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Major Article

Outcome of strict implementation of infection prevention control measures during an outbreak of Middle East respiratory syndrome

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Key Words:
Middle East Respiratory Syndrome (MERS)
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Background: The objective of this retrospective cohort study was to assess the impact of implementation of different levels of infection prevention and control (IPC) measures during an outbreak of Middle East respiratory syndrome (MERS) in a large tertiary hospital in Saudi Arabia. The setting was an emergency room (ER) in a large tertiary hospital and included primary and secondary MERS patients.

Methods: Rapid response teams conducted repeated assessments of IPC and monitored implementation of corrective measures using a detailed structured checklist. We ascertained the epidemiologic link between patients and calculated the secondary attack rate per 10,000 patients visiting the ER (SAR/10,000) in 3 phases of the outbreak.

Results: In phase I, 6 primary cases gave rise to 48 secondary cases over 4 generations, including a case that resulted in 9 cases in the first generation of secondary cases and 21 cases over a chain of 4 generations. During the second and third phases, the number of secondary cases sharply dropped to 18 cases and 1 case, respectively, from a comparable number of primary cases. The SAR/10,000 dropped from 75 (95% confidence interval [CI], 55-99) in phase I to 29 (95% CI, 17-46) and 3 (95% CI, 0-17) in phases II and III, respectively.

Conclusions: The study demonstrated salient evidence that proper institution of IPC measures during management of an outbreak of MERS could remarkably change the course of the outbreak.

Middle East respiratory syndrome (MERS) is an epidemic-prone viral disease with a high case fatality rate and ill-defined mode of transmission.[1-6] Currently, there is no safe and effective vaccine and chemoprophylaxis for the disease.[7] Major outbreaks of symptomatic MERS occurred in some major health facilities; these outbreaks were attributed to inadequate adherence of health care workers (HCWs) to infection prevention and control (IPC) guidelines.[8-10] Screening of HCWs and inpatients during outbreaks using polymerase chain reaction and serologic tests revealed more asymptomatic cases of MERS infections.[11] The role of HCWs with asymptomatic infections in further spreading the disease and amplification of outbreaks is not fully understood.[12] Preventing transmission of MERS in hospitals requires increased awareness of HCWs about the disease, triaging and isolation of patients who might have MERS infection, early detection, adherence to standard IPC procedures, and protocols and use of personal protective equipment (PPE), especially when performing aerosol-generating procedures.[6,13] Successful implementation of IPC measures depends on the presence of clear administrative policies and organizational leadership that promotes and facilitates adherence to IPC guidelines within the health care settings, including HCWs, patients, and visitors to the admitted patients.[14]

An outbreak of MERS occurred in an emergency room (ER) of a large tertiary hospital in Riyadh City (LTHR), Saudi Arabia; the ER

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has 150 beds and >1,000 HCWs.[12] The aim of this article is to demonstrate the outcome of strict implementation of IPC measures during the outbreak of MERS.

BACKGROUND

Materials and methods

The Ministry of Health of Saudi Arabia created a rapid response team (RRT) as part of its response to MERS outbreaks in public and private health care facilities in the Kingdom of Saudi Arabia. The main objective of the RRT is to ensure that all health care facilities are complying with Ministry of Health IPC guidelines and receive timely and appropriate technical support and supplies as deemed necessary. The RRT visits the health facilities, conducts independent assessments, audits IPC measures, and assesses the performances of the IPC team and HCWs. The RRT assesses the IPC performance within health facilities using a detailed structured checklist composed of 10 elements (approximately 125 specific observations). Each element is given a score of 0-2, depending on whether the health facility was fully, partially, or noncompliant. By the end of each visit, the RRT develops action plans with the hospital management to be immediately implemented.

According to the IPC guidelines, the hospital leadership is accountable for supporting the infection prevention activities that are relevant to the services provided and the patient populations cared for at the facility. The hospital ensures presence of ≥1 dedicated qualified IPC staff, adherence of HCWs to IPC measures, and presence of a designated triage area in the ER for suspected MERS that is physically separated from other areas in the ER. The IPC guidelines have a special section for collection of biologic specimens and for aerosol-generating procedures. Suspected MERS patients and other persons in the triage area (eg, persons accompanying suspected MERS patients) are instructed to wear facemasks and are placed in a separated area (by at least 1.5 m) from each other.

Demographic, epidemiologic, and clinical data about laboratory-confirmed MERS cases were obtained from the Health Electronic Surveillance Network of Saudi Arabia and LTHR paper and e-medical records of the patients. We used Microsoft Excel 2013 (Microsoft, Redmond, WA) for data entry; Epi Info 7 (Centers for Disease Control and Prevention, Atlanta, GA) was used for analysis of data and plotting epidemic curves for the outbreak. The collected data were used to construct 2 detailed chronologic time lines for each patient using 3- and 24-hour intervals to illustrate the dynamics of movements and outcome of patients throughout their stay in the hospital. We divided the outbreak into 3 phases based on the awareness of HCWs and implementation of IPC measures. At the beginning of the outbreak (phase I), there was inadequate awareness of HCWs at the LTHR about emergence of an outbreak of MERS in the hospital. When the hospital administration became aware about the increased number of MERS cases, additional but inadequate IPC measures were put in place (phase II). Toward the end of the outbreak (phase III), strict IPC measures were implemented. Then, the LTHR management decided to close the ER, suspend elective surgeries, and postpone all outpatient appointments and visits.[12] We obtained the number of patients that visited the ER seeking medical care during each phase of the outbreak. We calculated the crude secondary attack rate per 10,000 patients (SAR/10,000). SAR/10,000 was defined as the number of MERS cases that occurred within 14 days among patients visiting the ER for medical care after exposure to a primary or secondary case.

The RRT visited the LTHR 11 times during the outbreak: 5 times during phase II and 6 times during phase III. The RRT was not invited to visit the LTHR during phase I. The first assessment was conducted on August 6, 2015, and the last assessment was conducted on September 13, 2015. The RRT ascertained the level of awareness of HCWs of the case definition of a suspected case of MERS; presence of written IPC policies or guidelines for suspected or confirmed MERS patients; reporting, postexposure evaluation, and follow-up; and receipt of support of administration of the LTHR. The RRT also checked whether or not appropriate PPE for HCWs was made readily available in the ER at the LTHR. More HCWs were screened toward the end of the outbreak to alleviate and respond to a wave of panicking that swept the hospital, especially the staff working at the ER.

We used the time line, a well-defined algorithm, and the epidemiologic links to identify chains of secondary, tertiary, and quaternary generations of MERS cases that were acquired within the LTHR. Each chain of secondary cases was tracked back to a single primary case. We reviewed the medical records of each case (primary or secondary) admitted to the ER of LTHR to exclude exposure to MERS from a previous visit to the ER or other departments within the hospital where we conducted the study. Throughout the course of the outbreak, the LTHR screened 1,310 HCWs and inpatients for Middle East respiratory syndrome coronavirus (MERS-CoV). More details about the setup and workforce of the LTHR at the time of the outbreak are published elsewhere.[10]

RESULTS

Phase II (July 27-August 9)

The first RRT visit to the LTHR after the onset of the outbreak was on August 6, 2015 (ie, during phase II). The results of the assessments of the RRT during phases II and III are summarized in Table 1.

During the first visit to the ER, the RRT noted that the ER and the waiting area for the ER were overcrowded. There was no visual triaging for patients with respiratory infections and no specialized clinic for acute respiratory infections. Patients and escorts were close to each other (ie, <1 m from each other). A separate area was designated as a waiting area for suspected patients and their escorts. However, the waiting area was not controlled.

Some of the doctors serving at the ER did not know about the case definition of a suspected case of MERS and the appropriate IPC measures during management of suspected MERS cases. They were not aware of the potential risk of contracting MERS infection, of the high-risk procedures, and when they need to be tested and or abstain from work.

The HCWs were partially adhering to IPC guidelines because many HCWs were not putting on PPE when dealing with suspected MERS cases. Most nurses were using the same gowns and facemasks with all patients in the respiratory observation room. There was delayed admission and isolation of suspected MERS. Meanwhile, some HCWs were using double surgical masks. Others continued conducting their work in other patients' area without doffing their PPE. None of the HCWs used goggles or face shields. The availability of PPE was limited to the suspected isolation rooms. Some PPE (eg, N95 masks, face shield or goggles) was not readily available. HCWs were using aprons instead of gowns. Donning, doffing, and disposal of PPE was done incorrectly. There were no clear detailed instructions on what the HCW should do in case of suspecting MERS.

Nasopharyngeal swabs were taken in rooms without negative pressure. Cleaning workers were entering with all clean items and then providing the waste services with the same trolley. The LTHR has policies and guidelines on IPC but HCWs could not access MERS guidelines or were not even aware about them. Visual alerts (posters) were displayed in common waiting areas instructing HCWs to do IPC measures without specifying what should be done. There were IPC educational alerts for the patients visiting the ER seeking medical care, but in not in Arabic.

Table 1
Summary of assessments of the infection prevention and control rapid response teams*

Criteria	Questions asked	Visit on August 6, 2015	Visits on August 7, 2015	Visit on August 8, 2015	Visit on August 10, 2015	Visit on August 12, 2015	Visit on August 13, 2015	Visit on August 16, 2015	Visit on August 18, 2015	Visit on August 28, 2015	Visit on September 13, 2015
				Phase II					Phase III		
Level of awareness of HCWs of the case definition of a suspected case of MERS	Ask HCWs (doctors and nurses) about the signs and symptoms of suspected MERS	0†	0†	0†	0†	N/A	0†	0†	0†	0†	2‡
Presence of written IPC policies or guidelines for suspected or confirmed MERS patients	Ask to show a copy of the policy	N/A	N/A	2‡	2‡	2‡	2‡	2‡	2‡	2‡	2‡
Presence of written policies for reporting, postexposure evaluation, and follow-up of MERS cases	Ask to show a copy of the policy	N/A	N/A	2‡	2‡	2‡	2‡	2‡	2‡	2‡	2‡
	Ask to show evidence of implementation of policy (eg, last reporting documentation)	N/A	N/A	2‡	2‡	2‡	2‡	2‡	2‡	2‡	2‡
	Ask staff (1-2 staff) to tell you what to do in case of suspected or confirmed MERS-CoV exposure	N/A	N/A	1§	1§	1§	1§	1§	1§	0†	2‡
HCF administration/leadership support IPC and related activities for HCWs, patients, and patients visiting the ER seeking medical care	Ask CEO or medical director to show hospital-wide committee meeting minutes supporting IPC	N/A	N/A	2‡	2‡	2‡	2‡	2‡	2‡	2‡	2‡
	Ask staff (CEO and frontliners) if the leadership is supporting IPC; ask to give examples	N/A	N/A	2‡	2‡	2‡	2‡	2‡	2‡	2‡	2‡
Presence of ≥1dedicated (full-time) qualified IPC staff	Ask for IPC personnel file	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2‡
	Ask IPC questions to assess competency	2‡	2‡	2‡	2‡	2‡	2‡	2‡	2‡	2‡	2‡
	Total number of personnel responsible for infection control	1§	1§	1§	1§	1§	1§	1§	2‡	2‡	2‡
Adherence of HCWs to IPC measures, especially during aerosol-generating procedures	HCWs put on facemask or gown protection before entry into a MERS-CoV patient care area in the ER	1§	1§	1§	1§	2‡	1§	2‡	2‡	1§	2‡
HCWs at ER put on appropriate PPE during aerosol-generating procedures for MERS patients	HCWs put on gowns, gloves, eye protection, and a particulate respirator (N95 or higher)	N/A	N/A	1§	1§	1§	1§	2‡	1§	1§	1§
Presence of a designated triage area in ER for suspected MERS	ER triage area is physically separated from other areas	0†	0†	0†	2‡	2‡	1§	1§	2‡	1§	2‡
Patients and their escorts instructed to wear facemasks and stay in designated areas	Patients or escorts at waiting areas wear facemasks at least 1 m away from each other	0†	0†	0†	1§	1§	1§	1§	1§	1§	2‡
Appropriate PPE for HCWs were made readily available in the ER at the LTHR	Check availability of appropriate PPE for HCWs were made readily available in the ER at the HCF	1§	1§	1§	1§	1§	1§	2‡	2‡	1§	2‡

CEO, chief executive officer; *ER*, emergency room; *HCF*, health care facility; *HCW*, health care worker; *IPC*, infection prevention and control; *LTHR*, large tertiary hospital in Riyadh City; *MERS*, Middle East respiratory syndrome; *MERS-CoV*, Middle East respiratory syndrome coronavirus; *N/A*, data not available; *PPE*, personal protective equipment.
*The rapid response team did not do any audit or IPC assessment for LTHR during phase I.
†Noncompliant with IPC guidelines.
‡Fully compliant with IPC guidelines.
§Partially compliant with IPC guidelines.

On August 8, a 4-day intensive training of HCWs, respiratory therapists, radiograph technicians, and housekeeping workers started. The training focused on case definition, proper use of PPE, hand hygiene, and other IPC guidelines and was followed by a simulation exercise (drill) mimicking a patient with history of cough, fever, shortness of breath, and history of travel 1 week before onset of symptoms.

Phase III (August 10-26)

On August 10, the ER implemented a standardized checklist for triaging, an algorithm, and a clear pathway for a critical patient with acute respiratory symptoms. More visual alerts on MERS and educational messages on cough etiquette and hand hygiene were posted on the ER entrance. More high-efficiency particulate air filters were procured. Still, some HCWs were not following IPC guidelines; there were some HCWs with improper donning and or doffing of PPE, and some were not using eye protection. On August 11, the elective admissions were cancelled to decrease the congestion and crowdedness of the ER.

On August 12, the hospital distributed guidelines to the HCWs. The patients were separated, but their relatives continued to enter their rooms without PPE. Subsequent RRT visits did not note or document any significant violations of the IPC measures. On August 23, an immediate training and evaluation of IPC was completed to ensure compliance and enforce it, monitor physicians and nurses on their knowledge of case definition, monitor PPE use, monitor hand hygiene, and provide auditing and training for housekeeping staff on PPE use, hand hygiene, proper use of chemicals, proper dilution, changing mop heads between areas and proper laundry of mop heads.

On August 11, the LTHR administration recruited security officers to control movement of patients and escorts at the ER and hospital wards. A log for all HCWs working in the unit before starting their shifts was to be checked by the team leader or charge nurse for any signs and symptoms and for those that should abstain from work immediately and be tested with contact tracing and home isolation.

The charge nurse or team leader of each shift would randomly ask ≥1 HCW about the case definition of a suspected case of MERs, about PPE donning and doffing steps, and about other appropriate precautions for MERS. The RRT made more visits to the ER and hospital to ensure compliance with IPC guidelines. On August 23, the ER was evacuated and terminally cleaned. More high-efficiency particulate air filters were procured.

There were 130 laboratory-confirmed MERS cases diagnosed throughout the course of the outbreak period, including 20 (15%) primary and 110 (85%) secondary cases. Of all MERS secondary cases, there were 25 symptomatic and 18 asymptomatic (33%) secondary cases among HCWs. Except for 2 secondary cases, the epidemiologic links between primary and secondary cases across different generations were ascertained.

Through the course of phase I of the outbreak there were 6 primary cases that gave rise to a total of 48 secondary cases over 4 generations. One of the primary cases resulted in a total of 9 cases in the first generation, which ended with 21 cases over a chain of 4 generations. Notably, during phases II and III of the outbreak, the number of secondary cases sharply dropped to 18 and 1, respectively; however, the numbers of primary cases were equal or even more. During phase II, primary cases gave rise to a maximum of 2 generations of secondary cases; 3 primary cases did not give rise to secondary cases. The ratio of secondary cases per primary case fell from a range of 1-21 in phase I to 0-11 and 0-1 in phases II and III, respectively. Only 1 asymptomatic secondary case was actively detected after screening of the exposure of patients and HCWs in the ER to a MERS patient during phase III. The duration between the date of onset of symptoms and diagnosis of MERS among secondary cases dropped from 7 days in phase I to 1 day in phase III.

The SAR/10,000 was 42.3. The SAR/10,000 dropped from 75 (95% confidence interval [CI], 55-99) in phase I to 29 (95% CI, 17-46) and 3 (95% CI, 0-17) in phases II and III, respectively. Conversely, the number of infected HCWs increased from 2 in phase I to 10 and 31 in phases II and III, respectively. During the outbreak, screening of 2,868 HCWs and patients revealed that 1%, 2.1%, and 1.4% were positive for MERS-CoV in phases I, II, and III, respectively (Table 2).

DISCUSSION

The breakdown of the outbreak into 3 phases revealed salient evidence on the outcome of implementation of different levels of IPC measures that resulted in remarkable change in the course of the outbreak. Although, the number of primary cases of MERS and the patients visiting the ER seeking medical care were almost equal during the 3 phases of the outbreak, the SAR/10,000 dropped dramatically in the subsequent 2 phases of the outbreak. The fall tendency in SAR/10,000 across the 3 different phases of the outbreak could be caused by implementation of and more adherence to direct and indirect IPC measures (eg, triaging, use of PPE).

More HCWs were screened toward the end of the outbreak to alleviate and respond to a wave of panicking that swept the hospital, especially the staff working at the ER. Both symptomatic and asymptomatic infected HCWs were asked to stay home for 2 weeks. Increased awareness of HCWs at the ER about the MERS case definitions, hence improved surveillance activities, should have contributed in early detection of MERs cases and better implementation of appropriate IPC guidelines.[15] Because we have not studied the MERS virus, we could not rule out the role of virus attenuation in the drop of the number and generations of secondary cases.

Suspected cases of MERS were detected in relatively shorter periods after their onset of symptoms (shorter period from date of onset to the date of collection of the first sample and confirmation of diagnosis of MERS), biologic specimens were taken faster, and confirmed cases were moved away relatively quicker from the ER to other wards within the hospital in phase III. Paradoxically, more time was needed to confirm the diagnosis of MERS, probably because the laboratory was overtasked with an increased number of laboratory requests. Also, the delay in moving confirmed cases of MERS from the ER in phases I and II could have contributed to further spread of MERS within the ER.

Two primary cases gave rise to >5 secondary cases and could be labeled as super-spreaders. Similar infections have been seen in other MERS outbreaks.[16] One of the secondary cases was exposed to a case of MERS while he was in the ER and developed symptoms after he was moved to a ward within the hospital. He was tested 7 times over 4 weeks to confirm MERS diagnosis. As a result, he infected another patient within the ward and probably some HCWs. This incident highlights the importance of collection of a proper MERS test type, time, or technique.[17]

There were no secondary cases that could be linked to the very first primary case of MERS reported to the ER, probably because of the low infectivity of the virus.[18] In addition, the first primary MERS case diagnosed at the LTHR was not subjected to aerosol-generating procedure during his relatively short stay in ER, which act in spreading the virus because MERS-CoV virus affects the lower lobes of the lungs and spreads through droplets.[19]

Breakdown of the outbreak into 3 phases revealed some differences in management of cases of MERS related to case definition and implementation IPC measures. It is clear that IPC measures started to improve in phase II and were thoroughly implemented

Table 2
Secondary MERS cases distribution by different phases of the outbreak, large tertiary hospital in Riyadh City, June-August 2015

Phase (period)*	Total no. of patients visiting the ER seeking medical care	No. of MERS cases in different generations of the outbreak								
							HCW			
		Primary†	1st Gen	2nd Gen	3rd Gen	4th Gen	No. of screening tests‡	Tested positive	Total secondary cases§	Secondary attack rate per 10,000‖
Phase I (July 11-26), outbreak starts	6,402	6	23	15	7	3	192	2 (1.0%)	48	75 (95% CI, 55-99)
Phase II (July 27-August 9), MOH visit	6,190	8	15	3	0	0	471	10 (2.1%)	18	29 (95% CI, 17-46)
Phase III (August 10-26), ER closure	3,239	6	1	0	0	0	2,205	31 (1.4%)	1	3 (95% CI, 0-17)
Total	15,831	20	39	18	7	3	2,868	43 (1.5%)	67	42 (95% CI, 33-54)

CI, confidence interval; *ER*, emergency room; *Gen*, generations of secondary cases; *HCW*, health care worker; *MERS*, Middle East respiratory syndrome; *MOH*, Ministry of Health.
*Phase I: there was inadequate awareness of HCWs at the large tertiary hospital in Riyadh City about emergence of an outbreak of MERS in the hospital. No additional IPC measures were put in place. Phase II: the hospital administration became aware about the increased number of MERS cases, but inadequate IPC measures were put in place. MOH rapid response team visited the large tertiary hospital in Riyadh City and provided technical support. Phase III: strict IPC measures were implemented. The period ended with closure of the ER.
†From the first phase, 1 primary case was not included in calculating the secondary attack rate.
‡Some HCWs and inpatients were screened more than once.
§HCWs not included.
‖Not including HCWs.

in phase III. Based on the course of the outbreak, it is most likely that closure of the ER was unnecessary because the number of secondary cases in phase III is almost zero. Closure of ERs to new admission during outbreaks has been reported elsewhere to prevent occurrence of additional cases when the source of transmission was unknown and the decision was made only in consultation with public health authorities.[20]

Secondary MERS cases were detected relatively in shorter periods after their onset of symptoms, biologic specimens were taken faster, and confirmed cases were moved away relatively quicker from the ER to other wards within the hospital in phase III. This is most probably because of the increased awareness of HCWs about the MERS case definition. During phase III, IPC demonstrated improved IPC practice. It is difficult to estimate the contribution of each IPC element or intervention separately. The increase in the number of identified HCWs infected with MERS toward the end of the outbreak does not necessarily correlate to the date or the phase of the outbreak when they were infected. HCWs who tested positive for MERS in 3 different phases of the outbreak were counted as secondary cases, but we did not exclude them when we calculated the SAR/10,000, simply because it was not possible to link these secondary cases to specific primary MERS cases. If secondary MERS cases among HCWs were included, the SAR/10,000 would be even higher. Moreover, the secondary cases among HCWs were mostly detected toward the end of the outbreak during phase III after screening of HCWs, whereas reporting of primary cases continued to the date of its closure. The lesson learned from this outbreak is that continuous IPC assessment, audits, training, and supervision of HCWs and awareness of case definitions are crucial for reducing the number of secondary cases during outbreaks of MERS.

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