

Short Communication

Epidemiological and Clinical Characteristics of Patients with Middle East Respiratory Syndrome Coronavirus in Iran in 2014

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SUMMARY: The Middle East Respiratory Syndrome Coronavirus (MERS-CoV) was a great global concern in 2014. It has a wide range of manifestations that may differ in each area as well as high mortality. In this study, we report the epidemiological characteristics, history, clinical, and paraclinical information of all 5 patients from Iran with laboratory-confirmed MERS-CoV. All patients were from Kerman province. None of them had a history of travel, contact with animals, or consumption of camel milk products, however, all of the patients had contact with a person who had been in Saudi Arabia and experienced respiratory infection. One of the 5 patients was a man and 2 passed away from the disease. Fever and respiratory symptoms were the most common symptoms, and 2 patients had watery diarrhea. Alveolar patterns were observed in all available chest radiograms, and 3 patients had elevated liver aminotransferase levels. Two of these patients had leukopenia, and none had renal failure. In conclusion, the results of this study underscore the need for all patients with acute respiratory symptoms with contact with a person who has recently traveled to Saudi Arabia and experienced respiratory infection to be investigated for MERS-CoV.

The Middle East Respiratory Syndrome Coronavirus (MERS-CoV) was first diagnosed in a man with severe pneumonia in 2012 in Jeddah, Saudi Arabia. This man died of this new infectious disease (1). MERS-CoV has a very high mortality rate (2,3). Studies have indicated that this infection can present a wide range of respiratory and non-respiratory symptoms (4–9). Disease presentations may not start with respiratory symptoms. First MERS-CoV case in France initially presented with abdominal pain and diarrhea (8). In contrast, several MERS-CoV patients reportedly had mild respiratory symptoms that did not require admission (10–12).

In this study, we report the epidemiological, demographic, and clinical characteristics of all 5 patients with MERS-CoV in Kerman province, Iran in 2014. Five patients with laboratory-confirmed MERS-CoV including 3 non-medical individuals, 1 anesthesiologist, and 1 nurse assistant. We reviewed the history, clinical manifestations, laboratory data, and imaging findings of the 3 non-medical patients that were hospitalized in Afzalipoor Hospital in Kerman-Iran and as well as the data from the nurse assistant. The demographic and epidemiologic characteristics of all patients were also assessed. Data were gathered from their medical documents, including, interviews with patients or their families, as well as data from their infectious disease specialists.

Throat swab specimens and sputum samples were

collected and analyzed using real-time reverse transcription PCR (RT-PCR) as previously described by a method targeting the upstream E region and open reading frame 1b of the virus (13).

Five patients with laboratory-confirmed MERS-Cov disease were identified in Iran from May to July 2014. All patients were from and resided in Kerman province, Iran. None of the patients had a history of travel or known history of being in contact with animals or consumption of raw camel milk products within 14 days prior to becoming ill.

Patient 1 was a 52-year-old woman. She was referred to the hospital on May 11, 2014 and was admitted on the same day. She reported fever, productive cough, dyspnea both during physical activity and at rest, watery diarrhea, and loss of appetite from May 1, 2014 and a history of close contact with a woman who had an influenza-like illness and had traveled to Saudi Arabia to perform Umrah. She had a history of hypertension and had been under losartan treatment. Physical examination revealed a fever of 39.6°C, blood pressure of 115/80 mm Hg, respiratory rate of 36 breaths /min; oxygen saturation of 85% on oxygen (mask, 8 L/min) and 50% without oxygen, and bilateral coarse crackles at the base of her lungs.

She was admitted on the day of reference with the initial diagnosis of pneumonia. Chest radiograph (CXR) was taken, and bilateral alveolar infiltration at the basis of lungs was observed. Laboratory data revealed a leukocyte count of 3,900/ μ L with 79.3% neutrophils, normal urea and creatinine levels, and elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels (Table 1). Her electrocardiogram was normal. On the 2nd day of admission, echocardiography was done and showed no abnormality.

With an initial diagnosis of community acquired pneumonia, azithromycin and ceftriaxone were admin-

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istered for treatment. After 48 h, the antibiotics were changed to meropenem and vancomycin because her condition did not improve. Oseltamivir was started for a suspicion of influenza. On the basis of her close contact with the suspicious patient, RT-PCR was performed for coronavirus and influenza from nasopharyngeal swab and deep respiratory secretions collected on the day of admission. She was transferred to the intensive care unit (ICU) on May 14, 2014, because of her life-threatening respiratory symptoms. Bronchoscopy was performed on May 19, 2014, and a smear of the bronchial lavage sample showed no significant findings. The patient tested positive for MERS-CoV by RT-PCR on May 21, 2014. Her condition deteriorated, and she died on May 29, 2014, from severe respiratory distress.

Patient 2 was a 50-year-old woman who had close contact with her sister (Patient 1). She became ill on May 11, 2014, presenting with symptoms including a fever, watery diarrhea (3–4 times/day), and loss of appetite. She developed a productive cough and nausea on May 17, 2014. She was prescribed levofloxacin as outpatient therapy, but her symptoms did not improve. She was referred to the hospital and was admitted on May 19, 2014. She had a hysterectomy without any other past medical history. She had a temperature of 37.8°C, blood pressure of 110/65 mm Hg, respiratory rate of 21 breaths/min, oxygen saturation of 90% without oxygen, and fine crackles were detected at the base of her left lung.

Laboratory data on admission day showed normal renal function and abnormal AST level (Table 1). CXR revealed consolidation in the left lower lobe. Ceftriaxone, azithromycin, and oseltamivir were prescribed. Because of her close contact with her sister, RT-PCR was performed for coronavirus on a nasopharyngeal swab and deep respiratory secretions ob-

tained on the 2nd day of admission. The findings were positive. Her symptoms did not worsen, and she did not require ICU admission. She was discharged on May 30, 2014 in a stable condition.

Patient 3 was the assistant nurse of the 1st case, a 35-year-old woman working at the ICU. She developed a fever and a mild influenza-like illness on May 26, 2014 followed by a productive cough on May 28, 2014. She did not have vomiting or diarrhea and nothing remarkable in her past medical history. On the basis of her close contact with the 1st case, a throat swab taken on May 26, 2014 for suspicion of MERS-CoV, was positive (May 31, 2014). All her laboratory data were normal (Table 1). She was advised to stay home and follow infection control precautions. She became asymptomatic on June 3, 2014.

Patient 4 was a 44-year-old man, national health-care worker, anesthesiologist, and a resident of Kerman province, Iran. He developed mild symptoms of an influenza-like illness on June 6, 2014. He was reported to have chronic heart disease. His condition deteriorated as he developed dyspnea and was admitted to the hospital on June 17, 2014. Specimens were collected upon admission, and RT-PCR was negative for MERS-CoV on June 18, 2014. His condition continued to deteriorate, and he was transferred to the ICU on June 19, 2014. Additional specimens collected on that day tested positive for MERS-CoV on June 20, 2014.

He had close contact with a severe acute respiratory infection (SARI) patient during an intubation. This SARI patient had a fever, productive cough, and dyspnea and was admitted to Afzalipoor Hospital on May 17, 2014. He had a history of travel to Saudi Arabia to perform Umrah during May 5–15, 2014. RT-PCR test results for influenza and MERS-CoV on May 22, 2014, were negative. The SARI patient was transferred to the ICU and was intubated because of severe respiratory

Table 1. Laboratory data of the patients

	Patient 1	Patient 2	Patient 3	Patient 5	Normal range
Date of blood testing	May 11	May 19	May 26	June 25	
(days after 1st symptom)	Admission day (day 10)	Admission day (day 8)	Not admitted (day 1)	Admission day (day 3)	
Blood cells					
Leukocyte count (cells/ μ L)	3.6×10^3	3.8×10^3	4.0×10^3	7.7×10^3	$4\text{--}10 \times 10^3$
Neutrophils (%)	79.3	53.5	64.3	81.6	23–45
Lymphocytes (%)	18.5	37.3	33.5	8.1	35–65
Hemoglobin (mg/dL)	11.9	11.6	13.0	14.1	11.5–16.5
Platelet (cells/ μ L)	155×10^3	124×10^3	253×10^3	117×10^3	$150\text{--}450 \times 10^3$
Blood biochemistry					
Blood urea nitrogen (mg/dL)	15	15	21	30	17–53
Creatinine (mg/dL)	0.8	0.7	0.8	0.8	0.5–1.6
ALT (IU/L)	59	27	40	17	5–40
AST (IU/L)	101	60	23	59	5–40
Prothombin time (s)	13	—	—	14.3	
INR	1.0	—	—	1.2	
Blood sugar (mg/dL)	109	167	167	108	<140
RT-PCR					
Date of sample collection	May 14	May 20	May 26	May 28	
Type of specimen samples	Throat swab	Throat swab	Throat swab	Throat swab	
Underlying Disease	Hypertension	None	None	COPD	

ALT, alanine aminotransferase; AST, aspartate aminotransferase.

distress on May 26, 2014. His condition deteriorated, and he died on May 30, 2014 from severe respiratory distress.

Patient 5 was a 67-year-old woman with a history of chronic obstructive pulmonary disease (COPD) who was admitted to the hospital on June 6, 2014 owing to COPD exacerbation. She was discharged on June 14, 2014, and her treatment was continued at home. She was in a stable condition until she developed severe acute respiratory symptoms and was readmitted on June 25, 2014. During the 1st admission, she had a close contact with a SARI patient. The SARI patient's daughter had traveled to Saudi Arabia while having close contact and living with the SARI patient. However, the SARI patient was not investigated for MERS-CoV.

Patient 5 first experienced symptoms on June 22, 2014, including fever, productive cough and mild hemoptysis, pleuritic chest pain, moderate to severe dyspnea, night sweats, loss of appetite, and weight loss over the past month. Her past medical history over the previous 20 years revealed only COPD. She had a fever of 38.9°C, blood pressure of 110/80 mm Hg, respiratory rate of 32 breaths/min, oxygen saturation of 92% on oxygen (nasal cannula, 4 L/min) and 88% without oxygen. Physical examination revealed coarse crackles at base of both lungs and high-resonance bronchial sounds in the upper half of both lungs. Laboratory data on the day of admission showed elevated AST levels (59 IU/L), abnormal prothrombin time (PT, 14.3 s), and international normalized ratio (INR, 1.2) (Table 1). CXR showed consolidations in the left lower and right middle lobes. Antibiotic therapy including meropenem and vancomycin was started. The patient did not respond to antibiotics. Because she also had a close contact with a suspected patient RT-PCR was performed for MERS-CoV, and oseltamivir treatment was started.

Her respiratory symptoms worsened, and she was intubated and transferred to the ICU. Thereafter, the patient left the hospital with personal consent and went to a private hospital. Her condition deteriorated there, and she died from severe respiratory distress on July 4, 2014. The PCR testing confirmed MERS-CoV infection several days later.

In this report, we described the epidemiological links, demographic features, and clinical progression of patients with MERS-CoV in Iran. We could find no plausible reason to explain why all of the patients were from Kerman province in Iran. None of them had a history of travel or known history of being in contact with animals or consuming raw camel milk products, but all of them had contact with a confirmed MERS-CoV case or suspected cases with negative RT-PCR findings or who did not visit a practitioner. All of these suspected cases had severe acute respiratory syndrome except for the daughter of the SARI patient, and they had traveled to Saudi Arabia. The daughter of the SARI patient had traveled to Saudi Arabia but she did not develop respiratory syndrome.

One of the 5 patients was a man (man: woman ratio 1:4). In Saudi Arabia, 62–72% of MERS-CoV cases were men (14,15). In other countries with imported MERS-CoV cases, most of the patients were also men

(16,17).

Two of the 5 MERS-CoV patients in this study died (40% mortality rate). The mortality rate of MERS-CoV varied worldwide ranging from 22 to 100% (15,16,18,19). Saudi Arabia was the most involved country and had a reported MERS-CoV mortality rate of 60% (15). Both the patients who died, described in the current study, had medical comorbidities including hypertension and COPD, while the other 3 patients were otherwise healthy. A similar finding was reported in Tunisia; among them one patient having diabetes mellitus died, the other 2 patients without any medical comorbidities, recovered without any complications (17). In Saudi Arabia, 47 MERS-CoV cases were reported, and only 2 cases did not have any underlying medical comorbidities and steroids use. Malignant diseases, chronic lung diseases, and hypertension were the comorbidities most related to death (15). These findings are also similar to those of the current study.

All MERS-CoV cases had a fever and productive cough. Dyspnea and loss of appetite were the next-most common symptoms and were seen in 3 patients. Two patients had watery diarrhea, and one of which also had nausea. Myalgia and pleuritic chest pain were seen in 1 patient. Other studies also reported fever and cough as the most prevalent symptoms (15,20). The frequencies of the other symptoms were similar in Iran and Saudi Arabia (15).

CXR were available for 3 of the MERS-CoV patients in the current study, and all showed alveolar patterns (data not shown). In France, one of MERS-CoV cases had upper right lobe consolidation, but the other patient had no significant findings in CXR (20). In Saudi Arabia, all patients had CXR abnormalities including increased bronchovascular markings, patchy infiltration, patchy to confluent air-space consolidation, etc. (15). Another study in Saudi Arabia reported interstitial infiltrates in all MERS-CoV cases (21). A study of 12 MERS-CoV cases in Egypt reported that 5 cases had normal, and 5 cases had scattered patches of rather confluent airspace fillings within one or both lungs, and other 2 cases showed large consolidations (22).

Laboratory data were available for 4 of the 5 MERS-CoV patients. Two patients had only elevated AST levels. One patient had elevated ALT as well as AST levels. One patient had normal ALT and AST levels. Studies from France and Tunisia did not report liver test results, but the frequencies of elevated ALT and AST levels in Saudi Arabia cases were 11% and 15%, respectively, less than the frequencies in Iran (15). One of our cases had prolonged PT and high INR, and 2 had leukopenia. The French MERS-CoV cases reported severe renal failure (20), which was not observed in the 5 MERS cases in Iran.

Both MERS-CoV cases in France and 98% cases in Saudi Arabia were admitted to the ICU (15,20). Four of the five cases (80%) in Iran were also transferred to the ICU. Tunisia had one ICU admission among 3 patients, a rate less than that in other countries (17).

In conclusion, all patients with acute respiratory symptoms who report close contact with a person who recently traveled to Saudi-Arabia and experienced respiratory infection should be investigated for MERS-

CoV. Obtaining an accurate history, particularly regarding recent contacts, is a critical step in these cases.

This study was approved by Ethical Committee of Kerman University of Medical Sciences, and informed consent was obtained from all patients at baseline.

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Conflict of interest None to declare.

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