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Middle East Respiratory Syndrome-coronavirus infection: An overview

Jaffar A. Al-Tawfiq*

Specialty Internal Medicine Unit, Dhahran Health Center, Saudi Aramco Medical Services Organization, Saudi Aramco, Dhahran, Saudi Arabia

Received 28 May 2013; accepted 5 June 2013

KEYWORDS

Novel coronavirus;
MERS-CoV;
Middle East Respiratory
Syndrome

Summary Middle East Respiratory Syndrome-coronavirus (MERS-CoV) was reported from a number of countries in the Middle East and Europe with a reported high mortality rate. MERS-CoV was initially isolated from a patient from Bisha, Saudi Arabia. A recent outbreak of MERS-CoV infection was described in a healthcare facility. Although, the recent publications on this topic had shed light on the epidemiology of the disease, many questions remain to be answered.

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The coronavirus family of single-strand RNA viruses is a large group of viruses that usually cause upper respiratory tract infection in humans. The first two members, 229E and OC43, were recognized in the 1960s [1]. It was not until 2003 when this family of viruses attracted attention due to the discovery of a new virus that caused the pandemic severe acute respiratory syndrome (SARS) [2,3]. Later on, two additional novel coronaviruses, NL63 and HKU1, were identified in 2004 and 2005 [4,5]. These two viruses cause respiratory tract infections and they are widely spread within the human population [4]. Thus, these four known human coronaviruses, 229E, OC43, NL63, and HKU1, cause mild to moderate

upper-respiratory tract illness without significant morbidity.

Since September 2012, a novel coronavirus was found to cause sporadic cases of severe acute respiratory infection (SARI). The virus strain was not known previously and genome sequencing showed that this new virus belongs to the genus Beta-coronavirus and is distinct from other known coronaviruses and from SARS [6]. In a small number of patients with SARS, 7/28 (25%) had low titers of neutralizing antibodies for this newly discovered virus [7]. The newly discovered virus was recently named the Middle East Respiratory Syndrome-coronavirus (MERS-CoV) [8].

MERS-CoV was initially isolated from the respiratory tract of a patient from Bisha, Saudi Arabia. The patient developed severe pneumonia and acute renal failure in June 2012 [6]. This case was first published in ProMed in September 2012 [9]. The disease apparently runs a severe course in the

* Correspondence address: P.O. Box 76, Room A-428-2, Building 61, Dhahran Health Center, Saudi Aramco, Dhahran 31311, Saudi Arabia. Tel.: +966 3 877 3524; fax: +966 3 877 3790.

E-mail addresses: jaffar.tawfiq@aramco.com,
jaltawfi@yahoo.com

majority of patients. In a family cluster of four cases, a spectrum of disease severity was observed. One patient had atypical presentation of fever, urinary retention, flank pain, diarrhea, renal colic, and urinary tract infection. Another patient had severe disease and death, and milder illness in two young family members [10].

From 6 April to May 17, 2013, 21 confirmed cases of MERS-CoV infection were reported in the region of Al-Ahsa in the Eastern Province of Saudi Arabia (16 males and 5 females, median age 56 years) with nine deaths [11,12]. The majority of the initial cases were associated with a single health care facility. In addition, three family members of cases and two health care workers who had contact with laboratory confirmed cases developed the infection [11,12]. In addition, two cases were reported by France. The first case became ill after a 9-day vacation to Dubai, UAE. The second case, reported on 12 May, is a patient who shared a room at a health care facility with the first case [13]. In Tunisia, there were two laboratory confirmed cases, a brother and a sister, who are thought to have caught the virus from their father, who became ill three days after returning from a visit to Qatar and Saudi Arabia and died on 10 May [14]. Countries with reported cases are Saudi Arabia, Qatar, Jordan, and the United Arab Emirates. The United Kingdom, Germany, France and Tunisia also reported cases among people who had been to the Middle East or have had contact with travelers returning from these areas. Thus, globally, from September 2012 to end of May 2013, there are 49 laboratory-confirmed cases of infection with MERS-CoV, with a mortality rate of 55% [15].

The exact mode of transmission of the virus is not known. In February 2013, MERS-CoV infection was confirmed in an adult male in the United Kingdom [16]. The patient developed severe respiratory tract infection 10 days after traveling to Pakistan and Saudi Arabia. A contact tracing of 135 identified two secondary cases among family members without recent travel: one developed severe respiratory illness and died, the other had an influenza-like illness. No other severe cases were identified nor were MERS-CoV detected in respiratory samples among 135 contacts followed for 10 days.

Who is considered a close contact? In the UK study mentioned above [17] a close contact definition is shown in Table 1. From that study it was concluded that there was a limited human to human transmission [17]. Health care associated transmission of MERS-CoV was described in Jordan in April 2012. However, the first time healthcare workers were involved in healthcare transmission of MERS-CoV was diagnosed after exposure to patients with

Table 1 Definition of close contacts.

Setting	Definition
Airplane setting	Aircraft passengers in the same row and the two rows in front and behind a symptomatic case.
Household setting	Prolonged (>15 min) face-to-face contact with the confirmed case during the illness in a household setting.
Household setting who also visited the patient in hospital	As above and hospital visiting.
Healthcare setting	(i) Healthcare worker (HCW) who provided direct clinical or personal care to or examined a symptomatic confirmed case or was within close vicinity of an aerosol-generating procedure AND who was not wearing full personal protective equipment (PPE) at the time; or (ii) a visitor to the hospital who was not wearing PPE at the bedside of a confirmed case; full PPE was defined as correctly fitted high filtration mask (FFP3), gown, gloves and eye protection;
Other setting	A person who had prolonged (>15 min) face-to-face contact with a confirmed symptomatic case in any other enclosed setting.

Source: Adopted from Ref. [16].

MERS-CoV in May 15 2013. The Saudi Ministry of health announced two cases of MERS-CoV infection in healthcare workers who were exposed to patients with confirmed infection [18]. In a recent publication from Saudi Arabia, four patients' members of an extended family had a total of 28 persons living in the extended household, with frequent contact and more often between husbands and wives and their children. None of the family members apart from the four patients and none of 124 health care workers who had contact with the patients developed respiratory symptoms or illness [10]. The data indicates a clear evidence of limited, non-sustained, human-to-human transmission. The

exact route of transmission is not clear, but the most likely modes of transmission include droplet and contact transmission. But further studies are required to better understand the risks.

When caring for patients with suspected or confirmed cases of MERS-CoV, the following recommendations for infection control measures in hospital settings include: standard precautions, droplet precautions (wearing a medical mask when in close contact (within 1 m) and upon entering the room or cubicle of the patient); and performing hand hygiene in accordance with the World Health Organization's (WHO) 5 moments of hand hygiene. Additional measures include wearing a particulate respirator when performing aerosol-generating procedures in addition to other precautions as outlined by WHO document [19]. A recent publication of MERS-CoV outbreak in healthcare setting, there was evidence of person-to-person transmission and the outbreak was aborted by the implementation of basic infection control measures [12]. The center for Disease Control and prevention, United States, recommends the placement of the patient in an Airborne Infection Isolation Room (AIIR) [20].

As our understanding of the infection evolves, some questions remain to be answered and include: the exact routes of transmission, the incubation period, the true distribution in animals and humans, and how best to manage these patients. Does the virus cause mild and unrecognized disease and what is reported represents only the tip of an iceberg? To further answer this question, there is a need for a robust and deployable specific serological test to investigate mild cases and asymptomatic individuals.

Funding

No funding sources.

Competing interests

None declared.

Ethical approval

Not required.

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