

MERS Outbreak: Is India Prepared?

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Introduction

Middle east respiratory syndrome (MERS) belonging to the family *Coronaviridae* is a highly lethal viral respiratory illness affecting human beings. Among the four coronavirus genera identified, *Alphacoronavirus* (NL63 and HCoV-229E) and *Betacoronavirus* (HCoV-OC43, HCoV-HKU1, MERS-CoV, and SARS-CoV) cause diseases in humans [1]. MERS-CoV belongs to lineage C of the genus *Betacoronavirus*, and is closely related to *Tylonycteris* bat coronavirus HKU4 (BtCoV-HKU4), *Pipistrellus* bat coronavirus HKU5 (Bt-HKU5) and CoVs in *Nycteris* bats [2]. The genome is single-stranded, positive sense RNA. Fever, non-productive cough, shortness of breath, dyspnea and myalgia are the major symptoms observed in MERS patients. Chills, sore throat, headache, diarrhoea, coryza, nausea/vomiting, sputum production, abdominal pain and runny nose were also observed in some of the patients. People with comorbidities (such as diabetes, cancer, chronic lung, heart and kidney diseases) and weakened immune systems are at higher risk of becoming infected with MERS-CoV, or have a severe infection [3]. Case fatality of about 36% was observed among MERS-CoV infection confirmed cases [4]. According to WHO, since September 2012 globally about 1289 MERS-CoV laboratory confirmed cases (including 455 related deaths) have been reported [5].

The incubation period for MERS ranges from 2-14 days. Although the disease was first reported in Saudi Arabia (September 2012), retrospective studies showed the identification of MERS in Zarqa, Jordan as early as April 2012 [6]. MERS can affect any age group and gender. During admission of MERS-CoV infected patients, laboratory findings such as leukopenia, lymphopenia, thrombocytopenia, and elevated lactate dehydrogenase levels may be observed. As per the data available clinical spectrum of MERS disease ranges from asymptomatic infection to acute upper respiratory illness, severe pneumonia, respiratory failure, septic shock and multi-organ failure resulting in the death of the patients [7]. Radiographic findings such as unilateral or bilateral patchy densities (opacities), interstitial infiltrates, consolidation, and pleural effusions may be observed [7]. Cases of Co-infection with respiratory viruses (e.g., parainfluenza, rhinovirus, influenza A virus[H1N1]pdm09, herpes simplex virus, influenza B virus) and community acquired bacteria has been reported during admission of MERS-CoV infected patients [1]. Cases of nosocomial bacterial (including *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Acinetobacter* species) and fungal (*Candida* species) infections have also been reported in mechanically-ventilated patients [1].

MERS infection has been linked to countries in and near the Arabian Peninsula. Nine countries in or near the Arabian Peninsula have reported lab-confirmed MERS Cases (Saudi Arabia, United Arab Emirates (UAE), Qatar, Oman, Jordan, Kuwait, Yemen, Lebanon, Iran)

while nearly 17 countries have reported travel-associated MERS cases (United Kingdom, France, Tunisia, Italy, Malaysia, Philippines, Greece, Egypt, United States of America, Netherlands, Algeria, Austria, Turkey, Germany, South Korea, China, Thailand) [8]. Recent travellers from the Arabian Peninsula, close contacts of an ill traveller/confirmed MERS case from the Arabian peninsula, people having direct contact with infectious secretions of MERS cases (e.g., being coughed on), healthcare personnel, people with direct exposure to camels (contact) and people consuming raw camel milk/urine/undercooked camel meat are at increased risk of acquiring MERS [9]. MERS-CoV strains from camels were found to be identical to human MERS-CoV strains in countries such as Egypt, Oman, Qatar, and Saudi Arabia. Camels are most likely to be a major reservoir host for MERS-CoV and an animal source of infection in humans [4]. Based on viral genome analysis, it is hypothesized that MERS-CoV originated in bats and was transmitted to camels in the distant past. Genome sequence analysis has revealed that MERS-CoV has not mutated much during transmission in human populations, except for a single amino acid mutation (position 1020 of the surface protein) located in a region of the protein involved in fusion to host-cell membranes but not in binding to DPP4. MERS-CoV can bind to DPP4 from several species [1]. Thus, in addition to camels and human beings non-human primates, rabbits, goats, sheep and horses are thought to be susceptible to MERS Co-V infection. Possible role of camels and other animals in the transmission of MERS-CoV needs further investigation.

MERS-CoV spreads from infected patients to others through close contact (such as caring for or living with an infected person). Cases of MERS-CoV human-to-human transmission has been confirmed in hospitals as well as household settings. A recent report confirmed MERS-CoV infection in two healthcare providers from USA while caring the MERS infected patients. MERS-CoV can be diagnosed either by PCR or by using serological tests such as ELISA, Immunofluorescent assay (IFA) and neutralizing antibody assay respectively. Presence of viral nucleic acid can be confirmed either by positive real-time reverse transcription PCR on at least two specific genomic targets (*upE*, *ORF 1b*, *ORF 1a*) or by a single positive target with sequencing of a second positive PCR product (RdRp, N gene) [1]. FDA has authorized the use of CDC's 2012 real-time reverse transcription-PCR assay for testing MERS-CoV infection in clinical samples such as respiratory, blood, and stool specimens. For serological confirmation of infection, paired serum samples should be collected 14-21 days apart with the first taken during the first week of illness. A positive ELISA/Immunofluorescence assay (screening assay) should be followed by a neutralisation assay (confirmatory assay). MERS-CoV serological results should be carefully interpreted because of cross-reactivity against other coronaviruses [1]. MERS-CoV has been detected in faeces, serum and urine of infected patients. MERS-

CoV viral RNA load is at lower concentration in blood, urine, and stool specimens whereas higher in respiratory tract samples [1]. High viral load and longer duration of MERS-CoV can be detected in lower respiratory tract (tracheal aspirates and bronchoalveolar lavage fluid) when compared to upper respiratory tract (nasopharyngeal swabs) of the affected patients.

Following simple preventive actions daily will help people in protecting themselves from being infected by MERS-CoV. Preventive measures as recommended by CDC includes washing our hands with soap and water or an alcohol based hand sanitizer, proper disposal of tissues containing cough/sneeze secretions, avoiding personal contact such as kissing, or sharing cups or eating utensils, with sick people and finally cleaning and disinfecting frequently touched surfaces and objects (such as doorknobs). Healthcare personnel, household members and close contacts of MERS infected/suspected patients should wear personal protective equipment such as surgical masks, gowns, gloves, respirator (disposable N95 filtering facepiece respirator), eye protection (goggles or face shield), to prevent the spread of MERS-CoV. Drinking of pasteurised camel milk and properly cooked camel meat is necessary to destroy the virus and prevent its spread [1]. Consumption of raw camel urine for medicinal purposes should be avoided. People working at camel farms, slaughterhouses, markets, racing facilities and veterinarians, should practise good personal hygiene. If camels are showing signs of upper respiratory tract disease protective measures such as wearing of gloves and gowns is recommended [1].

Currently, there is neither an available vaccine nor a specific antiviral treatment recommended to prevent MERS-CoV infection. *In Vitro* studies have shown that MERS-CoV is readily inhibited by type 1 interferons (IFN- α and especially IFN- β), ciclosporin, mycophenolic acid, chloroquine, chlorpromazine, loperamide, and lopinavir [1]. The efficacy of these drugs in treating MERS-CoV infected patients needs further investigation. Human monoclonal neutralising antibodies and convalescent sera from recovered patients might be useful for treating MERS-CoV infected patients [1]. Symptomatic treatment is being offered to individuals infected with MERS to help relieve symptoms. For severe MERS cases care is being taken to support vital organ functions.

Ministry of Health and Family Welfare, Govt. of India has issued guidance for the Hajj and Umrah pilgrims (returning from Saudi Arabia) and travellers (returning from Saudi Arabia, Republic of Korea and/or any of the other MERS-CoV affected countries) to report immediately at the immigration desk if they are suspecting of being infected with MERS-CoV [8]. Although there are no confirmed reports of MERS in India, but the risk of transmission to the general public can't be ruled out and nationwide surveillance should be carried out at airports as a precautionary measure. Flight crews and Emergency Medical Service (EMS) units at airports should be instructed to report MERS suspected cases. MERS suspected patients should be kept in isolation and tested to prevent/restrict the spread of the disease to the general public. Proper implementation of infection prevention and control measures is the only way in stopping the spread of this deadly disease.

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