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Perspective

Healthcare worker exposure to Middle East respiratory syndrome coronavirus (MERS-CoV): Revision of screening strategies urgently needed

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ABSTRACT

Objectives: Middle East respiratory syndrome coronavirus (MERS-CoV) continues to cause frequent hospital outbreaks in Saudi Arabia, with emergency departments as the initial site of the spread of this virus.
Methods: The risk of transmission of MERS-CoV infection to healthcare workers (HCWs) was assessed in an outbreak in Riyadh. All HCWs with unprotected exposure to confirmed cases were tested after 24 h of exposure. Two negative results for MERS-CoV obtained 3 days apart and being free of any suggestive signs and symptoms were used to end the isolation of the HCWs and allow their return to duty.
Results: Overall 17 out of 879 HCWS with different levels of exposure tested positive for MERS-CoV. Of the 15 positive HCWS with adequate follow-up, 40% (6/15 HCWs) tested positive on the first sampling and 53% (8/15) tested positive on the second sampling. The time to negative results among the 15 positive HCWs ranged between 4 and 47 days (average 14.5 days) and the infected HCWs needed on average two samples for clearance. All positive HCWs were either asymptomatic or had mild disease.
Conclusions: The data obtained in this study support the widespread testing of all close contacts of MERS-CoV cases, regardless of the significance of the contact or presence or absence of symptoms. In addition, urgent careful review of guidance regarding the return of asymptomatic MERS-CoV-positive HCWs under investigation to active duty is needed.

Introduction

The Middle East respiratory syndrome coronavirus (MERS-CoV) is a pathogen of zoonotic reservoir that has caused many outbreaks in healthcare settings, involving many healthcare workers (HCWs) (Alfaraj et al., 2018a; Memish and Al-Tawfiq, 2014). As of February 2018, a total of 2143 laboratory-confirmed cases of infection with MERS-CoV including 750 deaths had been reported globally from 27 countries, including 12 countries of the Middle East (Anon, 2018). Emergency departments have been highlighted as the initial site of the spread of this virus in most of the recent outbreaks (Ghazal et al., 2017; Assiri et al., 2013; Balkhy et al., 2016).

A recent MERS-CoV outbreak occurred at King Saud Medical City (KSMC), concurrent with outbreaks at two other hospitals in the Riyadh region in June 2017 (Amer et al., 2018). This study was performed to better understand the best strategies to handle exposed HCWs. The risk of transmission of MERS-CoV infection to HCWs in this outbreak was assessed and all available literature reviewed in an attempt to improve future preventive and post-exposure management interventions.

Method

A descriptive report on exposure criteria and screening results of HCWs acquiring MERS-CoV infection during the June 2017

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outbreak at KSMC was produced. Real-time PCR (RT-PCR) of nasopharyngeal samples was used to test the traced contacts for MERS-CoV. All HCWs with unprotected exposure to confirmed cases were tested after 24 h of exposure. Two negative results for MERS-CoV obtained 3 days apart and being free of any suggestive signs and symptoms were used to stop their isolation and allow them to return to active duty. Further retesting depended on being symptomatic within the 14-day post-exposure monitoring period. Data were collected as part of the post-exposure management process.

Results and discussion

Considering the super-spreading phenomenon of some of the reported positive MERS-CoV cases during the KSMC outbreak and because some of the cases had been intubated in a multi-bed room before being suspected and isolated, the tracing of contacts was very inclusive and included all persons who had been in attendance in the same area where the patient had stayed. A total of 1055 subjects were traced at the time: 879 HCWs and 176 patients. HCWs who had experienced high-risk unprotected exposure or had performed or attended aerosol-generating procedures (even if protected) were swabbed twice, while those who had experienced unprotected low-risk exposure and protected HCWs not attending aerosol-generating procedures were swabbed once. A total of 2000 swabs were collected during the outbreak period.

Overall 17 HCWS tested positive for MERS-CoV linked to four index cases. The first two index cases were super-spreaders, with the first case infecting nine exposed HCWs and the second index case infecting six exposed HCWs. The third and fourth index cases infected one HCW each. Two of the nine affected HCWs related to the first index case are not included in this report (Table 1). The activities undertaken by the infected HCWs ranged from mild exposure, e.g., exposure during routine nursing care, being in the same clinical area, or just having a simple peer conversation, to more high-risk exposure, e.g., intubation and connecting infected patients on bilevel positive airway pressure (BiPAP). Of all the positive HCW contacts, 40% (6/15 HCWs) tested positive on the first sampling, 53% (8/15) tested positive on the second sampling, and only one HCW tested positive on the third sampling. Fortunately, none of the positive MERS-CoV HCWs had severe disease: 53% were asymptomatic and 46% had mild symptoms. The presence or absence of symptoms was found to be unrelated to the infected HCWs cycle threshold (CT) value. Among the 15 positive HCWs, the time to negative results ranged between 4 and 47 days (average 14.5 days) and the infected HCWs needed on average two samples for clearance.

Over the last 5 years, since the virus emerged in September 2012, it has been found that the incubation period for MERS-CoV cases in whom exposure is known is between 5.5 and 6.5 days, and evidence suggests that the incubation period could be as long as 14 days. The infection control community continues to be challenged by the lack of updated evidence-based infection control guidelines for handling HCWs in contact with cases positive for MERS-CoV. Some of the key questions include: (1) Which of the exposed HCWs are at risk of acquiring MERS-CoV and need to be tested? (2) What exposure justifies testing? (3) Should asymptomatic contacts be screened? (4) Are asymptomatic positive HCWs infectious? (5) How many samples need to be taken for confirmation of positivity

Table 1
Characteristics of confirmed MERS-CoV cases.

Demographic characteristics					Exposure			Screening				Progress		
No.	Specialty	Sex	Age, years	Nationality	Source case	Area	Level of care/contact	Days to positive from exposure	Sequence of 1st positive	CT value	Symptoms[a]	Isolation	No. of repeated positives	Days to negative
1	Nurse	F	29	Filipino	A	ER	Routine care	4	1st	30	Mild	Hospital	14	47
2	Nurse	F	32	Filipino	A	ER	Routine care	4	1st	32	Mild	Hospital	7	23
3	Nurse	F	30	Filipino	A	ER	Hooked BiPAP	4	1st	31	Mild	Hospital	6	21
4	RRT nurse	F	47	Filipino	A	Medical ward 1	Intubation	10	2nd	33	None	Dormitory	0	4
5	RRT nurse	F	27	Filipino	A	Medical ward 1	Intubation	11	3rd	27	Mild	Dormitory	2	10
6	ICU specialist	M	39	Indian	A	Medical ward 1	Intubation	10	1st	30	None	Home	6	26
7	Cardiology specialist	M	26	Saudi	A	ER	Attending the same area No direct care	8	2nd	26	Mild	Home	4	26
8	RRT nurse	F	30	Filipino	B	Medical ward 2	Intubation	6	2nd	33	Mild	Hospital	4	20
9	Bedside nurse	F	32	Filipino	B	Medical ward 2	Routine care	6	2nd	26	Mild	Hospital	4	21
10	Bedside nurse	F	26	Filipino	B	Medical ward 2	Routine care	6	2nd	21	None	Dormitory	1	8
11	Bedside nurse	F	28	Filipino	B	Medical ward 2	Routine care	8	2nd	31	None	Dormitory	1	11
12	RRT nurse	F	32	Filipino	B	Medical ward 2	Intubation assistance	6	2nd	23	None	Dormitory	2	17
13	RRT nurse	F	32	Indian	B	Medical ward 2	Intubation	3	1st	28	None	Home	0	4
14	Cardiology specialist	M	34	Egyptian	C	Office	Peer conversation	5	1st	33	None	Home	0	6
15	Nurse	F	31	Filipino	D	ER	Routine care	8	2nd	34	None	Dormitory	0	4

BiPAP, bilevel positive airway pressure; CT, cycle threshold; ER, emergency room; F, female; ICU, intensive care unit; M, male; MERS-CoV, Middle East respiratory syndrome coronavirus; RRT, rapid response team.

[a] Mild symptoms: dry cough or mild upper respiratory illness symptoms.

and clearance and how many days apart? (6) How long should HCWs be quarantined and when is it safe for them to return to active duty?

Although many reports of hospital outbreaks have been published to date, very few have discussed these key infection control questions in any detail. This is why national and international guidance on managing exposed HCWs has been inconsistent and sometimes confusing to the professional infection control community. The latest available guidance from the Saudi Ministry of Health published in 2017 still discourages the testing of asymptomatic HCWs and allows only one sample from HCWs who have had high-risk exposure to be cleared (Command and Control Center Ministry of Health Kingdom of Saudi Arabia Scientific Advisory Board, 2017). Similarly, the latest US Centers for Disease Control and Prevention guidance published in 2015 discourages the testing of asymptomatic contacts (CDC, 2015).

The World Health Organization (WHO), as always, has the most comprehensive guidance, which is balanced, evidence-based, considers the different levels of healthcare infrastructure, and most importantly is built on the consensus of expert opinion leaders from the six WHO regions. In their interim guidance released in June 2015, the WHO makes recommendations for inclusive testing in clusters/outbreaks associated with healthcare settings: "if feasible, all contacts of laboratory confirmed cases, especially HCW contacts and inpatients sharing rooms/wards with confirmed cases, regardless of the development of symptoms, should be tested for MERS-CoV using PCR" (WHO, 2018a). In 2015, the WHO also provided guidance on the management of asymptomatic persons who were PCR-positive, and in January 2018 published updated recommendations (WHO, 2018b,c). In both documents the WHO states: "Until more is known, asymptomatic RT-PCR positive persons should be isolated, followed up daily for symptoms and tested at least weekly – or earlier, if symptoms develop – for MERS-CoV until a first negative test and then every 24–48 hours, releasing positive contacts only after 2 negative PCR results 24 hrs apart".

Home versus hospital isolation of RT-PCR-positive persons depends on isolation bed capacity, the ability to monitor persons daily outside a healthcare setting, and the overall social conditions of the household and its occupants.

Unfortunately, due to the lack of scientific evidence at the time of guideline development, the same WHO guidance documents give member states the conditional permission to return their asymptomatic PCR-positive HCWs to active duty if there are a significant number of asymptomatic RT-PCR-positive HCWs and concerns exist about keeping the healthcare system functioning for all patients during an outbreak. Clearance is bound by the following conditions, which are almost impossible to comply with and monitor in a healthcare facility with an ongoing MERS-CoV outbreak: there should be good infection control infrastructure in the facility, HCWs should not work in areas with patients at risk of MERS-CoV infection complications, and all positive HCWs should be monitored by repeat PCR testing for virus clearance and for compliance with good infection control practices, including wearing masks when within 1 meter of others (HCWS or patients). This component of the guidance needs to be revised based on the recent evidence showing possible transmission from asymptomatic PCR-positive HCWs, which could put patients and other HCWs at unnecessary risk if the conditions mentioned in the WHO document are not strictly applied and monitored (Alfaraj et al., 2018b).

A recently published report from another hospital outbreak in Riyadh involving 153 HCW contacts with seven (4.5%) HCWs testing positive for MERS-CoV looked critically at the ideal infection control practices in handling HCWs in contact with positive cases (Alfaraj et al., 2018b). The findings of that report are consistent with those of the present study, confirming the lack of relevance regarding the extent of exposure or presence or absence of symptoms among HCW contacts of confirmed MERS-CoV cases (Alfaraj et al., 2018b). Both reports highlight the difficulties in ruling out positive HCWs from the first sample and stress the need for repeat sampling to confirm positivity and negativity. This report corroborates what has been published previously and calls for an urgent review and update of the available local and international guidance on handling HCWs in contact with MERS-CoV-positive cases and encourages critical monitoring of future outbreaks to answer any remaining infection control queries.

Five years after the emergence of the disease, significant new knowledge has been gained, but some gaps and challenges remain, including the definite source of infection and the exact routes of direct or indirect exposure, how to predict super-spreaders, clear guidance on handling exposed HCWS who can act as disease carriers spreading the disease to others, and finally how to detect cases early in the emergency room with the development of rapid, easy-to-use, highly sensitive and specific point-of-care testing.

In an effort to prevent any unnecessary risky exposure of HCWs and possibly compromising HCW and patient safety by propagating healthcare-associated outbreaks, the available evidence to date supports the 2015 WHO guidance in its call to be liberal in testing all 'close contacts' of MERS-CoV cases, regardless of the significance of contact or presence or absence of symptoms, as well as the need for repeat testing weekly until negative and every 24–48 h for release from isolation. In addition, urgent careful review of guidance regarding the return of asymptomatic MERS-CoV-positive HCWs under investigation to active duty is needed. All public health guidelines, especially those addressing emerging pathogens of international public health importance, need to be regularly updated based on new scientific evidence; furthermore, areas of ambiguity need to be addressed with focused research initiatives by the countries affected.

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Ethical approval

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Conflict of interest

All authors declare no conflict of interest.

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