
- Does this focus on the Middle East represent a bias in case detection due to a high degree of awareness and governments having a more proactive screening programme for MERS-CoV?
- Is there evidence of association with the genetic make-up of Middle Eastern populations that would make people more or less susceptible to infection with MERS-CoV, as reported for other infectious diseases (Blackwell *et al.* 2009; Apps *et al.* 2013)?
- What role does co-infection with other respiratory disease pathogens play in clinical presentations of MERS-CoV (Rizzo *et al.* 2010; Redford *et al.* 2014)?
- When was MERS-CoV actually introduced into human populations and how did it cross the species barrier?

During the 2012 and 2013 Hajj pilgrimages, 5 million pilgrims from 184 countries (including 500 000 from African countries) visited Makkah and Madinah in KSA, and no cases of MERS-CoV were detected during their stay in KSA or after the pilgrims returned home. As both camels and bats are found in all parts of Africa, there is a high likelihood of MERS-CoV infections being missed. There is certainly a lack of awareness of MERS-CoV across the African continent and beyond the Middle East amongst healthcare workers. Furthermore, diagnostic services for respiratory viral infections are virtually non-existent at most entry points in the health system and are scanty at referral centres.

In response to the potential threat of an influenza pandemic, several international institutions and governments, in partnership with 15 African countries, invested in the development of epidemiologic and laboratory influenza surveillance capacity in Africa, and the African Network of Influenza Surveillance and Epidemiology (ANISE) was formed (Kasolo *et al.* 2013). The project ‘Strengthening Influenza Sentinel Surveillance in Africa (SISA)’ is currently generating epidemiological and virological data and developing routine national, regional and international reporting mechanisms (Kebede *et al.* 2013) in liaison with WHO, national influenza laboratories and other stakeholders involved in influenza surveillance. This initiative must be extended to screening for MERS-CoV. A large percentage of pilgrims return to their home countries after the Hajj pilgrimage with symptoms of respiratory tract infections. Thus, there is a dire need for developing rapid diagnostic platforms for screening of multiple pathogens in patients presenting with acute respiratory tract infections at all points of care (Zumla *et al.* 2013a) so accurate and early identification can be made, allowing for appropriate treatment and infection control measures to be accorded. Meanwhile, it is important that a more proactive search for MERS-CoV infections is performed by healthcare workers in African countries using current guidelines for MERS-CoV screening and testing (CDC 2014; WHO 2014b) and that they keep a high degree of awareness of the possibility of MERS-CoV infection in all patients presenting with RTIs.

References

- Abubakar I, Gautret P, Brunette GW *et al.* (2012) Global perspectives for prevention of infectious diseases associated with mass gatherings. *The Lancet Infectious Diseases* **12**, 66–74.
- Aguilera JF, Perrocheau A, Meffre C *et al.* (2002) Outbreak of serogroup W135 meningococcal disease after the Hajj pilgrimage, Europe 2000. *Emerging Infectious Diseases* **8**, 761–767.
- Al Rabeeah A, Memish ZA, Zumla A *et al.* (2012) Mass gatherings medicine and global health security. *Lancet* **380**, 3–4.
- Alagaili AN, Briese T, Mishra N *et al.* (2014) Middle East respiratory syndrome coronavirus infection in dromedary camels in Saudi Arabia. *MBio* **5**, e00884–14.
- Alexandersen S, Kobinger GP, Soule G *et al.* (2014) Middle East respiratory syndrome coronavirus antibody reactors among camels in dubai, United arab emirates, in 2005. *Transboundary and Emerging Diseases* **61**, 105–108.
- Al-Tawfiq JA & Memish ZA (2012) Mass gatherings and infectious diseases: prevention, detection, and control. *Infectious Disease Clinics of North America* **26**, 725–737.
- Al-Tawfiq JA, Smallwood CA, Arbuthnott KG *et al.* (2013) Emerging respiratory and novel coronavirus 2012 infections and mass gatherings. *Eastern Mediterranean Health Journal* **19**(Suppl 1), S48–S54.
- Apps R, Qi Y, Carlson JM *et al.* (2013) Influence of HLA-C expression level on HIV control. *Science* **340**, 87–91.
- Assiri A, McGeer A, Perl TM *et al.* (2013) Hospital outbreak of Middle East respiratory syndrome coronavirus. *New England Journal of Medicine* **369**, 407–416.
- Blackwell JM, Jamieson SE & Burgner D (2009) HLA and infectious diseases. *Clinical Microbiology Reviews* **22**, 370–385, Table of Contents.
- CDC (2014) *Middle East Respiratory Syndrome (MERS)* [Online]. CDC, Atlanta. Available: <http://www.cdc.gov/coronavirus/mers/> Accessed 6 March 2014.
- Fagbo SF (2002) The evolving transmission pattern of Rift Valley fever in the Arabian Peninsula. *Annals of the New York Academy of Sciences* **969**, 201–204.
- al-Gahtani YM, el Bushra HE, al-Qarawi SM *et al.* (1995) Epidemiological investigation of an outbreak of meningococcal meningitis in Makkah (Mecca), Saudi Arabia 1992. *Epidemiology and Infection* **115**, 399–409.
- Government, U (2011) *2011 Report on International Religious Freedom* [Online]. US Government. Available: <http://www.state.gov/j/drl/rls/irfr/2011/> Accessed 6 March 2014.
- Haagmans BL, Al Dhahiry SH, Reusken CB *et al.* (2014) Middle East respiratory syndrome coronavirus in dromedary camels: an outbreak investigation. *The Lancet Infectious Diseases* **14**, 140–145.
- Hemida MG, Perera RA, Wang P *et al.* (2013) Middle East Respiratory Syndrome (MERS) coronavirus seroprevalence in domestic livestock in Saudi Arabia 2010 to 2013. *Eurosurveillance Weekly* **18**, 20659.
- Kasolo F, Yoti Z, Bakyaite N *et al.* (2013) IDSR as a platform for implementing IHR in African countries. *Biosecurity and Bioterrorism* **11**, 163–169.
- Kebede S, Conteh IN, Steffen CA *et al.* (2013) Establishing a national influenza sentinel surveillance system in a limited resource setting, experience of Sierra Leone. *Health Research Policy and Systems* **11**, 22.
- Lee N, Hui D, Wu A *et al.* (2003) A major outbreak of severe acute respiratory syndrome in Hong Kong. *New England Journal of Medicine* **348**, 1986–1994.
- Memish ZA, Mishra N, Olival KJ *et al.* (2013) Middle East respiratory syndrome coronavirus in bats, Saudi Arabia. *Emerging Infectious Diseases* **19**, 1819–1823.
- Memish Z, Zumla A, Alhakeem R *et al.* (2014a). The Annual Hajj Pilgrimage: Infectious Disease Surveillance and Control. *Lancet* in press.
- Memish ZA, Al-Tawfiq JA, Makhdoom HQ *et al.* (2014b). Screening for Middle East respiratory syndrome coronavirus infection in hospital patients and their healthcare worker and family contacts: a prospective descriptive study. *Clinical Microbiology and Infection* doi:10.1111/1469-0691.12562. [Epub ahead of print].
- Redford PS, Mayer-Barber KD, McNab FW *et al.* (2014) Influenza A virus impairs control of Mycobacterium tuberculosis coinfection through a type I interferon receptor-dependent pathway. *Journal of Infectious Diseases* **209**, 270–274.
- Reusken CB, Haagmans BL, Muller MA *et al.* (2013) Middle East respiratory syndrome coronavirus neutralising serum antibodies in dromedary camels: a comparative serological study. *The Lancet Infectious Diseases* **13**, 859–866.
- Rizzo C, Caporali MG & Rota MC (2010) Pandemic influenza and pneumonia due to Legionella pneumophila: a frequently underestimated coinfection. *Clinical Infectious Diseases* **51**, 115.
- WHO (2014a). *Middle East Respiratory Syndrome Coronavirus (MERS-CoV) Summary and Literature Update—as of 20 January 2014*. WHO, Geneva.
- WHO (2014b) *Revised Interim Case Definition for Reporting to WHO – Middle East Respiratory Syndrome Coronavirus (MERS-CoV)* [Online]. WHO, Geneva. Available: http://www.who.int/csr/disease/coronavirus_infections/case_definition/en/.
- Zaki AM, van Boheemen S, Bestebroer TM *et al.* (2012) Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. *New England Journal of Medicine* **367**, 1814–1820.
- Zumla AI (2014) Middle East Respiratory Syndrome Coronavirus – Epidemic Potential or ‘Storm in a Teacup’. *European Respiratory Journal*. [Epub ahead of print].
- Zumla A, George A, Sharma V *et al.* (2013a) WHO’s 2013 global report on tuberculosis: successes, threats, and opportunities. *Lancet* **382**, 1765–1767.
- Zumla A, Gant V, Bates M *et al.* (2013b) Rapid diagnostics urgently needed for killer infections. *The Lancet Respiratory Medicine* **1**, 284–285.

Corresponding Author Ziad A. Memish, Al-Faisal University, Riyadh 11176, Saudi Arabia. E-mail: zmemish@yahoo.com