

Perspective

Call to action for improved case definition and contact tracing for MERS-CoV

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MERS-CoV has plagued countries of the Eastern Mediterranean region since April 2012 and has since spread to 27 countries across the globe, with more than 2274 cases with 842 case fatalities (FAO Animal Health Service/EMPRES. MERS-CoV situation update 21 November 2018, 17:00 h; Rome, http://www.fao.org/ag/againfo/programmes/en/empres/mers/situation_update.html). The spread of MERS-CoV to countries outside the Arabian Peninsula has been through travellers incubating the disease with minimal/or no symptoms while travelling. To date, no documented transmission of MERS-CoV has been proved to be associated with the transportation systems or hubs.¹ The most recent travel incident was through a South Korean business traveller to the State of Kuwait who went back to South Korea (SK), and on arrival, he developed respiratory symptoms and was promptly isolated and the diagnosis of MERS-CoV was confirmed. This was the second incident of an MERS-CoV-positive returning traveller that SK had to deal with, but fortunately there was no transmission to other passengers on the same flight or in SK.^{2–4}

Saudi Arabia (KSA) so far has carried the greatest brunt of MERS-CoV since its emergence, with 85% of the total global reported cases being either diagnosed or originating in KSA, with a total of 1897 cases and 734 fatalities (FAO Animal Health Service/EMPRES. MERS-CoV situation update 21 November 2018, 17:00 h; Rome, http://www.fao.org/ag/againfo/programmes/en/empres/mers/situation_update.html).⁵ Progress has been made in KSA since the disease emerged in reducing the number and size of explosive healthcare facilities (HCF) outbreaks. This was achieved by increasing healthcare workers' (HCW) knowledge about the disease, improving infection prevention and control practices in HCFs, the application of a wide-net disease case definition and strict screening and triage in emergency room (ER) of all HCFs in KSA. This undoubtedly comes at a very high cost through excessive testing for MERS-CoV, increased workload for HCW,

prolongation of patient waiting time in emergency rooms and an unmeasured compromise in handling urgent cardiac and renal failure patients who often are mislabelled as suspected MERS-CoV patients on ER presentation. The financial toll of MERS-CoV and its preventative strategies is yet to be estimated, and the impact of MERS-CoV on the performance of other national communicable disease preventive programs is unknown.

The undoubtedly costly efforts to control MERS-CoV in KSA to date have not significantly impacted the number of primary/community MERS-CoV cases with or without animal exposure over the last 6 years. Despite the overall reduction in the number of HCF-associated outbreaks, we continue to be challenged with many HCWs affected by the disease (FAO Animal Health Service/EMPRES. MERS-CoV situation update 21 November 2018, 17:00 h; Rome, http://www.fao.org/ag/againfo/programmes/en/empres/mers/situation_update.html).

One of the strategies to assess the robustness of MERS-CoV case definition is to evaluate the cost-effectiveness of diagnostic testing at a national level. Healthcare in KSA is divided between the Ministry of Health (MoH) and other government sectors, at a ratio of 70:30%. Over the last 3 years, the KSA MoH has purchased between 125 000 and 140 000 MERS-CoV PCR kits annually. The estimated cost of doing one PCR test in the lab (inclusive of genetic extraction, PCR test, controls and consumables) is around 60 USD (personal communication KSA MoH). On a national level, between 10 and 11 million USD are spent annually on MERS-CoV testing alone. The yield of this testing is extremely low, based on a recent report from the Saudi MoH, which indicated that over a 10-month period (1 April 2015–1 February 2016) only 384/57 363 (0.7%) of MERS-CoV PCR tests were positive.⁶ This highlights an urgent need to re-evaluate the current case definition for MERS-CoV, even though its fifth version was just released on May 2018 (MIDDLE EAST

RESPIRATORY SYNDROME CORONAVIRUS; GUIDELINES FOR HEALTHCARE PROFESSIONALS 5th ed. May 2018. Available at: <https://www.moh.gov.sa/CCC/healthp/regulations/Documents/MERS-CoV%20Guidelines%20for%20Healthcare%20Professionals%20-%20May%202018%20-%20v5.1%20%281%29.pdf>). The wider case definition is usually recommended earlier in the course of any emerging epidemic to capture all suspected cases and limit disease spread nationally, regionally and globally. But as more knowledge about the disease accumulates over time, refinement of the case definition is needed to make it more precise and to refocus resources available to new areas in need of research and development.

Two key infection prevention and control questions with MERS-CoV have challenged the national and global infection control community: the first is early identification of MERS-CoV-infected patients presenting to HCFs with respiratory symptoms for immediate application of proper isolation precaution to prevent further spread of the disease to other patients and HCWs.⁷ The second challenge has been to accurately identify all significant asymptomatic/symptomatic contacts of confirmed MERS-CoV cases at risk of acquiring the disease. More than 20% of MERS-CoV cases occurred in HCWs, and strict measures are needed to decrease this high rate (FAO Animal Health Service/EMPRES. MERS-CoV situation update 21 November 2018, 17:00 h; Rome, http://www.fao.org/ag/againfo/programmes/en/empres/mers/situation_update.html).

The ideal strategy to detect MERS-CoV cases early is to develop Point of Care Testing (POCT) that is sensitive, specific, affordable, rapid, automated and can be easily applied. Multiple POCTs have been developed and others are under development, all waiting to be validated nationally in KSA.^{8,9} The KSA MoH attempted to address the early detection of suspected MERS-CoV cases among patients presenting with respiratory symptoms through a visual triage system which was developed and continues to be adopted at the national level since its development in 2016. It is a scoring system applied on every patient presenting with respiratory symptoms to any ER or haemodialysis unit nationally. The score takes into account certain demographic, clinical signs and symptoms and risky exposures. A score of 4 was selected randomly to represent a high risk of MERS-CoV requiring directing the patient to a respiratory pathway, prompt medical assessment and isolation and testing. A recent small-scale evaluation of this system indicated the lack of sensitivity and specificity in detecting MERS-CoV-positive patients even if the score was increased to 8.¹⁰ Large-scale, national evaluation of this system is needed to make a decision regarding its use.

Protecting the lives of the HCWs from emerging fatal viral diseases should be one of the highest priorities of any healthcare system. Over the last 6 years, evidence has emerged that super spreading events are a hallmark of corona viruses, with multiple detailed HCF outbreak investigations revealing the following key infection control facts: exposed patients/HCWs can be infected if they are in the same space with the index case (with no relation to time spent or distance from the index case), HCWs can test positive for the virus any time during the full incubation period (14 days) and, finally, asymptomatic infections are common among HCWs and are infectious and to rule out infection among HCWs a minimum of two tests spanning the whole incubation period are needed.^{11–13}

Updated WHO guidelines on handling outbreak investigations in HCFs kept the above infection control challenges in mind while developing the updated standards released in January 2018. The WHO guidance encourages liberal testing of all contacts, with special focus on HCWs, and stressed the need for isolating all asymptomatic RT-PCR-positive persons from HCF outbreak investigations with repeat testing at least weekly or earlier, if symptoms develop, releasing positive contacts only after two negative PCR results 24–48 h apart (WHO Management of asymptomatic persons who are RT-PCR positive For Middle East respiratory syndrome coronavirus (MERS-CoV): Interim Guidance 3 January 2018, WHO/MERS/IPC/15.2 Rev.1. 2018, http://apps.who.int/iris/bitstream/handle/10665/180973/WHO_MERS_IPC_15.2_eng.pdf?sequence=1. [Accessed November 2018].). This contrasts with the fifth version of the Saudi MoH MERS-CoV case definition and National IC guidance, which underplays the need for liberal testing or isolating asymptomatic HCF outbreak contacts, in addition to introducing criteria like presence of symptoms, significance of contact based on distance and time spent with the index case and finally requiring HCW contacts to resume work after one negative result.

Dealing with a new emerging viral outbreak has proven to be extremely challenging to manage and extremely costly, especially when no vaccine or therapeutic agents are approved and when limited data on the value of post-exposure prophylaxis among healthcare workers are available.¹⁴ Data on the economic impact of MERS-CoV on individual HCF and on the national healthcare infrastructure in KSA have not been documented and its availability would help decision-makers in re-channelling the money to more cost-effective programs.

The MERS-CoV case definition needs to be streamlined further and, based on the available evidence to date, it should not focus on all patients with severe pneumonia or ARDS or unexplained deterioration of a chronic condition of patients with congestive heart failure or chronic kidney disease on haemodialysis without a risky exposure. But the definition should ensure that the above 2-patient categories are triaged through POCT mechanisms in hospitals and dialysis centres across the whole healthcare systems in KSA. For the two other categories of the case definition which are linked to risky exposure and includes fever and gastrointestinal symptoms, a critical review of the national database of MERS-CoV reported cases should be undertaken to test its sensitivity and specificity. In addition, investment in liberal testing of contacts of confirmed MERS-CoV cases in HCF should be encouraged and staff and contacts should be quarantined until the incubation period has lapsed.

The KSA MoH efforts need to be commended and with 6 years since the emergence of MERS-COV, the knowledge and expertise gained by MoH staff is tremendous and need to be better utilized. Identification of research priorities to address the key knowledge gaps in controlling MERS-CoV is urgently needed. Although global concerns about the role of travel in spreading MERS-CoV among the rising Hajj and Umrah pilgrims and causing pandemic have been justified, it never materialized. We should continue to spread evidence-based recommendations to limit the number of pilgrims who are very old, very young, immunocompromised, with multiple chronic diseases and comorbidities from attending the Hajj and to promote staying away from farms and contact with camels during their visit to

KSA, which has been clearly shown to be the key reservoir for the disease identified to date.

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