

Outbreak Control Policies for Middle East Respiratory Syndrome (MERS): The Present and the Future

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Abstract

Middle East Respiratory Syndrome coronavirus (MERS-CoV) is the latest coronavirus to have emerged in the human population. The Saudi Arabian Ministry of Health (MoH) quickly came up with guidelines for the public and healthcare workers. This article looks at the policies recommended by International Organizations and the MoH. Like Ebola, the MERS-CoV is speculated to have come from bats, which harbour similar Coronaviruses. The article uses the principles of One Health to look at the outbreak and compares the MERS outbreak to the Ebola virus disease outbreak in West Africa. Besides highlighting key policy recommendations for the MERS-CoV outbreak, some recommendations have been brought about. The article intends to explain the MERS-CoV outbreak in a more holistic approach, taking in to consideration the One Health implications of the outbreak.

Commentary

The Middle Eastern Respiratory Syndrome (MERS), caused by a Coronavirus (MERS-CoV) (Beta Coronavirus), was first isolated in September 2012, from a 60 year old person in Saudi Arabia who eventually succumbed to the infection [1]. The MERS-CoV infects cells, which have CD26 (also known as dipeptidyl peptidase 4 (DPP4)) receptor of human beings and bats. Such receptors are seen in human non-ciliated bronchial epithelial cells, which are the cells that are mostly infected during the disease [2-4]. Once the virus enters the host, it takes about 5 days for the disease to manifest, i.e. the median incubation period of MERS is about 5 days (Range: 2-14 days) [5, 6]. So for a suspected case of MERS, a contact history for a period of 14 days needs to be taken into consideration. MERS-CoV causes both upper and lower respiratory tract infection [6]. The severity of the illness varies widely, from asymptomatic infection to severe illness as observed in patients with pneumonia and acute respiratory distress syndrome (ARDS) [5,7]. Some patients have also exhibited acute kidney injury [8]. MERS-CoV is particularly important as 40 out of 100 people it infects, would die [9].

Outbreaks of MERS have been mostly seen in the Middle East. Although imported cases have been observed in Europe, Asia and North America. A total of 971 laboratory confirmed cases of MERS have been reported by the WHO. MERS-CoV seems to have a predilection for adult males (63.5% cases are male and the median age is 48 years) [10]. This is important as certain activities carried out by men could contribute to risk factors for MERS and these could be dealt with while designing outbreak control policies.

MERS coronavirus is a zoonotic disease that is transmitted from infected dromedary camels (camels having rhinorrhea) to human beings upon close contact [11]. The outbreaks that have occurred in the past have actually perpetuated owing to the limited person-to-person transmission that have been attributed to droplet and contact transmission [12]. The ultimate culprit in the zoonotic origin of the MERS-CoV however seem to be the Egyptian cave bats [13,14]. Although the MERS-CoV and the bat-CoV are closely related, bats are not the immediate contact for human MERS-CoV infection [15].

The outbreak has not gone out of control unlike Ebola in West Africa. This could be attributed to the lower human-to-human transmission rates, less mortality rates for the CoV, lower human

population density in the MERS-CoV affected area, and quick response from the Government. The perfect comparison would be to compare the SARS-CoV outbreak with the ongoing MERS-CoV outbreak. Unlike the SARS outbreak, MERS has so far been restricted to the Middle East, besides a few imported cases as mentioned before. Genomic analysis of the two coronaviruses could point towards the differences between the two CoVs, which allowed SARS-CoV to escalate to a level of an epidemic [16].

The Saudi Arabian Ministry of Health (MoH) has laid down specific guidelines for the control and prevention of MER-CoV infection for Health care workers (HCWs), patients and family members of patients. The MoH has established MERS designated hospitals (MDH) to treat MERS patients where they have Airborne Infection Isolation Rooms (AIIR) as per WHO guidelines. The MoH has laid down diversion plans for Hajj with respect to MERS-CoV and Ebola virus disease as well [17].

The recommendations mentioned by CDC for hospitalized patients focus on standard, contact and airborne precautions. Home care isolation is also recommended but after strict assessment of the suitability of the house for home care.

Looking at current policies in place regarding the MERS outbreak, MoH's Command and Control Center reviewed data related to MERS-CoV from 2012-14, which helped the center develop policies to minimize the spread of MERS-CoV [18]. The policies in place are primarily for improving the efficiency of surveillance i.e. case reporting as well as to ensure the reliability of the data collected. Focusing on increasing the efficiency, quality and capacity of the standardized laboratory settings was yet another step taken to improve data collection [18].

Currently there is no vaccination or treatment available for this

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disease [19]. However, Centers for Disease Control and Prevention (CDC) does not advice travelers to cancel their travel plans to the effected countries [19].

CDC works with the World Health Organization (WHO) to closely monitor the spread of the virus along with the source and risks associated with the same. To deal with this effectively, CDC improved their data collection tools and methods, made recommendations for prevention and infection control and increased the capacities and efficiency of laboratories to detect the cases. CDC disseminates knowledge about MERS-CoV to the general population and potential travelers by publishing advisories for patient care and travel [19]. They utilize Advanced Molecular Detection (AMD) methods to further evaluate and describe the characteristics of the virus [19].

Neither MoH nor CDC have designed specific policies for the control of the MERS-CoV, they have recommended quarantine measures for an infected person and have listed out guidelines to be followed before the person can resume regular activities [20].

Since camels are being speculated as the source of transmission of the MERS-CoV to humans, the WHO has stated few precautionary measures that any traveler visiting the effected country must observe. Travelers are advised to practice basic safety techniques including proper hand washing before and after touching an animal, not eating undercooked or raw meat and milk [21,22].

The MoH has provided guidelines for airport staffs to follow in the event of an infected patient arriving at the airport. Quarantine stations are installed at airports to obtain information about the exposures associated with ill traveler [23].

On May 13th, 2014, Ministry of Health of Saudi Arabia announced new measures to deal with the challenges in the future. A more accurate case definition was made and guidelines with regards to international standards were established on how to contain the spread of MERS-CoV. This information was made public to all the stakeholders immediately [24]. Rapid intervention teams were brought together and were designated specific jobs and roles in the strategy. Recommended provisions were made for the intervention to progress smoothly; the capacity and capability of health care facilities were increased to deal with future potential cases of MERS [24]. This was a great step as the Saudi Arabian MoH had initiated necessary steps for outbreak control and was prepared for a full-blown MERS-CoV epidemic.

The Ministry of Health in conjunction with the WHO launched a campaign regarding informing the general public about the benefits of exercising good personal hygiene, and the precautionary actions which should be taken while eating meat or drinking camel milk [25]. Thus a major component of One Health, education and raising awareness were immediately implemented.

CDC and the MoH, Saudi Arabia have suggested preventative measures when sick, such as, staying home, covering the face while sneezing, avoiding touching eyes, ears, face and nose, exercising good personal hygiene, using face masks, washing hand adequately and eating healthy [20,26]. Educating the local community and travelers did seem to go a long way in allowing people to make informed choices.

MERS-CoV could possibly cause an epidemic given the right setup. The question remains, why hasn't this virus gone beyond sporadic outbreaks? To understand this, we would first need to know what factors lead to an epidemic or a pandemic, which has been described in this BBC article [27]. Several factors play a role in allowing a virus to spiral out of control. It's quite possible that the MERS-CoV has not

attained its full potential yet.

David Quammen, the author of *Spillover* mentions MERS-CoV to be a virus that requires close watching and rigorous measures to contain it [28]. More people the virus gets into, greater chances for it to mutate exist. Thus it was important to control this virus in the very beginning.

The virus has so far maintained a low profile and the healthcare system of Saudi Arabia has been able to handle current outbreaks. To answer the question if this virus could pose a real pandemic threat is a little too early as of now. It has not seemed to go beyond the Middle East, besides a few imported cases in other countries. This could possibly hint at camels being a necessary host for the survival of the virus. The virus has not attained sustained human-to-human transmission yet. This would explain the lack of large number of healthcare worker deaths unlike Ebola virus disease. MERS-CoV could become a significant threat if it acquires more efficient person-to-person transmission.

In order to assess the pandemic potential of MERS, R0 value has to be taken into consideration. R0 tells us about the number of persons the index case could potentially infect. During the initial period of the emergence of MERS in 2013, it was estimated that MERS has a R0 value of 0.69 (95% CI- 0.50-0.92) which was lower than SARS-CoV during the pre-pandemic era (R0 for SARS-0.80 (CI – 0.54-1.13) in pre-pandemic period) [29]. But a recent outbreak in Jeddah and Riyadh showed a R0 value of 3.5-6.7 and 2.0-2.8 respectively [9]. This variability in the R0 value can be ascribed to multiple factors. When the same virus (without major antigenic shift) has a variable R0 value, it implies that environmental factors, and to a lesser extent host factors, play an important role. This is where control and preventive measures kick in. In the past, knowledge about R0 value has led policy makers to design specific control strategies.

Among the various guidelines laid down by the MoH, home isolation is something we are a little skeptical about. As per this guideline, the approval of suitability of the home to be used for isolation purpose might be granted through a telephonic phone call. This could create inadequacy in the control measure. A strict vigilance needs to be followed in case home isolation is required in a MERS suspected or confirmed case. We recommend a proper physical assessment by MoH officials to declare the house to be fit for home isolation. Patients need to warn the healthcare workers (HCWs) prior to their hospital visit about their MERS-CoV infection [30]. Such complicated instructions for patients might create ambiguity and adherence to the guideline would then become questionable.

Ebola control measures include 21 days contact tracing as outlined by the CDC. This method led to the containment of the infection in United States [31]. We would recommend a similar 14 day contact tracing to be put in place for the MERS-CoV as well.

Controlling MERS-CoV, or any emerging disease for that matter requires interdisciplinary efforts. This is where the concept of One Health kicks in, a discipline through which we examine how the interactions of humans, animals and the environment come together to allow an infectious threat to arise, develop and become a sustained outbreak. There are several lessons to be learnt from the recent Ebola outbreak in West Africa. The Ebola virus disease (EVD) outbreak highlights the importance of both humans and animals and their interaction. Bats, which are the reservoirs for Ebola, can spread the virus to humans and non-human primates, with almost always fatal consequences for both [32].

What we have learnt from past outbreaks and from the campaign

to eradicate smallpox and polio is the importance of vaccination. Currently two vaccines against EVD are being tried out in West Africa. The gorilla population in Africa has declined by one-third due to Ebola outbreaks [33]. This calls for vaccination for non-human primates too. Vaccinating the animal reservoir species if possible, or the amplifying hosts, can prevent the transmission of zoonotic viruses to humans. This highlights the importance of vaccination in curbing the spread of a disease.

For MERS, there is significant data pointing to zoonotic transmission of the virus, but the exact dynamics are vastly unknown. Understanding the reservoir dynamics and the spillover dynamics for the MERS-CoV would help in preventing future cases of MERS and the policies could also address other zoonotic emerging diseases in the region. Whether bats and camels are the only animals harboring such a virus is questionable. Thus, wildlife surveillance is an important factor for monitoring emerging infectious diseases.

Also, incentive for large-scale pharmaceuticals to produce these vaccines need to be considered. For example, Ebola is endemic in Central Africa but it was the dramatic increase in the number of cases in West Africa, which prompted the global community to come up with a solution eventually. Is that what would take the scientific community to find a solution to MERS? A large-scale epidemic threatening a potential pandemic? Although a MERS vaccine candidate was successfully tested in mice in 2014, it is still awaiting clinical trials [34]. In order to prevent drastic consequences like that of Ebola, we need to avert delays. We as a scientific community need to also have a policy in place for future emerging diseases. World Health Organization (WHO) Director-General Margaret Chan announced a contingency fund of US\$100 million to support emergency response capacity in future outbreaks [35]. This is definitely a step in the right direction.

Understanding the cultural setting in an outbreak region also helps in containing the outbreak. This was observed in West Africa, where cultural difference was a massive hindrance to outbreak control efforts initially. Involving the local community is a great idea to convince the locals about the infection control techniques [35]. This needs to be done at the very beginning of an outbreak, since gaining the trust of locals takes considerable amount of time, time that can be saved.

Wildlife researchers need to quickly identify the mode of transmission of MERS-CoV from the reservoir species, bats, to dromedary camel population. Identifying the routes of transmission (bat-to-camel, camel-to-human, bat-to-human? and human-to-human) can help in designing specific strategies to control the outbreak. The policies being designed to control MERS-CoV need to consider the values of every stakeholder. For example, banning the consumption of raw camel milk seems like a good option to prevent the spread of MERS, but would the locals really comply? Would they change their long drawn traditions? Finding alternatives, which would respect the values of every stakeholder, is a component of One Health as well.

Every outbreak is different and presents unique challenges by itself. Teams of interdisciplinary expertise need to be on standby for such outbreaks. The government of the effected country would need to notify International Health agencies (WHO, CDC) at the earliest about a potential emerging infection. This would allow experts to quickly swing into action. We have been lucky with the MERS-CoV, but we might not be lucky the second time. The Ebola outbreak was a lesson learnt, as we aspire to better understand the interconnectedness of humans, animals and the environment.

Conflict of Interest

The authors declare no conflict of interest. All authors contributed equally.

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