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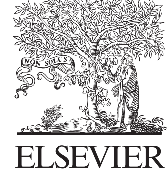

ORIGINAL ARTICLE

Middle East Respiratory Syndrome Coronavirus Outbreak in the Republic of Korea, 2015

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Abstract
Objectives: The outbreak of Middle East respiratory syndrome coronavirus (MERS-CoV) infection in the Republic of Korea started from the index case who developed fever after returning from the Middle East. He infected 26 cases in Hospital C, and consecutive nosocomial transmission proceeded throughout the nation. We provide an epidemiologic description of the outbreak, as of July 2015.
Methods: Epidemiological research was performed by direct interview of the confirmed patients and reviewing medical records. We also analyzed the incubation period, serial interval, the characteristics of superspreaders, and factors associated with mortality. Full genome sequence was obtained from sputum specimens of the index patient.
Results: A total of 186 confirmed patients with MERS-CoV infection across 16 hospitals were identified in the Republic of Korea. Some 44.1% of the cases were patients exposed in hospitals, 32.8% were caregivers, and 13.4% were healthcare personnel. The most common presenting symptom was fever and chills. The estimated incubation period was 6.83 days and the serial interval was 12.5 days. A total of 83.2% of the transmission events were epidemiologically linked to five superspreaders, all of whom had pneumonia at presentation and contacted hundreds of people. Older age [odds ratio (OR) = 4.86, 95% confidence interval (CI) 1.90—12.45] and underlying respiratory disease (OR = 4.90, 95% CI 1.64—14.65) were significantly associated with mortality. Phylogenetic analysis showed that the MERS-CoV of the index case clustered closest with a recent virus from Riyadh, Saudi Arabia.
Conclusion: A single imported MERS-CoV infection case imposed a huge threat to public health and safety. This highlights the importance of robust preparedness and optimal infection prevention control. The lessons learned from the current outbreak will contribute to more up-to-date guidelines and global health security.

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1. Introduction

Middle East respiratory syndrome (MERS) is a viral respiratory illness caused by a novel human beta-coronavirus (CoV) [1,2]. Since it was first reported from Saudi Arabia in September 2012, 1,211 patients have been detected worldwide, as of June 5, 2015 [3]. Secondary infection through human-to-human transmission was confirmed from previous outbreaks [4,5,6], and outbreaks in healthcare settings comprise a large proportion of the outbreak [4,7]. Although the exact route of transmission is still unclear, the respiratory droplet route is currently most likely [8]. Until June 2015, most of the cases of MERS-CoV infection occurred in the Middle East. Although a few cases were reported in other countries, none exceeded five [3].

The outbreak of MERS-CoV infection in the Republic of Korea started when a 68-year-old South Korean man developed fever and myalgia on May 11 after returning from a business trip to Bahrain, United Arab Emirates, and Saudi Arabia. MERS-CoV infection was diagnosed on May 20. However, by then he had already contacted approximately 600 people during his visits to two clinics and admission to a secondary hospital (Hospital C) located in Pyeongtaek, Gyeonggi-do. Twenty-six cases of MERS-CoV infection were confirmed among these initial contacts, and consecutive transmission based on nosocomial infection rapidly proceeded throughout the nation.

This unprecedented nationwide MERS-CoV outbreak in the Republic of Korea imposed a huge threat not merely to public health and safety, but also to the economy, the tourist industry, and social activity. The forecast for gross domestic product was downgraded by 0.3%, >135,000 foreign tourists canceled their visit to the Republic of Korea, >2,700 schools were closed, and >16,000 people underwent house quarantine. These highlight the importance of appropriate infection control intervention. However, although evidence-based investigation is essential for effective intervention, information concerning the epidemiology of MERS-CoV infection is currently limited. Herein, we provide an overall epidemiologic description of the MERS-CoV infection outbreak in the Republic of Korea, which is the largest outbreak outside of the Arabian Peninsula.

2. Materials and methods

2.1. Definitions

A person was defined as a confirmed MERS-CoV infection case when there was laboratory evidence of MERS-CoV infection, irrespective of clinical signs and symptoms. The onset of illness was defined as the time when a patient newly developed any symptom relating to MERS-CoV infection such as fever, chills, myalgia, shortness of breath, cough, sore throat, headache, nausea, vomiting, diarrhea, or abdominal pain. Cases were classified into healthcare personnel (doctor, nurse, and radiologic technologist), patient, caregiver (both paid and family caregivers), and others. Close contact was defined as a person who did not wear appropriate personal protective equipment (gloves, gown, N95 mask, goggles, or face mask), and: (1) stayed within 2 m of the patient; (2) stayed in the same room or ward with the patent; or (3) directly contacted respiratory secretions of the patient [9]. In order to describe patients who caused sizable subsequent infection transmission, we arbitrarily defined a superspreading event as one patient transmitting the infection to more than four patients. The patient who caused the superspreading event was defined as a superspreader.

2.2. Data source and assessment of exposure

We carried out an epidemiological research by direct interview of the patients who were confirmed with MERS-CoV infection. Data concerning demographic characteristics, the initial symptom and date of its onset, healthcare facilities for the case visited, presence of personal protective equipment, and a list of contacts were collected. The duration and route of exposure were further determined through reviewing closed circuit television and tracking the health insurance review and assessment service, global positioning system of the patient's cellular phone, and recent credit card inquiry transactions. Based on these data, potential exposures were identified for each confirmed case. When a confirmed case had multiple potential exposures, the most probable exposure was determined through the consensus of the authors. Simultaneously, we thoroughly reviewed the medical records of the patients in order to identify underlying comorbidities, radiological evidence of pneumonia, aerosol generating procedures, and final prognosis. National health insurance data was used to validate underlying diseases of the confirmed patients.

2.3. Clinical samples and laboratory confirmation

Sputum or tracheal-aspirate samples of the patients were collected in a sterile cap and transferred to qualified national, local, or commercial facilities immediately. For patients whose sputum specimen was not acquirable, a specimen from a nasopharyngeal or oropharyngeal swab was obtained. Laboratory diagnosis was performed according to the World Health Organization guidelines of the MERS laboratory test [10]. For molecular detection of MERS-CoV RNA, two real-time reverse-transcription polymerase chain reaction assays targeting an upstream of MERS-CoV envelope protein gene and the open reading frame 1a (ORF 1a) gene were used [11].

2.4. Sequencing and phylogenetic analysis

Full genome sequence using Sanger and Illumina sequencing was obtained from direct polymerase chain reaction products using sputum specimens from the

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