

## Editorial

### **MERS may not be SARS; but India is still vulnerable**

In 2012, a new virus emerged in the Middle-East causing clinical features ranging from asymptomatic or mild upper respiratory tract infection to acute respiratory distress syndrome and multi-organ failure resulting in death. The outbreak of Ebola virus disease in Africa had eclipsed the news about this new virus. Now it is emerging from shadows of Ebola, and its potential to become a global health threat is being discussed. The virus was first isolated from a patient who died from severe respiratory illness in Jeddah, Saudi Arabia and reported in June 2012<sup>1</sup>. The new virus belongs to family of coronaviruses. It was named Middle East Respiratory Syndrome - Coronavirus (MERS-CoV), after its appearance in that Region.

Globally, since September 2012, WHO has been notified of 1,366 laboratory-confirmed cases of infection with MERS-CoV, including at least 487 related deaths, as of July 7, 2015<sup>2</sup>. Frustratingly even after three years of circulation there is sketchy and limited understanding of the transmissibility and transmission dynamics of the virus. Laboratory confirmed cases of MERS have been reported from 26 countries from Middle-East (Iran, Jordan, Kuwait, Lebanon, Oman, Qatar, Saudi Arabia, the United Arab Emirates, and Yemen); Europe (Austria, France, Germany, Greece, Italy, The Netherlands, Turkey, and the United Kingdom); Africa (Algeria, Tunisia and Egypt); Asia (China, Malaysia, Republic of Korea, the Philippines and Thailand); Americas (the United States of America)<sup>3</sup>. The vast majority of these cases in the Middle-East has so far occurred in Saudi Arabia. Outside the Middle-East the largest outbreak has been in South Korea<sup>4</sup>.

The incubation period of MERS ranges between 2 and 14 days (median 5.4 days). The patient complains of fever, cough, chills, body aches and joint pains. Symptoms of pneumonia quickly set-in, there is shortness of breath, difficulty in breathing. Clinical examination shows typical signs of pneumonia. The condition rapidly deteriorates. Severe cases may go

into respiratory and/or other organs like kidney failure, requiring admission in ICU. About a third of patients complain of vomiting and diarrhoea. If untreated, one in three patients dies within 10-12 days from the onset of symptoms<sup>5</sup>. Symptoms are more severe in those who are immune-compromised, elderly, or those with underlying medical conditions like diabetes, cancer, chronic lung disease. Not all who get infected develop full blown pneumonia, some have only mild flu-like symptoms or no symptoms at all<sup>6</sup>. As of today there is neither a specific drug (though ribavirin and interferon alpha 2a are reported to have been used in Saudi Arabia<sup>7</sup>, clinical trial of serum containing antibodies from MERS survivors is planned<sup>8</sup>, and treatment with antibodies from cattle engineered to carry human immunoglobulin genes have shown promising results<sup>9</sup>) nor a vaccine for MERS-CoV (several are in various stages of development). The treatment remains symptomatic and supportive.

The Centers for Disease Control and Prevention (CDC), Atlanta developed real-time reverse transcription PCR (RT-PCR) assays for detection of MERS-CoV in respiratory, serum, and stool samples<sup>10</sup>. There are also some serologic tests available for detecting MERS-CoV antibodies.

MERS-CoV is a zoonotic virus. The natural habitat of coronaviruses is believed to be bats. Strains of this virus have been identified in camels in several countries of Middle-East. Serological tests done on camels and calves in Saudi Arabia show that close to 90 per cent have antibodies to MERS-CoV<sup>11</sup>. RT-PCR done on nasal swab samples of 96 live camels showed close to 30 per cent positive for MERS-CoV, whereas of the 91 camel carcasses, 60 per cent lung tissues were positive<sup>12</sup>. Genomic structures of MERS-CoV isolated from humans and dromedary camels have matched 99.9 per cent<sup>13</sup>. A dromedary camel was confirmed to be source of MERS-CoV that infected a patient who had a close contact with camel's nasal secretions.

The presence of identical sequences in the two MERS-CoV isolates recovered from the patient and from the camel suggests direct cross-species transmission<sup>14</sup>. But how do humans get infected is still not clear, as many of the patients do not give history of contact with camels. It is possible that there may be intermediate hosts other than camel that are source of infection to humans. Other animals, including goats, cows, sheep, water buffalo, swine, and wild birds, have been tested for MERS-CoV, but so far none have been found positive<sup>2</sup>.

Interestingly dromedary camels (*Camelus dromedarius*) are most common type of camels found across the world - in Middle-East, Asia and also in Africa. Why no human cases have been detected in African countries with large camel populations, though it is believed that MERS is circulating in camels in many parts of Africa. Are the serious cases going undetected or the symptoms are very mild and do not get reported.

Initially the virus did not appear to pass easily from person to person. Based on available information, it has been stated in mid-May, 2015 that 'the cases of Middle East Respiratory Syndrome (MERS) recently exported to other countries have not resulted in sustained onward transmission to persons in close contact with these cases on aircraft or in the respective countries outside the Middle East'<sup>15</sup>. However, if the virus is to transmit efficiently from person to person it would have to undergo a mutation. This scenario has changed rapidly.

A South Korean developed respiratory illness after returning from a trip to several countries in the Middle-East (Bahrain, Qatar, United Arab Emirates and Saudi Arabia). By July 7, 2015, a total of 185 MERS-CoV cases, including 33 deaths, have been reported from South Korea. The median age of the cases is 55 yr (ranging from 16 to 87 yr). The majority of cases are men (59%). Twenty six cases (14%) are health care professionals. To date, all cases (excluding the index case) have been linked to a single chain of transmission and are associated with health care facilities<sup>2</sup>. There is evidence in South Korea of secondary, tertiary and perhaps quaternary cases of MERS from single patient<sup>16</sup>. This transmission has happened without the virus undergoing a major mutation.

It is generally agreed that MERS-CoV is transmitted through respiratory secretions of an infected person. It has been shown to spread through close contact with an infected person - living together or health care personnel providing care in hospitals. All cases

reported so far have clear transmission routes from the initial infection.

On May 28, 2015, a traveler from South Korea to Huizhou, China, was admitted into hospital. MERS-CoV infection was confirmed on May 29, marking the first laboratory confirmed case in China. This patient was the son of a South Korean patient. The Chinese health authorities promptly placed 78 close contacts under surveillance, though none presented with symptoms and all tested negative for MERS-CoV<sup>17</sup>.

Scientists in the Republic of Korea and China have completed full genome sequencing of coronaviruses from the current outbreak. Findings were analyzed by a group of virologists convened by WHO. Preliminary analysis of these findings suggests that the MERS-CoV isolated in Korea are similar to those isolated in the Middle East<sup>2</sup>.

The sudden emergence of and spread of MERS reminds one of the early days of SARS (severe acute respiratory syndrome) - a related disease that appeared in 2003 in Asia had an estimated 8,000 cases and more than 750 deaths in over a dozen countries<sup>18</sup>. Both SARS and MERS are coronaviruses. Both are thought to have originated in bats. They spread through other animals to humans. SARS circulated in forest animals like civets, and MERS in camels. MERS seems to jump more easily to humans, but spreads less readily than SARS between humans.

Of the 26 countries which have reported MERS cases, except for countries in Middle-East and South Korea secondary cases have been few<sup>6</sup>. On one hand we have countries which have been able to contain the infection to the travelers, on the other are the countries where secondary and tertiary transmissions have taken place. The virus has not mutated to become more transmissible between humans, then why this differential spread? Perhaps what separates these two sets of countries is presence or absence of robust health systems, infection prevention and control measures to prevent the possible spread of MERS-CoV in health care facilities, policies for prevention of nosocomial infections and their effective implementation, observance of isolation/quarantine protocols and efficient public health surveillance. Some countries in our Region have been alive to the potential of MERS to spread. For example, the Chinese Government developed and issued MERS Prevention and Control Plan in 2013. After the first imported case was detected in China, it promptly revised its Plan in June 2015 based on first-hand experience. China also has health-check

at entry points in mainland China and MERS related questions are asked from travelers returning from the Middle-East<sup>19</sup>.

MERS has by and large circulated in a Region with which India enjoys special relationship. The strategic partnerships with countries of the Middle-East have strengthened remarkably and expanded in several key areas. Given the heavy passenger traffic between India and the Middle-East, not only for pilgrimage but also for employment, tourism, and business purposes, the risk of getting MERS-CoV infected individuals on one of the many flights from Middle-East cannot be ignored. India has had a brush with two respiratory infections outbreaks in the recent past- one was a coronavirus infection (SARS). Both had created panic and chaos. Measures needed to prevent spread of MERS-CoV and manage cases are similar to SARS. If a MERS-CoV infected individual were to land in India, would India be able to contain the infection and limit it to that individual alone? India knows what to do, the question is will that be done effectively? India remains vulnerable.

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#### References

- Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus AD, Fouchier RA. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. *N Engl J Med* 2012; 367 : 1814-20.
- World Health Organization (WHO). Middle East respiratory syndrome coronavirus (MERS-CoV) - Republic of Korea. Disease outbreak news. 7 July 2015. Available from: <http://www.who.int/csr/don/07-july-2015-mers-korea/en/>, accessed on July 8, 2015.
- World Health Organization (WHO). Frequently asked questions on Middle East respiratory syndrome coronavirus (MERS-CoV). Available from: [http://www.who.int/csr/disease/coronavirus\\_infections/faq/en/](http://www.who.int/csr/disease/coronavirus_infections/faq/en/), accessed on July 7, 2015.
- World Health Organization (WHO). MERS-CoV outbreak largest outside Kingdom of Saudi Arabia. Available from: <http://www.who.int/mediacentre/news/mers/briefing-notes/2-june-2015-republic-of-korea/en/>, accessed on July 8, 2015.
- Centers for Disease Control and Prevention (CDC). MERS Clinical Features. Available from: <http://www.cdc.gov/coronavirus/mers/clinical-features.html>, accessed on July 8, 2015.
- World Health Organization (WHO). Middle East respiratory syndrome coronavirus (MERS-CoV). Fact Sheet No. 401. 2015. Available from: <http://www.who.int/mediacentre/factsheets/mers-cov/en/>, accessed on July 8, 2015.
- Omrani AS, Saad MM, Baig K, Bahloul A, Abdul-Matin M, Alaidaroos AY, *et al.* Ribavirin and interferon alfa-2a for severe Middle East respiratory syndrome coronavirus infection: a retrospective cohort study. *Lancet Infect Dis* 2014; 14 : 1090-5.
- Sakamoto S, Tanaka H, Morimoto S. Towards the prophylactic and therapeutic use of human neutralizing monoclonal antibodies for Middle East respiratory syndrome coronavirus (MERS-CoV). *Ann Transl Med* 2015; 3 : 35.
- Matsushita H, Sano A, Wu H, Jiao JA, Kasinathan P, Sullivan EJ, *et al.* Triple immunoglobulin gene knockout transchromosomal cattle: bovine lambda cluster deletion and its effect on fully human polyclonal antibody production. *PLoS One* 2014; 9 : e90383.
- Lu X, Whitaker B, Sakthivel SK, Kamili S, Rose LE, Lowe L, *et al.* Real-time reverse transcription-PCR assay panel for Middle East respiratory syndrome coronavirus. *J Clin Microbiol* 2014; 52 : 67-75.
- Hemida MG, Perera RA, Wang P, Alhammadi MA, Siu LY, Li M, *et al.* Middle East Respiratory Syndrome (MERS) coronavirus seroprevalence in domestic livestock in Saudi Arabia, 2010 to 2013. *Euro Surveill* 2013; 18 (50) : pii=20659.
- Khalalafalla AI, Lu X, Al-Mubarak AI, Dalab AH, Al-Busadah KA, Erdman DD. MERS-CoV in upper respiratory tract and lungs of dromedary camels, Saudi Arabia, 2013-2014. *Emerg Infect Dis* 2015; 21 : 1153-8.
- Hemida MG, Chu DK, Poon LL, Perera RA, Alhammadi MA, Ng HY, *et al.* MERS coronavirus in dromedary camel herd, Saudi Arabia. *Emerg Infect Dis* 2014; 20 : 1231-4.
- Azhar EI, El-Kafrawy SA, Farraj SA, Hassan AM, Al-Saeed MS, Hashem AM, *et al.* Evidence for camel-to-human transmission of MERS coronavirus. *N Engl J Med* 2014; 370 : 2499-505.
- Ben Embarek PK, Van Kerkhove MD. Middle East respiratory syndrome coronavirus (MERS-CoV)-current situation 3 years after the virus was first identified. *Wkly Epidemiol Rec* 2015; 90 : 245-50.
- Cowling BJ, Park M, Fang VJ, Wu P, Leung GM, Wu JT. Preliminary epidemiological assessment of MERS-CoV outbreak in South Korea, May to June 2015. *Euro Surveill* 2015; 20 : pii=21163.
- Wu J, Yi L, Zou L, Zhong H, Liang L, Song T, *et al.* Imported case of MERS-CoV infection identified in China, May 2015: detection and lesson learned. *Euro Surveill* 2015; 20 (24) : pii=21158.
- World Health Organization (WHO). Summary of probable SARS cases with onset of illness from 1 November 2002 to 31 July 2003. Available from: [http://www.who.int/csr/sars/country/table2004\\_04\\_21/en/](http://www.who.int/csr/sars/country/table2004_04_21/en/), accessed on July 8, 2015.
- Gao J, Song P. China upgrades surveillance and control measures of Middle East respiratory syndrome (MERS). *Biosci Trends* 2015; 9 : 203-4.