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Clinical aspects and outcomes of 70 patients with Middle East respiratory syndrome coronavirus infection: a single-center experience in Saudi Arabia

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SUMMARY

Objectives: To report the experience with Middle East respiratory syndrome coronavirus (MERS-CoV) infection at a single center in Saudi Arabia.
Methods: Cases of laboratory-confirmed MERS-CoV occurring from October 1, 2012 to May 31, 2014 were reviewed retrospectively. Information sources included medical files, infection control outbreak investigations, and the preventive medicine database of MERS-CoV-infected patients. Data were collected on clinical and epidemiological aspects and outcomes.
Results: Seventy consecutive patients were included. Patients were mostly of older age (median 62 years), male (46, 65.7%), and had healthcare acquisition of infection (39, 55.7%). Fever (43, 61.4%), dyspnea (42, 60%), and cough (38, 54.3%) were the most common symptoms. The majority developed pneumonia (63, 90%) and required intensive care (49, 70%). Infection commonly occurred in clusters. Independent risk factors for severe infection requiring intensive care included concomitant infections (odds ratio (OR) 14.13, 95% confidence interval (CI) 1.58–126.09; $p = 0.018$) and low albumin (OR 6.31, 95% CI 1.24–31.90; $p = 0.026$). Mortality was high (42, 60%), and age ≥65 years was associated with increased mortality (OR 4.39, 95% CI 2.13–9.05; $p < 0.001$).
Conclusions: MERS-CoV can cause severe infection requiring intensive care and has a high mortality. Concomitant infections and low albumin were found to be predictors of severe infection, while age ≥65 years was the only predictor of increased mortality.

1. Introduction

Middle East respiratory syndrome coronavirus (MERS-CoV) is an emerging virus that was first isolated from a patient in Jeddah, Saudi Arabia, in June 2012.[1] Since then, there have been 699 cases of laboratory-confirmed MERS-CoV infection, including at least 209 deaths, reported in 21 countries from four continents.[2] Since its emergence in 2012, MERS-CoV infection has been diagnosed in sporadic cases and in family and healthcare clusters of infection.[3] The disease activity has recently appeared to increase, with a large healthcare-associated cluster in multiple hospitals in the western region of Saudi Arabia; 402 new cases were reported from Saudi

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Arabia alone during the period April 11 to June 9, 2014.[2] This in turn has raised concerns about the pandemic potential of MERS-CoV infection.

MERS-CoV is capable of causing a spectrum of illness ranging from asymptomatic infection to severe pneumonia requiring intensive care unit (ICU) admission.[4] While the infection is still associated with high mortality, specific antiviral therapy is lacking and management remains mainly supportive.[2,5]

The available literature describing the clinical and epidemiological features and outcomes of MERS-CoV infection is limited to case reports and descriptions of relatively small cohorts.[3,6–14]

We describe herein our clinical experience with 70 laboratory-confirmed MERS-CoV infection patients diagnosed at Prince Sultan Military Medical City (PSMMC) over a period of 20 months. PSMMC is a 1200-bed, tertiary medical center in Riyadh, Saudi Arabia, with around 40 000 annual admissions and 118 000 emergency room visits per year.

2. Methods

This was a retrospective study of all patients who were diagnosed with a laboratory-confirmed MERS-CoV infection at our center over the period October 1, 2012 to May 31, 2014. Patients were identified from the microbiology and infection control records. In addition to the medical file review, data were collected from infection control outbreak investigations and the preventive medicine database of MERS-CoV-infected patients. Demographic and clinical details, epidemiological exposures, laboratory investigations, and outcomes were collated. A consultant radiologist reviewed and summarized all radiological investigations. Patients were followed until discharge from the hospital or death. MERS-CoV infection was diagnosed by reverse transcriptase PCR (RT-PCR) testing of respiratory tract samples for the MERS-CoV upE, ORF 1b, and N genes.[15] All RT-PCR tests for MERS-CoV were performed at the Saudi Ministry of Health National Laboratories in Jeddah and Riyadh, Saudi Arabia. The study was approved by the institutional research ethics committee.

2.1. Definitions

Infection was classified as healthcare-associated if the onset of MERS-CoV illness was more than 48 h after the current admission, or if the onset of illness was within 14 days of discharge from a clinical area where cases of MERS-CoV infection had been documented. A cluster was defined as two or more persons with onset of symptoms within the same 14-day period, and who were associated with a specific setting (healthcare or household).[4] Concomitant infections included all bacterial, fungal, and viral infections that occurred within 14 days of the diagnosis of MERS-CoV infection. Severe infection requiring care in an ICU and death were considered poor outcomes.

2.2. Statistical analyses

The Chi-square test or Fisher's exact test was used to compare categorical data, while the Student's *t*-test was used to compare continuous variables. All *p*-values were two-tailed and considered statistically significant at a cut-off of <0.05. Risk factors for a poor outcome were initially assessed in a univariate analysis. Those factors that were found to be significant were then entered into competing logistic regression (ICU care) or Cox regression (death) in order to determine the independent risk factors for a poor outcome. Graphical and statistical tests indicated that the proportional hazard assumption was not violated. A forward stepwise method was used to identify the determinants of a poor outcome, with the probability of entry set at ≤ 0.05.

Statistical analyses were performed using Microsoft Excel 2007 (Microsoft Corp., Redmond, USA) and IBM SPSS Statistics software, version 21.0 (IBM Corp., Armonk, NY, USA).

3. Results

3.1. Characteristics of the study patients

A total of 70 consecutive patients were included in the study. The majority of patients were males (46, 65.7%), of older age (median 62 years), residents of Riyadh (57, 81.4%), and of Saudi nationality (57, 81.4%). Comorbid conditions were documented in 57 (81.4%) patients, with a median age-adjusted Charlson comorbidity index (CCI) score of 5 (interquartile range (IQR) 0.25–6.0). Over half of MERS-CoV infections (39, 55.7%) were healthcare-associated. Only seven (10.0%) patients were obese and nine (12.9%) were smokers. A history of exposure to animals, including camels, within the 2 weeks preceding the onset of MERS-CoV infection was very uncommon (Table 1).

The majority of patients (67, 95.7%) with confirmed MERS-CoV infection were symptomatic. The most common symptoms were fever (43, 61.4%), shortness of breath (42, 60.0%), and cough (38, 54.3%). Non-respiratory symptoms were also relatively common, including generalized fatigue (29, 41.4%), vomiting or diarrhea (21, 30.0%), abdominal pain (17, 24.3%), confusion (18, 25.7%), and myalgia or arthralgia (14, 20%). Most patients had pneumonia (63, 90%). The most common radiological abnormality on chest X-rays was bilateral pulmonary infiltrates, which were reported in 53 (75.7%) patients. For patients with community-acquired MERS-CoV infection, the median time from onset of symptoms to hospital admission was 5.0 (IQR 3.0–8.5) days (Table 2). Overall, the median time from illness onset to diagnosis was 7 (IQR 3.0–13.8) days.

Table 1
Epidemiological characteristics of 70 patients with laboratory-confirmed MERS-CoV infection

Characteristic	Value
Total, *n* (%)	70 (100)
Age, years, median (range)	62 (1–90)
Age group, *n* (%)	
0–5 years	1 (1.4)
6–18 years	2 (2.9)
19–50 years	20 (28.6)
51–64 years	14 (20.0)
≥65 years	33 (47.1)
Gender, *n* (%)	
Male	46 (65.7)
Female	24 (34.3)
Nationality, *n* (%)	
Saudi Arabia	57 (81.4)
Philippines	9 (12.9)
Yemen	3 (4.3)
Egypt	1 (1.4)
City of residence, *n* (%)	
Riyadh	57 (81.4)
Al Kharj	6 (8.6)
Other	7 (10.0)
Occupation, *n* (%)	
Healthcare worker	10 (14.3)
Non healthcare worker	60 (85.7)
Age-adjusted Charlson comorbidity index, median (IQR)	5 (0.25–6.0)
Obese, *n* (%)	7 (10.0)
Pregnant, *n* (%)	1 (1.4)
Smoker, *n* (%)	9 (12.9)
Animal exposure within 2 weeks before illness onset, *n* (%)	
Camels	1 (1.4)
Cats	2 (2.9)
Acquisition of infection, *n* (%)	
Community-acquired	31 (44.3)
Healthcare-associated	39 (55.7)

IQR, interquartile range; MERS-CoV, Middle East respiratory syndrome coronavirus.