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MERS-CoV - are we on the verge of a pandemic?

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Editorial

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Coronaviruses are single stranded RNA viruses found throughout the world. The six well-known human coronaviruses are 229E, OC43, NL63, HKU1, SARS-CoV[1,2] and the most recently discovered Middle Eastern Respiratory Syndrome coronavirus (MERS-CoV). Coronaviruses, commonly associated with colds and upper respiratory tract infections, are also known to cause pneumonia in the elderly and immunocompromised individuals.

The most well-known outbreak caused by a coronavirus in recent times was the SARS outbreak (2002-2003) which began in China and rapidly spread throughout the world leading to about 8000 cases and 700 deaths.[3] The origin was later linked to bats which are commonly sold in markets in China, primarily as food for civet cats, which in turn serve as a delicacy for humans. With stringent infection control measures worldwide, the outbreak was eventually curtailed and there have been no new reported cases after 2004.

MERS-CoV-related illness was first recognized in early 2012. The origin of the virus however, remains unknown. MERS-CoV virus is thought to be an animal virus; humans are infected sporadically. The "alternative explanation to explain the sporadic appearance of severe human cases with long periods of time between them, and the wide geographical area over which the virus was apparently distributed, is unrecognized ongoing transmission in people. Surveillance efforts since the discovery of the virus and retrospective testing of stored respiratory specimens suggest this is not the case."[4]

The evidence for animal origin of the virus is circumstantial and once again, bats are being considered as the most likely source of MERS-CoV. The virus has been placed in lineage C of the genus beta coronavirus and is the only human virus in that group; the other two members are bat coronaviruses.[5,6] All cases reported thus far have not been directly exposed to bats raising the possibility of an intermediary host or consumption of contaminated raw and unprocessed food items, e.g. sun-dried fruits[4] like dates and olives, which are avidly consumed in the middle-east. Apart from bats, rodents and domesticated animals like camels, sheep, goats and household pets may serve as sources of possible exposure for human cases and are a subject of study.[4]

Viruses have been known to jump species, e.g the SARS CoV, which jumped from bats to civet cats and then to humans. For now however, the origin of MERS-CoV remains unknown.

The first reported case of MERS-CoV infection was that of a 60 year old male patient in Saudi Arabia who became ill in June 2012 with fever, cough and dyspnea and later died of respiratory and renal failure after prolonged hospitalization.[6] The virus was eventually identified by cell culture and genome sequencing as a novel coronavirus. Later, another case was reported from Qatar[7] with similar respiratory illness. This was followed by a case cluster in a healthcare facility in Jordan, which was reported retrospectively when some of the saved respiratory samples were tested for MERS-CoV.[8] Since then, other case clusters have been reported from Saudi Arabia,[9] UK,[10] France[11] and Tunisia[12] with evidence of human — human transmission after close contact. Some of these infections were transmitted in healthcare facilities either among patients who shared the same rooms, family members visiting their ill relatives or healthcare workers caring for these patients. All of the reported cases have been either from the middle east or had a history of recent travel to the region.

Clinical data that is available from the published case reports reveals that most patients have had predominantly respiratory symptoms, although atypical presentation with diarrhoea has also been documented. ARDS and renal failure are common complications requiring intensive care. Common laboratory findings have been lymphopenia, thrombocytopenia, rising creatinine, and radiographic findings of either consolidation or bilateral infiltrates consistent with ARDS. Mean age of affected individuals has been 51 years (varying from 2-94 years) and majority of the patients

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(65%) have been males.[13] Many of the patients who developed severe disease had multiple co-morbid conditions or were immunocompromised either due to a disease or medication. Mortality of MERS-CoV infection has been high at approximately 56%; 45 of the 80 confirmed cases reported to-date have died.[12] Although this may be due to the fact that only severe cases have been reported and patients with mild symptoms may not have been diagnosed.

Diagnosis of MERS-CoV infection can be confirmed by reverse transcriptase PCR (RT-PCR) on respiratory, blood and stool samples. Deep respiratory samples like sputum, endotracheal aspirate and bronchial lavage are recommended because of a higher yield.[13] Of the reported cases, nasopharyngeal swabs were negative in many patients in whom deep respiratory samples were found to be positive.[10,11]

The mode of transmission remains unknown but is most likely to be by droplet transmission although airborne transmission is also a possibility. Based on this and the fact that there is a high morbidity and mortality associated with this virus and currently no available effective treatment, the WHO[14] and CDC[15] have jointly recommended that suspected and confirmed cases should be placed in airborne isolation rooms with limited movement outside the room. However, where these facilities are not available, healthcare workers should be provided with a surgical face mask when entering the patient's room and an N95 respirator to be used only for aerosol generating procedures like endotracheal intubation, nebulization, suctioning, tracheostomy, bronchoscopy etc.[14]

Only limited human-human transmission has been reported so far but since the first reported case, the number of cases identified in the last several months have increased with a relatively large cluster of 25 cases reported from Saudi Arabia.[16] When this virus achieve the ability of sustained human-to-human transmission, cannot be predicted with precision. What is evident is the opportunity MERS-CoV (like any other less-well adapted pathogen) will acquire during the huge congregations in Ramadan and Hajj. Person-person transmission, which is facilitated by close contact among people from all parts of the world, makes the threat of a pandemic, real.

Until such a time that more information is available on stability and transmission of MERS-CoV, healthcare workers need to be vigilant especially when dealing with patients returning from the middle eastern states and those indigenous patients with respiratory symptoms which are not responding to routine therapy. The suspected cases should be identified and appropriate infection control measures must be implemented to limit transmission. Additionally, steps need to be taken both by the medical community and at the government level to increase awareness among the healthcare workers about the symptoms, diagnostic criteria and infection control measures. No effective anti-viral treatment is available and management remains largely supportive — a situation analogous to the SARS-CoV infection. A non-commercial RT-PCR based diagnostic test is currently available at limited facilities in Pakistan. Every effort should be made to confirm the diagnosis in suspected cases so that appropriate supportive and infection control measures are instituted as early as possible.

The medical community has learned a lot from the SARS epidemic which was contained - not by a vaccine and not by antiviral therapy but by stringent infection control measures.

"The impact of any intervention depends on its efficiency as well as efficacy."[17] Exploring the possible impact of quarantine, it was the progressive reduction in onset-to-isolation intervals which eventually contributed to SARS control.[17]

MERS-CoV is a highly pathogenic virus with a real potential for causing outbreaks. However, at the moment its ability for sustained transmission appears to be limited. Applying the same principals of control as were used during the SARS epidemic, it may yet be possible to contain MERS-CoV close to its source of origin and thus prevent a coronavirus pandemic.

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