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Clinical Course and Outcomes of Critically Ill Patients With Middle East Respiratory Syndrome Coronavirus Infection FREE

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Article, Author, and Disclosure Information

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Abstract

Background: Since September 2012, 170 confirmed infections with Middle East respiratory syndrome coronavirus (MERS-CoV) have been reported to the World Health Organization, including 72 deaths. Data on critically ill patients with MERS-CoV infection are limited.

Objective: To describe the critical illness associated with MERS-CoV.

Design: Case series.

Setting: 3 intensive care units (ICUs) at 2 tertiary care hospitals in Saudi Arabia.

Patients: 12 patients with confirmed or probable MERS-CoV infection.

Measurements: Presenting symptoms, comorbid conditions, pulmonary and extrapulmonary manifestations, measures of severity of illness and organ failure, ICU course, and outcome are described, as are the results of surveillance of health care workers (HCWs) and patients with potential exposure.

Results: Between December 2012 and August 2013, 114 patients were tested for suspected

included 3 HCWs. One HCW became critically ill and was the 12th patient in this case series. Median Acute Physiology and Chronic Health Evaluation II score was 28 (range, 16 to 36). All 12 patients had underlying comorbid conditions and presented with acute severe hypoxemic respiratory failure. Most patients (92%) had extrapulmonary manifestations, including shock, acute kidney injury, and thrombocytopenia. Five (42%) were alive at day 90. Of the 520 exposed HCWs, only 4 (1%) were positive.

Limitation: The sample size was small.

Conclusion: MERS-CoV causes severe acute hypoxemic respiratory failure and considerable extrapulmonary organ dysfunction and is associated with high mortality. Community-acquired and health care–associated MERS-CoV infection occurs in patients with chronic comorbid conditions. The health care–associated cluster suggests that human-to-human transmission does occur with unprotected exposure.

Primary Funding Source: None.

Editors' Notes

Context

- Middle East respiratory syndrome coronavirus (MERS-CoV) is an emerging pathogen with a clinical spectrum that is not yet fully delineated.

Contribution

- Twelve hospitalized patients found to have MERS-CoV infection all required intensive care, including mechanical ventilation. Underlying comorbid disease was present in all patients. Extrapulmonary involvement was common. Various treatments were tried. Mortality was high. Three cases were nosocomially acquired, and 1 health care worker was among the case patients.

- A small case series may not be representative of all patients presenting to hospitals with MERS-CoV infection.

Implication

- Additional information on optimal management of MERS-CoV infection is urgently needed.

—The Editors

In September 2012, a new coronavirus was isolated for the first time from a patient in Saudi Arabia, who presented with acute pneumonia and renal failure (1). The virus was identified as a human β-coronavirus and was subsequently named "Middle East respiratory syndrome coronavirus" (MERS-CoV) (2). Since then, 170 laboratory-confirmed cases of infection with MERS-CoV have been reported to the World Health Organization, including 72 deaths (3). The disease has a high fatality rate and has several clinical features that resemble the infection caused by the severe acute respiratory syndrome coronavirus (SARS-CoV) (4). As such, there has been concern that the virus has the potential to cause a pandemic. World knowledge about this virus is accumulating, but data on critically ill patients infected with MERS-CoV are limited.

We describe the clinical course and outcomes of 12 critically ill patients with MERS-CoV admitted to 3 intensive care units (ICUs) in 2 tertiary hospitals in Saudi Arabia.

Methods

The study was approved by the Institutional Review Board of the National Guard Health Affairs, Riyadh, Saudi Arabia, and consent was not required.

Setting

The Saudi Arabian National Guard Health Affairs serves close to 1 million individuals of the

from 1 ICU (a medical–surgical ICU referred to as "ICU 1") at King Abdulaziz Hospital, Al-Ahsa, and from 2 ICUs (a medical–surgical ICU and a cardiac ICU, referred to as "ICU 2" and "ICU 3," respectively) at King Abdulaziz Medical City, Riyadh. Although ICU 2 and ICU 3 are located in the same hospital, they are in geographically separate locations and have limited staff crossover.

Both hospitals have board-certified intensivists who treat patients in closed medical–surgical ICUs and provide consultations to patients in the cardiac ICU as required. The hospitals are accredited by the Joint Commission International and have Infection Prevention and Control programs that work collaboratively with the ICU staff. Hand-hygiene compliance in the ICUs for 2012 was 85% to 98%, and the influenza vaccination rate among health care workers (HCWs) was 83%.

Since the first case of MERS-CoV was identified in Saudi Arabia in September 2012, the National Guard hospitals along with all other health care facilities in Saudi Arabia implemented the guidelines for testing of suspected cases and screening (surveillance of potential exposures) for MERS-CoV according to Ministry of Health directives. The multidisciplinary outbreak committee was reactivated to manage the current MERS-CoV outbreak. The infection control precautions for suspected MERS-CoV included placement of patients in a single-bed negative-pressure room and the use of personal protective equipment (N-95 mask, gown, and gloves) by HCWs. This study includes all cases encountered from December 2012, the date of the first suspected case, until August 2013. The first confirmed case of MERS-CoV was in May 2013 in Al-Ahsa and in June 2013 in Riyadh. The time frame overlaps with that of a previously reported case series, and the authors cannot entirely exclude the possibility that 1 or 2 of the patients in the current report have been included in the previous case series.

Patients

Infection with MERS-CoV was suspected in patients presenting with acute respiratory illness and chest radiographs suggestive of pneumonia and the acute respiratory distress syndrome (ARDS), especially if the patient required ICU admission. Suspected cases were tested for MERS-CoV with real-time polymerase chain reaction (RT-PCR), using the recommended sampling technique (nasopharyngeal swab and tracheal aspirates or bronchoalveolar lavage in intubated patients). In suspected cases with negative RT-PCR

Samples were tested at the regional reference laboratory of the Saudi Arabian Ministry of Health and the hospital laboratory at King Abdulaziz Medical City, Riyadh, as described elsewhere (5). The RT-PCR amplification targeted both the upstream E protein (*upE* gene) and ORF1a for confirmation.

Definitions

We included all patients admitted to ICUs with confirmed or probable MERS-CoV infection as defined by the World Health Organization (6). A confirmed case was defined as a suspected case with a positive result for MERS-CoV on RT-PCR. A probable case was defined as a suspected case if the RT-PCR result for MERS-CoV was unavailable, negative, or inconclusive in a patient with an epidemiologic link to a patient with confirmed MERS-CoV (6).

Data on demographic characteristics, contact history with a MERS-CoV confirmed case patient, underlying comorbid conditions, presenting symptoms, and radiographic findings were collected from the medical records. On the day of intubation, we assessed severity of illness by using Acute Physiology and Chronic Health Evaluation II scores and Sequential Organ Failure Assessment (SOFA) scores (7). On days 1, 3, 7, and 14 of intubation, we documented laboratory and ventilator variables and arterial blood gases. Leukopenia was defined as leukocyte count less than 4.0×10^9 cells/L, lymphopenia as a lymphocyte count less than 1.5×10^9 cells/L, and thrombocytopenia as a platelet count less than 140×10^9 cells/L. Aspartate aminotransferase and alanine aminotransferase levels were considered elevated if they were more than twice the upper reference limit (34 U/L and 55 U/L, respectively).

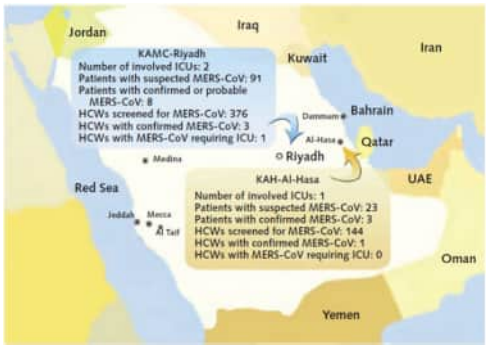
We recorded the time course of the patient's illness, microbiological test results, and treatments received. We also recorded the following outcomes: duration of mechanical ventilation, ICU length of stay, and survival to ICU discharge, at day 28 and at day 90.

Role of the Funding Source

This study did not receive external funding.

During the 9-month study period in the 2 hospitals, 114 patients were suspected of having and were tested for MERS-CoV infection (Figures 1 and 2). Of these, 10 ICU patients (9%) met the definition of confirmed cases, and 1 (1%) was a probable case. Among these cases, 8 were community-acquired, and 3 occurred in patients in ICU 3 (the cardiac ICU) who were part of a health care–associated cluster that included HCWs. In the latter patients, the initial hospitalization was for aortic valve replacement, coronary artery bypass graft surgery, or pericardiectomy for constrictive pericarditis. All of the hospitalized patients with confirmed MERS-CoV infection required ICU admission.

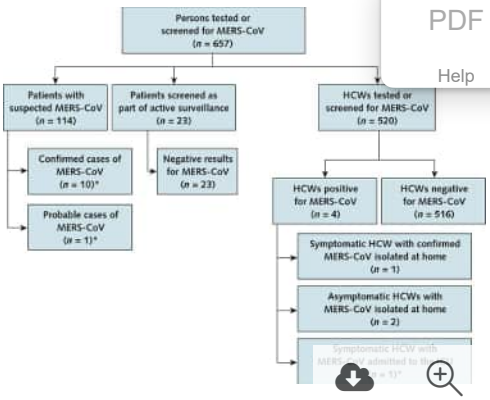
FIGURE 1.



Map of the Kingdom of Saudi Arabia showing the 2 study hospitals, the number of suspected and confirmed MERS-CoV infections in patients, and the number of HCWs screened and cases confirmed in HCWs.

ICU 1 is located in Al-Ahsa and ICU 2 and ICU 3 in Riyadh. HCW = health care worker; ICU = intensive care unit; KAH = King Abdulaziz Hospital; KAMC = King Abdulaziz Medical City; MERS-CoV = Middle East respiratory syndrome coronavirus; UAE = United Arab Emirates.

FIGURE 2.



Study flow diagram.

HCW = health care worker; ICU = intensive care unit; MERS-CoV = Middle East respiratory syndrome coronavirus.

* Cases described in this report.

In addition, 23 cardiac ICU patients were screened as part of active surveillance because of

the infections in HCWs occurred as a part of the health care–associated MERS-CoV cluster. These HCWs were nurses reported to have had exposure, without the use of personal protective equipment, to patients who were subsequently confirmed to have MERS-CoV infection. Only 1 of the HCWs (patient L), who had asthma, became severely ill and required ICU admission and is fully described in this series along with the other 11 patients. The other HCWs were mildly symptomatic or asymptomatic and were managed at home until the RT-PCR result was negative. Figure 1 shows the distribution of these cases between the 2 hospitals in Al-Ahsa and Riyadh.

Clinical Presentation

The demographic and clinical characteristics of the 12 critically ill patients with confirmed or probable MERS-CoV infection are shown in Table 1 and Appendix Tables 1, 2, and 3. The median age of the patients was 59 years (range, 36 to 83 years). Eight patients (67%) were male.

Table 1. Characteristics of Patients With Confirmed or Probable Middle East Respiratory Syndrome Coronavirus Infection

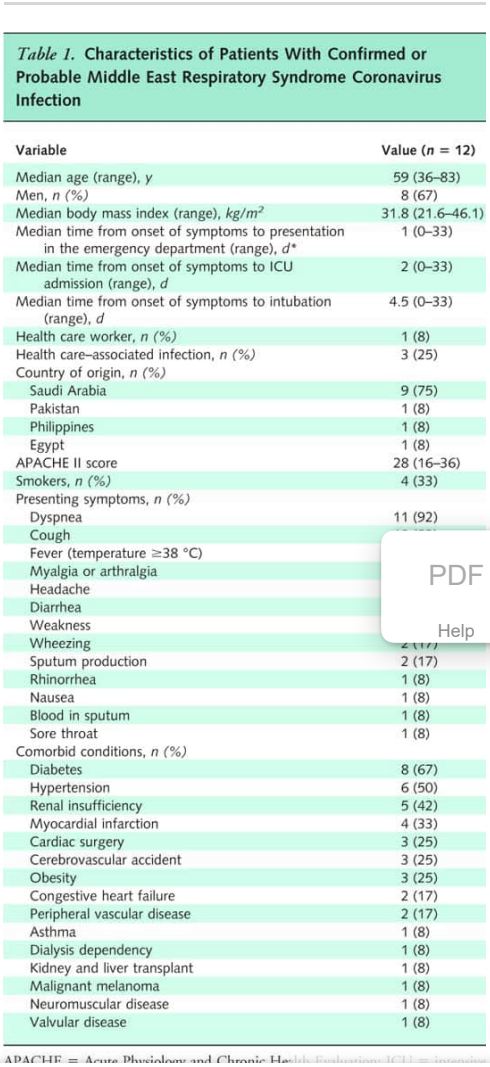


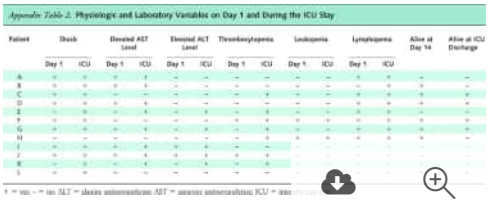
Table 1. Characteristics of Patients With Confirmed or Probable Middle East Respiratory Syndrome Coronavirus Infection

Variable	Value (*n* = 12)
Median age (range), *y*	59 (36–83)
Men, *n (%)*	8 (67)
Median body mass index (range), *kg/m²*	31.8 (21.6–46.1)
Median time from onset of symptoms to presentation in the emergency department (range), *d**	1 (0–33)
Median time from onset of symptoms to ICU admission (range), *d*	2 (0–33)
Median time from onset of symptoms to intubation (range), *d*	4.5 (0–33)
Health care worker, *n (%)*	1 (8)
Health care–associated infection, *n (%)*	3 (25)
Country of origin, *n (%)*	
Saudi Arabia	9 (75)
Pakistan	1 (8)
Philippines	1 (8)
Egypt	1 (8)
APACHE II score	28 (16–36)
Smokers, *n (%)*	4 (33)
Presenting symptoms, *n (%)*	
Dyspnea	11 (92)
Cough	
Fever (temperature ≥38 °C)	
Myalgia or arthralgia	
Headache	
Diarrhea	
Weakness	
Wheezing	
Sputum production	2 (17)
Rhinorrhea	1 (8)
Nausea	1 (8)
Blood in sputum	1 (8)
Sore throat	1 (8)
Comorbid conditions, *n (%)*	
Diabetes	8 (67)
Hypertension	6 (50)
Renal insufficiency	5 (42)
Myocardial infarction	4 (33)
Cardiac surgery	3 (25)
Cerebrovascular accident	3 (25)
Obesity	3 (25)
Congestive heart failure	2 (17)
Peripheral vascular disease	2 (17)
Asthma	1 (8)
Dialysis dependency	1 (8)
Kidney and liver transplant	1 (8)
Malignant melanoma	1 (8)
Neuromuscular disease	1 (8)
Valvular disease	1 (8)

APACHE = Acute Physiology and Chronic Health Evaluation; ICU = intensive

Appendix Table 1. Individual-Patient Characteristics and Primary Therapies During the Intensive Care Unit Stay

Appendix Table 2. Physiologic and Laboratory Variables on Day 1 and During the ICU Stay



Appendix Table 3. SOFA Score, by Study Day

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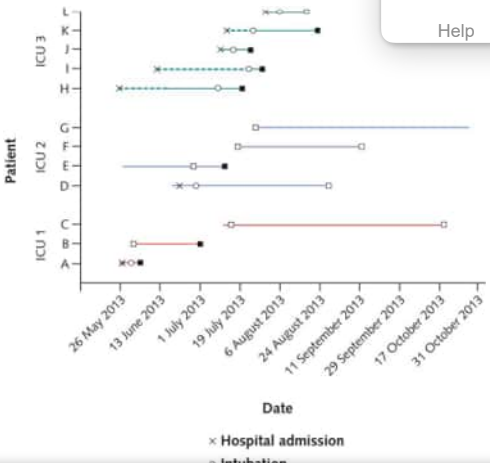
Variable	Median SOFA Score (Range)			
	Day 1	Day 3	Day 7	Day 14
Respiration	4 (2–4)	3 (2–4)	3 (1–4)	3 (2–4)
Platelet count	0 (0–1)	1 (0–3)	0 (0–4)	1 (0–4)
Bilirubin level	0 (0–2)	0 (0–3)	0 (0–3)	0 (0–3)
Hypotension	3 (0–4)	2 (0–4)	3 (0–4)	3 (0–4)
Glasgow Coma Scale score	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)
Creatinine concentration	2 (0–4)	1 (0–4)	0 (0–3)	1 (0–4)
Total	9 (3–12)	9 (4–13)	7 (0–14)	5 (0–14)

SOFA = Sequential Organ Failure Assessment.

The presenting symptoms were mainly those of lower respiratory tract infection (dyspnea in 11 patients [92%], cough in 10 [83%], and fever in 8 [67%]); in contrast, symptoms of upper respiratory tract infection were infrequent (Table 1). The median interval from onset of symptoms to the emergency department visit was 1 day; to ICU admission, 2 days; and to intubation, 4.5 days (range for all time frames, 0 to 33 days). Figure 3 summarizes the time course of disease.

FIGURE 3.



Timeline of the clinical course of the study patients. The beginning of the solid lines refers to the onset of MERS-CoV symptoms. The different line colors indicate the 3 different intensive care units (ICU 1 in Al-Ahsa and ICU 2 and ICU 3 in Riyadh). The dashed line indicates the time in the hospital before the onset of MERS-CoV symptoms in patients with health care–associated infection. Patient G was still in the hospital

The median Acute Physiology and Chronic Health Evaluation II score was 28 (range, 16 to 36), and the median SOFA score was 9 (range, 3 to 12). Each patient had at least 1 comorbid condition (Table 1); the median number of comorbid conditions was 3 (range, 1 to 6). Animal exposure was documented for 2 patients; in both instances, the animals (a camel and a domestic cat) were not apparently ill.

Respiratory Manifestations and Support

Acute severe hypoxemic respiratory failure was the prominent feature of the presentation, and all patients required invasive mechanical ventilation (Table 2). Before intubation, 5 patients had received a failed trial of noninvasive positive-pressure ventilation (NIPPV). Chest radiography at the time of intubation showed airspace changes that ranged from unilateral lobar to bilateral diffuse involvement consistent with ARDS (Appendix Figure). Chest computed tomography was performed in 3 patients and confirmed the same patterns (Figure 4).

APPENDIX FIGURE.

Chest radiographs from the 12 patients with Middle East respiratory syndrome coronavirus infection on the day of intubation, demonstrating airspace disease that ranged from lobular to bilateral lung involvement.

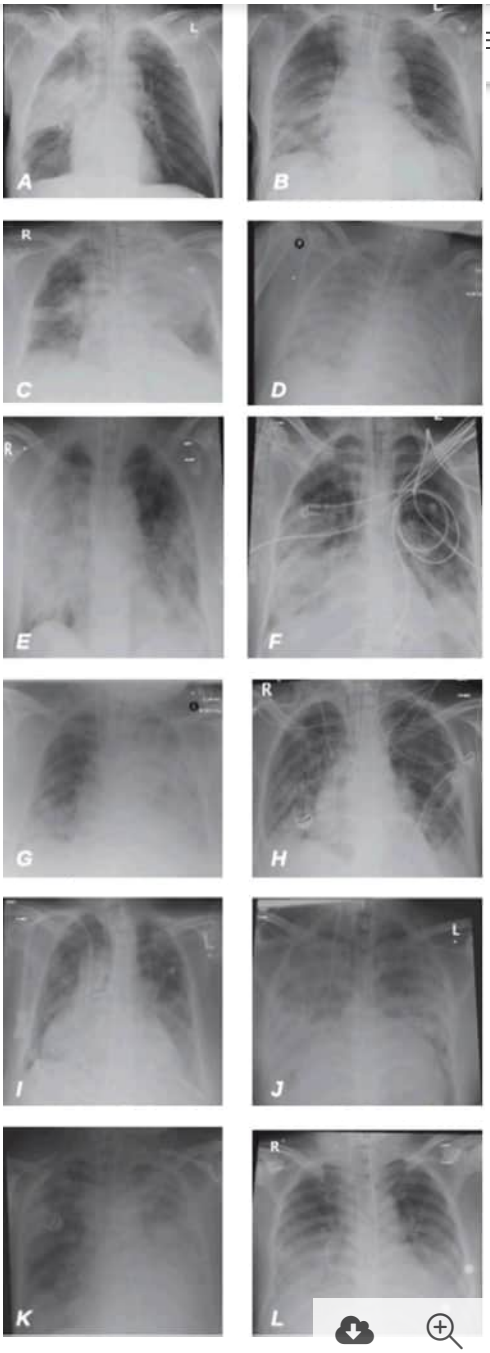
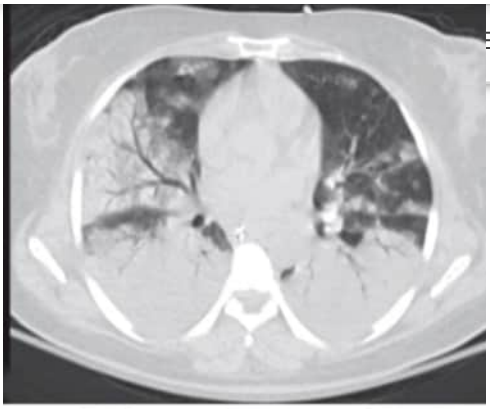
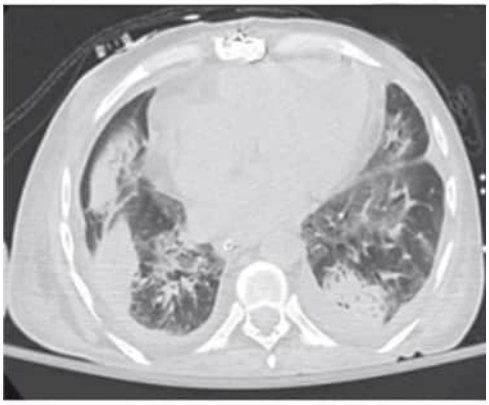


FIGURE 4.

Computed tomography images from 3 patients, showing bilateral airspace disease.





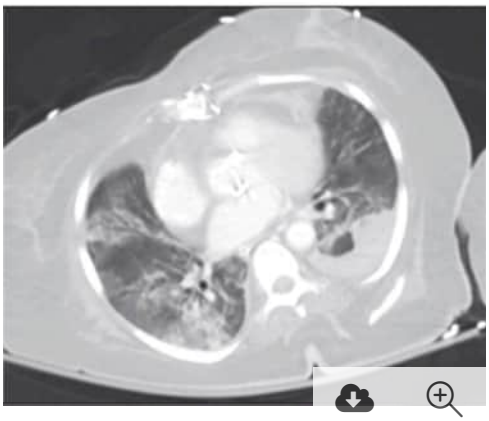
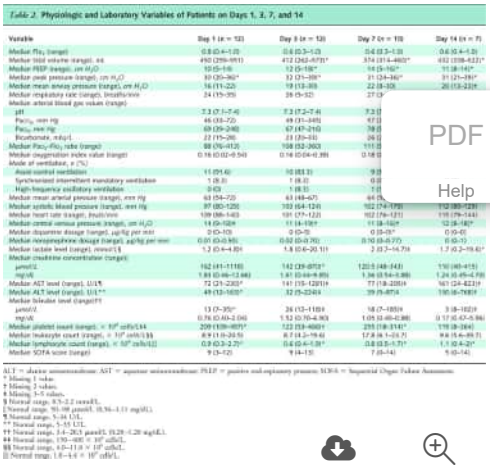


Table 2. Physiologic and Laboratory Variables of Patients on Days 1, 3, 7, and 14



All patients received intravenous sedation, and 4 (33%) patients received neuromuscular blockade. Because of refractory hypoxemia, nitric oxide was used in 6 (50%) patients,

median duration of mechanical ventilation was 16 days (range, 4 to 30 days). Tracheostomy was performed in 3 patients (25%).

Nonrespiratory Manifestations and Support

Eleven patients (92%) had at least 1 extrapulmonary manifestation. Individual organ components of the SOFA score are shown in Appendix Table 3.

Circulatory

Vasopressors were required in 8 patients (67%) on day 1 and in 11 patients (92%) during the ICU stay. Echocardiography was performed in 11 patients, and all showed no acute change in myocardial function.

Renal

Acute kidney injury that required renal replacement therapy occurred in 7 patients (58%).

Hepatic

The aspartate aminotransferase level was elevated in 6 patients on day 1 and in 8 patients during the ICU stay. The alanine aminotransferase level was elevated in 2 patients on day 1 and in 5 patients during the ICU stay.

Hematologic

Nine patients (75%) had lymphopenia on day 1, and 11 (92%) had it during the ICU stay. Thrombocytopenia was noted in 2 patients on day 1 and in 7 patients (58%) during the ICU stay.

Gastrointestinal

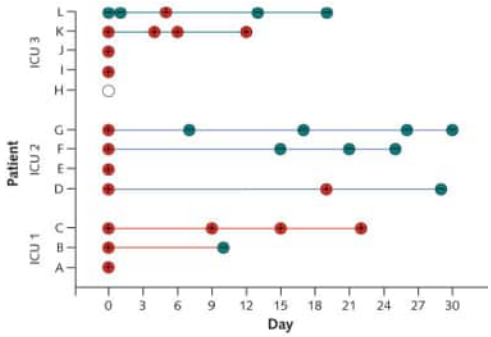
Diarrhea was noted in 2 patients. Three patients had acute abdomen during the ICU s
One patient, who had diabetes and peripheral vascular disease, developed ischemic bowel; abdominal computed tomography revealed pneumatosis intestinalis, and the patient required hemicolectomy. The other 2 patients had negative laparotomies.

Microbiological Investigations

One patient was co-infected with methicillin-resistant *Staphylococcus aureus* and influenza B and another with *Streptococcus pneumoniae*.

Figure 5 shows the results of sequential RT-PCR testing. Eleven patients had positive results. Infection with MERS-CoV was considered probable in 1 patient because of high clinical suspicion and an epidemiologic link to a confirmed positive MERS-CoV case that was identified after he had died; hence, no test was performed for this patient.

FIGURE 5.



Results of sequential real-time polymerase chain reaction.

The red circles indicate a positive result for MERS-CoV; green circles indicate negative results. The open circle indicates that patient H did not undergo testing because he was a probable MERS-CoV case patient. ICU = intensive care unit; MERS-CoV = Middle East respiratory syndrome coronavirus.

Antimicrobial Therapy, Corticosteroids, and Intravenous Immunoglobulin

All patients received broad-spectrum antimicrobials, and 7 patients (58%) received oseltamivir empirically. None of the patients received ribavirin or interferon-β. Low-dose hydrocortisone (≤300 mg/d) was given to 5 patients (42%) for shock and methylprednisolone (120 to 1000 mg/d) was given to 5 other patients (42%). One patient received intravenous immunoglobulin and high-dose corticosteroids for thrombocytopenia, with an improvement in platelet count.

Outcomes

Among the 12 patients, 7 (58%) were alive at day 28, 5 (42%) were alive at ICU discharge, and 5 (42%) were alive at day 90. The median ICU length of stay was 30 days (range, 7 to 104 days). The median hospital length of stay was 41 days (range, 8 to 96 days), excluding 1 patient who was still in the hospital at the time of submission. Table 3 summarizes other outcomes.

Table 3. Main Interventions and Outcomes

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Variable	Value
Noninvasive positive-pressure ventilation, *n* (%)	5 (42)
Invasive ventilation, *n* (%)	12 (100)
Neuromuscular blockade, *n* (%)	4 (33)
High-frequency oscillation ventilation, *n* (%)	2 (17)
Nitric oxide, *n* (%)	6 (50)
Prone positioning, *n* (%)	3 (25)
Barotrauma, *n* (%)	2 (17)
Vasopressors, *n* (%)	11 (92)
Renal replacement therapy, *n* (%)	7 (58)
Tracheostomy, *n* (%)	3 (25)
Median duration of mechanical ventilation (range), *d*	16 (4–30)
Alive at day 28, *n* (%)	7 (58)
Alive at day 90, *n* (%)	5 (42)
ICU survival, *n* (%)	5 (42)
Median ICU length of stay (range), *d*	30 (7–104)
Median hospital length of stay (range), *d*	41 (8–96)*

ICU = intensive care unit.
* One patient is still in the hospital.

Discussion

We report on 12 critically ill patients with confirmed or probable MERS-CoV infection. Among these cases were 3 cardiac ICU patients who were part of a health care–associated MERS-CoV cluster in 1 ICU. This cluster also included 3 HCWs, one of whom became critically ill. All critically ill patients had underlying comorbid conditions and developed acute respiratory failure that was characterized by severe hypoxemia and illness, a high incidence of extrapulmonary manifestations, and a high mortality rate.

The clinical features of MERS-CoV disease observed in our patients bear some resemblance to those in critically ill patients with disease caused by SARS-CoV (5). For example, patients with MERS-CoV infection presented with acute hypoxemic respiratory failure requiring invasive mechanical ventilation, therapy with NIPPV frequently failed in these patients, and they often had severe hypoxemia necessitating rescue therapy.

However, our case series also demonstrates some important differences from SARS-CoV infection. All of our patients had underlying comorbid conditions, including asthma, diabetes, renal failure, cardiac disease, recent surgery, or heart failure. This high prevalence of comorbid conditions may be explained in part by the high prevalence of diabetes and hypertension in the Saudi population. However, it also strongly suggests that patients with such conditions are susceptible hosts for MERS-CoV. There were no hospitalized patients with MERS-CoV infection outside the ICU, which differs from a Canadian study of SARS in which only 19% of patients were critically ill (8).

To date, the diagnostic characteristics of MERS-CoV on RT-PCR, including the sensitivity

and technique, as well as transportation time to the reference laboratory. In 2 of our patients, the result remained positive for several weeks, and it seems that a persistent positive result may not necessarily be associated with worse outcome or infectiousness to others.

Use of a lung protective strategy with a small tidal volume is the mainstay of management of ARDS (9). Recent studies showed significant survival benefit with prone positioning and neuromuscular blockade in patients with ARDS (10, 11). Although the use of inhaled nitric oxide in patients with severe ARDS causes a transient improvement in oxygenation, it has not been shown to improve survival and may be harmful (12). Of note, in vitro studies have shown that nitric oxide inhibits the replication cycle of SARS-CoV (13). The clinical therapeutic relevance of this finding to MERS-CoV infection is unknown.

The routine early use of HFOV in ARDS is not recommended because 2 recent trials showed no benefit and possible harm (14, 15). However, HFOV may still have a role as a rescue therapy, which was the case in our patients. There have been concerns about aerosol generation and possible increased risk for disease transmission with HFOV (16). A study examining SARS transmission to HCWs did not show an association between HFOV and staff infection, but the sample size was insufficient to exclude secondary transmission with HFOV (17). In our patients, we used filtered circuits because it has been suggested to reduce transmission (18).

Extracorporeal membrane oxygenation was used during the SARS and H1N1 influenza epidemics. However, it was not used in any of our patients because of the presence of multiple comorbid conditions, thrombocytopenia, and extrapulmonary involvement.

Data are limited on the use of NIPPV in viral pneumonia in general. Although its use in acute lung injury is associated with early physiologic improvement, it has not been shown to decrease the need for intubation or to reduce mortality. In fact, it may increase adverse effects (19). Furthermore, NIPPV is associated with aerosol generation and may increase disease transmission (16). Five of our patients were treated with NIPPV initially; all eventually required invasive ventilation.

The use of corticosteroids in viral pneumonia and ARDS remains controversial. The

admission (23). The potential benefit of corticosteroids in ARDS may be limited to the fibroproliferative phase of the disease (24), patients with ARDS and shock (25), or use of low-dose corticosteroids (26). A randomized, controlled trial found that the use of methylprednisolone for persistent ARDS was associated with improvement in physiologic end points but did not reduce mortality. In fact, patients who started methylprednisolone therapy more than 2 weeks after the onset of ARDS had increased risk for death (27). Whether there is a specific role for corticosteroids in MERS-CoV is unknown. The potential role of ribavirin and interferon-β for the treatment of MERS-CoV is drawn from limited use in patients with SARS and from in vitro studies on SARS-CoV (28–30).

The pathogenesis of organ dysfunction in MERS-CoV is unknown. A striking finding in our cases is the high incidence of extrapulmonary manifestations, including circulatory, renal, hepatic, and hematologic. It remains to be studied whether the main pathogenic mechanism of organ dysfunction is related to cytokine dysregulation, given the high prevalence of lymphopenia in our patients. Other possible mechanisms include direct viral invasion; the virus was recovered from urine and stool in one report (31). The response of severe thrombocytopenia to intravenous immunoglobulin in one of our patients suggests a possible autoimmune mechanism.

Acute kidney injury requiring renal replacement therapy occurred in our patients more often than has been reported in SARS. Renal replacement therapy was required in 58% of our patients, compared with 5% of critically ill patients during the SARS epidemic in Canada (8). The high prevalence may be related to preexisting comorbid conditions, such as diabetes, old age, and hypertension. The isolation of MERS-CoV from urine in one study suggests the possibility of direct viral involvement of the kidneys (31).

The low rate of transmission among HCWs in our study is consistent with previous re[illegible] from the Kingdom of Saudi Arabia and the United Kingdom (32–34). We believe that the low rate of transmission to HCWs was related to effective infection control, lack of susceptible hosts, and poor adaptability of the virus to human transmission observed in this emerging pathogen thus far. However, it is clear from the health care–associated cluster that human-to-human transmission occurs with unprotected exposure. Therefore, there is a concern that MERS-CoV may become highly infectious to humans with sustained human-to-human transmissibility. In such an event, along with the high pathogenicity of the virus, MERS-CoV will become a major public health threat worldwide (35).

Given the high mortality rate of this emerging infection and the lack of evidence for specific therapies, our findings call for an urgent collaborative study to examine therapeutic options, such as convalescent plasma or ribavirin, interferon, or other novel drugs (36).

In conclusion, MERS-CoV infection causes severe respiratory and substantial nonpulmonary organ dysfunctions and has a high mortality rate. Community-acquired and health care–associated MERS-CoV infection occurs in patients with chronic comorbid conditions. Transmission to HCWs seems to be low, although human-to-human transmission does occur with unprotected exposure.

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