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Special Article

Middle East respiratory syndrome: A new global threat

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ABSTRACT

The outbreak of Middle East respiratory syndrome (MERS) is reported from Saudi Arabia and the Republic of Korea. It is a respiratory disease caused by coronavirus. Camels are considered as a source for MERS transmission in humans, although the exact source is unknown. Human-to-human transmission is reported in the community with droplet and contact spread being the possible modes. Most patients without any underlying diseases remain asymptomatic or develop mild clinical disease, but some patients require critical care for mechanical ventilation, dialysis and other organ support. MERS is a disease with pandemic potential and awareness, and surveillance can prevent such further outbreaks.

Key words: Corona virus, infection, Middle East respiratory syndrome, outbreak

INTRODUCTION

"Between 10th and 13th October 2015, the Kingdom of Saudi Arabia notified World Health Organization (WHO) of four additional cases of Middle East respiratory syndrome corona virus (MERS-CoV) infection": Disease outbreak news, 22nd October 2015 on the WHO website.[1]

The first case of MERS was reported from Saudi Arabia in June 2012 in a patient with severe respiratory illness and acute kidney injury.[2] MERS-CoV was isolated from his sputum and it was considered as a serious public health problem with a pandemic potential because millions of pilgrims from all over the world visit Saudi Arabia each year for the Hajj and Umrah pilgrimages. The 2014 outbreak of MERS in Saudi Arabia raised the concern that this virus has mutated and become more transmissible or virulent. The outbreak of CoV is also reported from the Republic of Korea where 36 mortalities have been reported from May 2015 to 19th August 2015.[3] Recent outbreak of CoV has affected more than 186 persons worldwide including Middle East countries, Republic of Korea, Jordan, Kuwait and some parts of Europe. Till date probably no case of MERS has been detected from India. Since September 2012, WHO has been notified of 1599 laboratory-confirmed cases of infection with MERS-CoV, including at least 574 related deaths.

MERS is a respiratory disease with high mortality, caused by a single-stranded RNA CoV. This virus was initially called as CoV 2012 or camel flu, which was then renamed as MERS-CoV.[4] The genomic sequence of MERS-CoV was identified and it has been found that host-cell receptor for cell entry is dipeptidyl-peptidase 4 (DPP4, also known as CD26).[5]

DEFINITION

Case definitions have been proposed by WHO for MERS.[6] Confirmed case is defined as a person with laboratory confirmation of infection with MERS-CoV irrespective of clinical signs and symptoms. A probable case is a patient with acute febrile illness for which testing is inconclusive or not available,

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and that patient either has a direct epidemiological relation with confirmed MERS-CoV case or resides in or travelled to the Middle East or countries where MERS-CoV is known to be circulating. As per WHO, laboratory confirmation includes detection of viral nucleic acid or acute and convalescent serology. The WHO recommends that probable and confirmed cases are to be reported within 24 h of classification through the Regional Contact Point for International Health Regulations at the appropriate WHO Regional Office.[7]

DISEASE TRANSMISSION

Transmission of MERS-CoV might have originally occurred from bats to camels and other, unidentified intermediate hosts. The MERS virus circulated in camel populations in Africa and the Arabian countries for many years. In 2012, MERS-CoV spread to human populations, with camels being the most likely source. Various possible routes of spread from camels to humans exist. Among human beings, it is transmitted by droplet, contact and airborne spread. The incubation period for cases associated with limited human-to-human transmission ranges from 2 to 14 days. The virus is most commonly found in the lower respiratory tract of symptomatic patients and shedding may persist for up to 2 weeks. Lower respiratory tract shedding of MERS-CoV RNA can be detected after 1 month of illness in most patients, suggesting that prolonged shedding could be a source for spread in outbreaks.[8]

CLINICAL FEATURES

Most patients without any underlying disease remain asymptomatic or develop mild clinical disease and typically present with fever, cough, chills, sore throat, myalgia and arthralgia. In some patients, it is followed by dyspnoea with rapid progression to pneumonia within a week, requiring mechanical ventilation (MV) and other organ support like haemodialysis.[9] A few patients may also present with gastrointestinal symptoms such as vomiting, anorexia, abdominal pain, and diarrhoea. Co-infection with other respiratory viruses, nosocomial bacterial and fungal infections is also common in these patients.

In patients with immunosupression or with other co-morbidities such as obesity, diabetes, cardiac disease, lung disease and acute renal failure (ARF), the symptoms can be severe. In its lethal form, MERS causes highly fatal acute pneumonia. ARF is common in these patients which may be either due to hypoxic damage or infection of the kidney. The higher rate of kidney infection can be because of high expression of DPP4 in the kidney.

Arabi *et al*.[10] reported that 11 out of 12 critically ill patients of MERS had extrapulmonary manifestations with shock and seven had ARF. One patient, who was immunocompromised presented with fever, diarrhoea, and abdominal pain without any respiratory symptoms. All 12 patients needed MV, 11 needed vasopressors, renal replacement therapy was needed in seven patients, and median duration of MV was 16 days. Only five patients survived till Intensive Care Unit (ICU) discharge and at day 90. The median duration of ICU stay was 30 days and median hospital stay was of 41 days.

In another study by Assiri *et al*.,[11] 45 patients out of 47 had other co-morbidities including diabetes (68%), hypertension (34%), chronic cardiac disease (28%) and chronic kidney disease (49%). In those 47 patients, 46 presented with fever, 41 had fever with chills and 34 presented with shortness of breath. About 8–10 patients had haemoptysis, sore throat, myalgia, diarrhoea, vomiting and abdominal pain. All patients had an abnormal chest radiograph, and 42 patients needed critical care and 34 needed MV. The median time for onset of symptoms to MV was 7 days and to death was around 14 days (mortality rate 60%).

LABORATORY FINDINGS

Common laboratory findings of MERS include leucopaenia, consumptive coagulopathy, raised creatinine, lactate dehydrogenase and deranged liver enzyme levels.[12] Chest imaging of MERS show features of viral pneumonitis and acute respiratory distress syndrome, with bilateral hilar and patchy infiltrates with small pleural effusions in some cases. Lower respiratory tract specimens are of first priority for collection and real-time reverse-transcriptase polymerase chain reaction testing. If respiratory samples are not available, virus can be obtained from blood, urine, and/or stool specimens, but their concentration in these is very low in comparison to respiratory sample.

PREVENTION AND MANAGEMENT

No specific vaccine exists for MERS till date, and corporates do not seem to be interested in the

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development of vaccine due to low infectivity of MERS and due to the huge amount of money and time involved in the development of a vaccine. It is hoped that by the time vaccine is developed, the virus may be contained.[13] There is no specific treatment for MERS and supportive treatment remains the mainstay of management. In Korea, hundreds of schools and few hospitals were closed during the outbreak. The healthcare authorities traced thousands of suspected contacts and monitored them for 14 days – the maximum incubation period of the disease. Any person who began to show symptoms was quarantined. Healthcare workers and other patients were protected by treating the infected in negative pressure rooms. The government had also created separate spaces at some emergency rooms to deal specifically with suspected MERS patients. WHO and United States Centers for Disease Control and Prevention and the Saudi Ministry of Health have issued various recommendations for prevention of MERS.[14] The infection prevention and control measures are droplet precautions (wearing a surgical mask within 1 m of patients) and contact precautions (wearing gown and gloves on entering patient's rooms and removing them on leaving). Droplet precautions should be added to the standard precautions when providing care to all patients with signs of acute respiratory infection.[15] The use of personal protective equipment such as gowns, gloves, goggles or face shield and respiratory protection equivalent as disposable N95 filtering facepiece respirator are recommended. Patients with MERS should be placed in negative pressure rooms or in rooms in which room exhaust is filtered through high-efficiency particulate air filters. Airborne preventive measures with at least six air changes per hour should be used in treatment rooms, especially during high-risk procedures such as bronchoscopy, intubation, nebulisation therapy or tracheal suction.[16] These recommendations are evidence-based and have proven to be effective in hospitals in affected countries. The WHO recommends that individuals who are at high risk of virulent disease such as immunocompromised hosts, diabetics, patients with chronic lung disease or preexisting renal failure should take precautions when visiting areas where camels are present. Regarding travel to these areas, WHO has neither recommended any special screening or quarantine at the entry points nor restricted applications of travel and trade. However, countries outside the affected region should maintain a high level of vigilance, especially countries with large numbers of travellers or guest workers returning from the Middle East.[17]

After Swine flu and Ebola, the MERS-CoV is the new global threat with a fatality rate of around 40.7% that has put India on high alert.[18] The Union Ministry of Health and Family Welfare, India has issued an advisory for general public to be alert about MERS. The advisory has been issued for travellers visiting to/from Saudi Arabia, Republic of Korea and other affected countries. The ministry has recommended that all travellers who have fever, cough, respiratory discomfort or distress should report at the immigration counter. Travellers are advised to be vigilant for symptoms of MERS-CoV for 14 days after return back. The immigration officials are advised to direct all travellers to the proper medical facility at the airport for further management. All primary health centres and hospitals are advised to notify any case of fever or communicable disease.

SUMMARY

MERS is a disease with pandemic potential but many questions regarding epidemiology, pathogenicity, transmission and management are still unanswered. Global awareness of MERS along with surveillance for MERS-CoV should be increased to prevent such further outbreaks. The recent MERS epidemic of 2015 of Korea and Saudi Arabia can be taken as wake up call for a country like India, with inadequate health facilities and a huge population.

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Conflicts of interest

There are no conflicts of interest.

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Announcement

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Cut Off Date	Name of Award / Competition	Application to be sent to
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30 June 2016	Late Prof. Dr. A. P. Singhal Life Time Achievement Award	Hon. Secretary, ISA
30 June 2016	Rukmini Pandit Award	Hon. Secretary, ISA
30 June 2016	Dr. Y. G. Bhoj Raj Award	Hon. Secretary, ISA
30 Sept. 2016	Kop's Award	Chairperson, Scientific Committee ISACON 2016 with Copy to Hon. Secretary, ISA
30 Sept. 2016	Prof. Dr. Venkat Rao Oration 2017	Hon. Secretary, ISA
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10 Nov. 2016	Late Dr. T. N. Jha Memorial & Dr. K. P. Chansoriya Travel Grant	Hon. Secretary, ISA, copy to Chairperson Scientific Committee of ISACON 2016
20 Oct. 2016	Awards (01 Oct 2015 to 30 Sept 2016) 1. Best City Branch 2. Best Metro Branch 3. Best State Chapter 4. Public Awareness – Individual 5. Public Awareness – City / Metro 6. Public Awareness - State 7. Ether Day (WAD) 2016 City & State 8. Membership drive 9. Proficiency Awards	Hon. Secretary, ISA
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