

World Health Organization's Disease Outbreak News, Advisory and Mitigation of Middle East Respiratory Syndrome

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Abstract

Middle East Respiratory Syndrome Coronavirus (MERS-CoV) is a fatal infectious disease that till date, since September 2012, has infected 2103 people and killed, 733 of them. MERS-CoV has infected people in almost all the habitable continents of the world except South America and Australia. The World Health Organization (WHO), in response, has taken a number of measures to eradicate it and giving advisory through, its MERS-CoV related disease outbreak news (DON) is one such measure. This research analyses the WHO advisory published in the, MERS-CoV, DON, from 25th September 2012 till 10th November 2017 and its role in generating awareness and preparedness by different governments of the world against the spread of MERS-CoV. The research was based on meta-analysis. The secondary data was collected from WHO's, disease outbreak news and also, from the ministry of health portals of the MERS-CoV affected countries. Data was also collected from various other sources reporting MERS-CoV infections. Since the beginning of MERS outbreak in 2012, the number of WHO, MERS DON, which was the highest in the year 2015, has gradually declined and reached the lowest in 2017. As the DON declined, so did the number of infected and deaths over the years. The highest percentage increase in the number of infected and deaths was seen in the year 2013 and 2014, which almost plummeted in the year 2016 but surprisingly there has not been a substantial decline since and has almost remained the same till the last reported, WHO MERS disease outbreak news on the 10th of November 2017. The researchers conclude that local communities should be taken into confidence, camels should be vaccinated, pharmaceutical companies should be incentivized and other important developments should be dynamically updated on DON, which in turn, could help stop further causalities.

Keywords: Advisory; Disease outbreak news; Middle East Respiratory Syndrome; World Health Organization; Policy

Abbreviations: AIIR: Airborne Infection Isolation Rooms; CDC: Centers for Disease Control and Prevention; DON: Disease Outbreak News; EMRO: Eastern Mediterranean Regional Office; IHR: International Health Regulations; IPC: Infection Prevention And Control; MERS-CoV: Middle East Respiratory Syndrome Coronavirus; MoH: Ministry of Health; NCoV: Novel Coronavirus; PHEIC: Public Health Emergency of International Concern; SARI: Severe Acute Respiratory Infections; UK: United Kingdom; UN: United Nations; WHO: World Health Organizations

Introduction

MERS is an illness caused by a virus (more specifically, a Coronavirus) called Middle East Respiratory Syndrome Coronavirus (MERS-CoV). Most MERS-CoV patients develop serious respiratory sickness with signs of high temperature, cough and breathlessness. 3 to 4 patients of MERS-CoV have died, out of every 10 reported cases [1]. Initially called novel coronavirus 2012 or simply novel coronavirus, MERS-CoV was first identified in September 2012 in the Kingdom of Saudi Arabia, after genome sequencing of a virus isolated from sputum samples from a person who fell ill in a 2012 outbreak of a new flu. [2]. Retrospective study, done by health officials, later revealed that first known case of MERS happened in April 2012, in Saudi Arabia's neighbouring country, Jordan. Thus far, all the reported incidence of this disease, have been suggested to have originated through travel from countries in and near the Arabian Peninsula [3]. Republic of South Korea was affected the most in 2015, by MERS-CoV. It was the largest outbreak of the disease outside the Arabian Peninsula and was linked with people coming back from Middle Eastern gulf countries [4]. Since 2012, as per WHO, MERS-CoV has been identified in twenty seven countries, which include Algeria, Austria, Bahrain, China, Egypt, France, Germany, Greece, Islamic Republic of Iran, Italy, Jordan, Kuwait, Lebanon, Malaysia, the Netherlands, Oman, Philippines, Qatar, Republic of Korea, Kingdom of Saudi Arabia, Thailand, Tunisia, Turkey, United Arab Emirates, United Kingdom, United States, and Yemen. Saudi Arabia has reported the maximum percentage of cases, amounting to about 80%. People reported to be infected by this disease outside the Arabian Peninsula are believed to have been infected in the Arabian Peninsula and moved to places outside the Middle East. But on only rare occasions, sudden occurrences of this disease have been identified in regions outside the Middle East [5]. 2,103 laboratory-confirmed occurrence of MERS-CoV cases with a minimum of 733 deaths have been reported to WHO, since September 2012 [6].

WHO is the body of the UN responsible for directing and coordinating health [7]. WHO thrives to achieve this through many ways and one of it is by providing guidelines, which includes recommendations, with regards to wellbeing interventions, which can be clinical, community health or policy recommendations [8]. On 25th September 2012, following the confirmation of the novel Coronavirus, WHO-under the International Health Regulations-right away notified all the Member States regarding the Coronavirus. Moreover, it has ever

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since, taken a lead in coordinating and providing direction to health establishments and technical health agencies [9]. This research analyses the WHO advisory published in the, MERS-CoV disease outbreak news (DON), under the Coronavirus infections section and its part in generating responsiveness against the spread of MERS-CoV.

Objective of the Study

The main objective of the research is to analyses the WHO advisory published in the, MERS-CoV disease outbreak news, under the Coronavirus infections section from 25th September 2012 till 10th November 2017 and its role in generating awareness and preparedness against the spread of MERS-CoV. This is with the intention to understand the effect of WHO guidelines on the implementation of awareness and preparedness policies laid down by various governments to tackle dreaded infectious diseases like MERS-CoV.

To achieve the main objective, the following sub objectives were set: (1) Assess WHO MERS-CoV awareness and preparedness disease outbreak news; (2) Assess MERS-CoV awareness and preparedness initiatives of the worst affected countries in the Middle East, Asia, Europe and America.

Research Methodology

The research is based on secondary data collected from WHO, Coronavirus infections, disease outbreak news sections and also, from the ministry of health portals of the MERS-CoV affected countries. Furthermore, data was collected from various other sources reporting MERS-CoV infections. Thus, in an attempt to understand the effect of WHO MERS-CoV preparedness and response guidelines, in addition to, the subsequent initiatives laid down by various governments, the available literature is reviewed.

Literature Review

Assess WHO MERS-CoV awareness and preparedness disease outbreak news

On 22nd of September 2012, WHO informed through its DON that on 22 September 2012, United Kingdom (UK) informed WHO of an incidence of serious respiratory syndrome with kidney failure with travel history to Kingdom of Saudi Arabia and Qatar. WHO also included a brief about what Coronavirus is and said that it is currently in the process of obtaining further information to determine the public health implications of these two confirmed cases. With respect to these findings, WHO did not recommend any travel restrictions [10]. On 25th of September 2012, under the International Health Regulations-WHO right away notified all the Member States about the illness and that WHO has been taking the lead in coordinating and providing direction to health establishments and technical health agencies. A group of Coronavirus specialized laboratories were identified by WHO for the affected countries. It said that WHO would work closely with Saudi Arabia, as in previous years, to support the country's health measures for all visitors participating in the Hajj pilgrimage to the holy city of Mecca [11]. On 28th September 2012, WHO updated, that the novel coronavirus cannot be easily transmitted from person-toperson and that no travel or trade restrictions were recommended by WHO for Saudi Arabia or Qatar with respect to the novel coronavirus infections [12]. On 29th September 2012, WHO came up with a revised interim case definition, in order to make sure a suitable and useful recognition and study of MERS-CoV affected people, who may have been infected with MERS-CoV, without exhausting the health care systems with needless testing. And also, WHO did not recommend

specific health checks at the entry point nor did it advice that any travel or trade constraints be enforced [13]. On 10th October 2012, WHO reported that it is supporting the national authorities in their ongoing investigation, and deployed experts to Saudi Arabia and Qatar as part of an international team. These and future epidemiological and scientific studies it said would lead to a better understanding of the novel coronavirus [14]. In a major development, after more than a month, WHO, reported that further epidemiological and scientific studies were needed to better understand the virus. WHO said that it is prudent to believe that MERS-CoV was probably more extensively spread than only the 2 countries which had identified cases. Member States ought to think about testing of affected people, with unknown pneumonias for the new coronavirus even when the patient has not travelled or other links with the two affected countries. Furthermore, any group of severe acute respiratory infections (SARI) or SARI in employees, working in the healthcare system, must be completely investigated, not considering, of where in the world they occur [15]. In the last update of the year 2012, other than informing about additional infections and deaths due to the virus, WHO informed that the MoH, Jordan requested WHO's support in diagnosing infections. A mission from WHO Eastern Mediterranean Regional Office (EMRO) and head office came on 28th of November 2012, to Amman, in order to help in further epidemiological observation and to strengthen the SARIs [16]. So, by the end of 2012, WHO was actively assisting in investigating the identified corona infected countries i.e. Qatar, Kingdom of Saudi Arabia and Jordan.

After almost two months on 11th February 2013, WHO updated that a confirmed case with infection of the novel coronavirus (NCoV) was reported from United Kingdom and that the new case indicated that the virus was persistent. According to the situation at that time and accessible information WHO encouraged all Member States to carry on their close watch for SARI and to cautiously check any strange patterns. Any group of SARI or SARI in employees working in the healthcare system, must be completely investigated, not considering of where in the world they occur. New human cases and clusters should be promptly reported both to national health authorities and to WHO. But WHO did not recommend particular checks at the entry point with regard to this event nor did it advocate that any travel or trade limitations are applied [17]. On 9th of May 2013, WHO suggested healthcare sector to be watchful among recent travellers coming back from regions affected by the virus who develop acute SARI. WHO also directed that, where possible specimens from patients' lower respiratory tracts must be obtained for diagnosis [18]. On 12 May 2013, WHO reminded the Clinicians that nCoV infection should be considered even with atypical signs and symptoms in patients who are significantly immune compromised [19]. On 18th May 2013, WHO, advised that health care systems that offer care for cases with suspected nCoV infection must take suitable measures to mitigate the danger of spread of the virus to other patients, healthcare employees and attendants. Health care providers were reminded of the significance of methodical execution of infection prevention and control (IPC) [20]. It was on 23rd of May 2013, WHO changed the title of its disease outbreak news update to Middle East respiratory syndrome-Coronavirus [21]. On 4th October 2013, WHO came up with a very important update where it said that WHO had convened an Emergency Committee under the International Health Regulations (IHR) to advise the Director-General on the status of the current situation. The Emergency Committee, which comprised international experts from all WHO Regions, unanimously advised that, with the information now available, and using a riskassessment approach, the conditions for a Public Health Emergency

of International Concern (PHEIC) had not at present been met [22]. On the 31st of December 2013, WHO, advised that people coming back from the gulf countries who develop SARI have to be tested for MERS-CoV as suggested in the recent surveillance recommendations. Furthermore, WHO advised that people at high risk of severe illness due to MERS-CoV must restraint from close interaction with animals when going to farms or barn areas where the virus is believed to be potentially circulating. For the population at large, when going to the farm or a barn, general cleanliness measures, such as frequent hand washing prior to and after touching animals, avoiding interaction with sick animals, and following food hygiene practices, must be followed [23]. WHO advised on the 11th of March 2014, that since it is not always possible to make out patients with MERS-CoV early on, due to mild or unusual symptoms, it is important that healthcare employees use benchmark precautions without fail, with all patientswith or without considering their diagnosis-consistently in all work activities. Droplet safety measures ought to be added to the standard precautions when giving care to each and every one with symptoms of acute respiratory infection. Contact precautions and eye protection should be supplemented when caring for suspected or confirmed patients of MERS-CoV infection. When doing aerosol generating procedures airborne precautions should be used [24]. On 11th of June 2014, WHO advised that until more is known regarding MERS-CoV, diabetics, kidney failure patients, patients with respiratory disease, and immunocompromised people should be regarded to be at high threat from MERS-CoV infection. So, these individuals must keep away from close contact with animals, predominantly camels, when going to farms, market places, or barn areas where the virus is understood to be potentially circulating. Public should refrain from consuming raw camel milk or camel urine, or eating meat that has not been properly cooked [25]. From 14th July 2014, WHO started giving countrywise updates[26]. Then on 3rd July 2015, WHO advised that due the absence of substantial data of sustained person-to-person transmission in the society, WHO does not advice travel or trade restrictions with regard to this event. Generating understanding about MERS-CoV among travellers to and from affected regions is an excellent community health exercise. And also, DON regarding MERS-CoV in the Republic of Korea will be published on a bi-weekly basis (on Tuesdays and Fridays). Due to the scale of the existing outbreak, DONs will concentrate on describing the development of the outbreak and epidemiological trends, instead of concentrating on person to person case details [27].

On 20th September 2016, WHO threat assessment, WHO broke the news that MERS has caused acute human infections resulting in high case fatality rate and has shown the capability to spread between individuals especially in healthcare environment, with the potential to lead to large scale outbreaks [28]. In 2017, there was no additional advice from WHO, other than what was advised before, since the MERS-Cov cases remarkably declined.

Assess MERS-CoV awareness and preparedness initiatives of the worst affected countries in the Middle East, Asia, Europe and America

South Korea: The WHO carried out a joint mission with the Republic of Korea's Ministry of Health & Welfare in South Korea, in light of the outbreak of MERS-CoV [29]. The outbreak, the largest outside Saudi Arabia, fuelled public anxiety and hit spending, with thousands in quarantine and the number of schools closed to 2,474, including 22 universities. Many people on the streets were seen wearing face masks, public transport was disinfected and attendance at movie theaters and baseball games tumbled [30]. The WHO then urged

South Korea to re-open thousands of closed schools over MERS fears, stated that the virus was unlikely to spread among healthy children. But WHO advised that hospitals and clinics should strengthen infection control measures and health professionals should ask about MERS in anyone showing up with respiratory symptoms [31]. South Korea started taking tough steps to stop its citizens from getting in touch with affected people. Hospital workers started taking additional safety measures with those patients who were suspected of having MERS. Workers also started measuring temperature of students at schools, as well as, disinfecting and carefully cleaning the public transport [32]. South Korean agencies gave course of action, recommending citizens to "avoid visiting crowded places as much as possible" and to wear face masks at outside their homes. It also advised against "close contact with people who have fever and heavy breathing".

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Some buildings set up temperature screening booths at their receptions. Health workers sprayed down subway stations and the insides of train carriages. It also launched a website dedicated to MERS updates. The acting Prime Minister of South Korea Choi Kyung-hwan was photographed shaking hands with shop owners, and President Park Geun-hye postponed a trip to the US vowing to put a "quick end" to the outbreak. More than 3,800 people remained under quarantine-either monitored in hospitals or at home. Those at home were tracked by their mobile phones. One entire village was put on lockdown. More than 100 residents of Jangduk in North Jeolla province were barred from leaving and from receiving visitors, when one case of MERS was confirmed. Health workers took residents' temperatures twice a day, and the government and other villages provided food and supplies [33].

The longest incubation period of MERS is fourteen days. Hence, making 28 days as the waiting period, as well as, including days from identification of the most recent case on July 4, 2015, the earliest date the South Korean government could have declared the end of outbreak was August 2 if it adhered to WHO criteria. Nevertheless, to highlight safety for the homeland and to intercontinental travellers at an earlier time, the South Korean government in the beginning decided to announce the end of the MERS outbreak on July 27, the date the last quarantined MERS patient was discharged from movement restriction. Because the government of South Korea was worried regarding the validity of strict adherence to the WHO criteria, they without prejudice calculated the likelihood of observing additional cases at a given time and compared that likelihood with the WHO criteria [34].

Saudi Arabia: On the 7th of May, 2014, his Excellency Eng. Adel bin Mohamed Fakieh, the Health Minister in charge, launched a public awareness campaign to combat the MERS Coronavirus. The campaigns objective was to empower the public with crucial up to date information [35]. The health minister of Saudi Arabia, created MERS task forces and designated treatment centers, intensified MERS communication on Twitter and Facebook, and began disclosing more particulars on each new confirmed case. Meanwhile, the Ministry of Education announced its first infection-prevention campaign for MERS in the country's 34,000 schools [36]. The Saudi Arabian, MoH, gave explicit guidelines for the control and prevention of MER-CoV infection for Health care workers (HCWs), patients and attendants of the patients. The MoH established MERS designated healthcare centres, to take care of MERS affected individuals, where they have Airborne Infection Isolation Rooms (AIIR) according to WHO recommendations. The MoH also gave diversion strategies for Hajj regarding MERS-CoV and also for Ebola virus illness [37]. Looking at the policies with respect to the MERS outbreak, MoH's Command

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and Control Center reviewed information regarding to MERS-CoV from 2012-14, which assisted the center build policies to mitigate the transmission of MERS-CoV. The laid down policies were first and foremost for improving the effectiveness of surveillance i.e. infection reporting and to make sure, the dependability of the collected data. Focusing on growing the competence, excellence and capability of the standardized laboratory environment was yet another measure taken to advance collection of data [38]. On 13th of May, 2014, MoH, of Saudi Arabia, announced new measures to deal with the future challenges. A more precise case definition was prepared and course of action with respect to global standards were established on how to control the spread of this dreaded disease. This information was announced to all the stakeholders at once. Quick intervention teams were got together and were given precise assignments and roles in the strategy. Recommended provisions were made for the intervention to progress efficiently; the competence and ability of health care providers were improved to deal with potential future infections of MERS. This was a great step as the Saudi Arabian MoH had started essential measures for outbreak control and was equipped for a full-blown MERS-CoV epidemic [39]. The MoH in coordination with the WHO started a drive about informing its citizens about the benefits of living a life of, good individual cleanliness, and the preventative measures which must be taken while consuming meat or drinking camel milk [40]. Thus a foremost element of Health, education and raising awareness were right away implemented. The MoH, Saudi Arabia, recommended precautionary ways when sick, such as, stay at home, covering the face while sneezing, avoiding touching eyes, ears, face and nose, exercising good personal hygiene, using face masks, washing hand sufficiently and having healthy food habits [41]. Educating the local population, as well as, visitors and travellers, helped in making individuals make informed choices [42].

United States of America: The risk of the spread of MERS in this country is very low. Of over 2000 reported cases of MERS, 800 have tested negative for the disease, while as, only two U.S. patients have ever tested positive for the disease and that too both in the Month of May 2014. Centers for Disease Control and Prevention (CDC), USA maintains a close vigil on the situation. CDC, along with, other agencies carry on, to closely monitor the MERS situation. CDC fully understands the probability of MERS-CoV to spread further and that it may cause more infections in the United States and globally. This is the precise reason that they have uninterruptedly collaborated with global agencies on epidemiologic and laboratory studies to better understand MERS. Inspite of this, CDC still, doesn't suggest that people alter their travel plans because of MERS. The current CDC travel notice is an Alert (Level 2), which gives special precautions for travellers [43].

United Kingdom: Although the risk of MERS-CoV in individuals who meet the case definition for a possible case in the UK following travel to/from the Middle East is low, testing for MERS-CoV is warranted together with rapid implementation of appropriate infection control measures while awaiting results of testing. Public Health England remains vigilant and minutely watches developments in the Middle East and in the rest of the world where new cases have emerged, and continues to liaise with international colleagues to assess whether recommendations need to change [44].

Results

As depicted in Table 1, since the beginning of the MERS outbreak in 2012, the number of WHO, MERS disease outbreak news, which was the highest in the year 2015, has gradually declined over the years and reached the lowest in 2017 (Table 1). As the disease outbreak news has declined, so has the number of infected and deaths over the years, as has been evident from Table 2. On the other hand, one of the highest numbers of WHO disease outbreak news and one of the highest number of deaths from MERS are both from the year 2015. Furthermore, the highest percentage increase in the number of infected and deaths was seen in the year 2013 and 2014, which almost plummeted in the year 2016 but surprisingly there has not been a substantial decline since and has almost remained the same till the last reported WHO MERS disease outbreak news on the 10th of November 2017. Thus, the total number of infected people, stands at 2103, and while as, deaths due to MERS stand at 733 as of 10th of November 2017 (Table 2).

The researchers point out that the maximum number of infected people and deaths due to MERS have been reported in the Middle East region. Kingdom of Saudi Arabia witnessed the maximum number of infected cases at the start of 2017 at about 1561 including 633 deaths. By mid of 2016, United Arab Emirates had 80 reported cases, Jordan 26, Qatar 16, Oman 8. Till the end of 2015 Iran reported only 6, Kuwait 4, Tunisia 3, Algeria 2, while as, Egypt, Bahrain, Yemen, Lebanon all reported only one case and all these countries have not reported any further cases. In Asia, China, Malaysia, Thailand and Philippines, all reported less than 5 cases and there has been no further reported case of MERS since 2015. On the other hand, South Korea was badly affected by the MERS virus and had reported 185 cases till the mid of 2015, but since then no further cases have been identified. In Europe, eight countries were affected; United Kingdom reported the maximum number of infected cases at 4. But here also, as in the case of Asian countries MERS outbreak was brought under control and no further cases were reported since 2015. In America, United States of America reported only 2 incidences in 2014.

Furthermore, the researchers observe that, it was in September 2016 that WHO recognized that MERS can spread between person to person, especially in healthcare environment with the potential to lead to large scale outbreaks. Thus, WHO advisory for the containment of MERS-Cov is that WHO encourages all Member States to carry on their monitoring for severe acute respiratory infections (SARI), as well as, to cautiously examine any odd patterns. Infection prevention and control measures are vital in stopping the likely spread of MERS-

Year	Number			
2012	7			
2013	66			
2014	58			
2015	95			
2016	38			
*2017	22			
*As of 10 th of November 2017				

Table 1: Number of MERS WHO disease outbreak news

Year	No. of infected	No. of deaths	Percentage increase/decrease infected	Percentage increase/decrease deaths
30-Nov-12	9	7		
31-Dec-13	167	67	1856%	957%
26-Dec-14	765	273	358%	307%
4-Dec-15	680	237	-11%	-13%
19-Dec-16	243	75	-64%	-68%
10-Nov-17	239	74	-2%	-1%

 Table 2: Yearly MERS related infected cases and deaths percentage (%) increase/ decrease.

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CoV in health care facilities. Employees working in the healthcare sector, must always apply standard safety measures, without fail, with all patients, regardless of their diagnosis. Droplet precautions should be added to the standard safety measures, when giving care to patients with indications of acute respiratory infection; contact precautions and eye protection should be added when caring for possible or established patients of MERS-CoV infection; airborne precautions must be used, when performing aerosol generating procedures. Community and household awareness of MERS and MERS prevention measures in the home possibly will reduce household transmission and prevent community clusters. Diabetics, kidney failure, respiratory illness, and immune compromised individuals are considered to be at high risk of severe disease from MERS-CoV infection. Thus, in addition to avoiding close interaction with suspected or confirmed human cases of the disease, individuals with these conditions must avoid close contact with animals, mainly camels, when going to farms, market places, or barn areas where the virus is known to be or potentially circulating. General cleanliness measures, such as regular hand washing prior to and after touching animals and avoiding contact with sick animals, should be adhered to. Healthy eating habits should be maintained. People should avoid drinking raw camel milk or camel urine, or eating meat that has not been properly cooked. WHO does not recommend special checking at the entry points of countries, nor at present does it suggest the application of any travel or trade restrictions.

Discussion

Although the incidence of MERS-CoV have considerably dropped over the years; but it has certainly not stopped from spreading. On the other hand, WHO's DON updates have declined over the years, which certainly should not have been the case. On the contrary, it should have increased, with regular updates about the progress that the scientific community is making towards making a vaccine or finding a treatment for MERS-CoV affected patients. At present no vaccination or treatment exits for this disease, and WHO should play a vital part in decimating news regarding developments in this area of concern through its DON. The MoH, Kingdom of Saudi Arabia in collaboration with WHO started a campaign with respect to informing its citizens, is regarding the benefits of exercising good personal hygiene, and the protective steps which should be taken while consuming meat or drinking camel milk. This and many more steps apparently helped in containing the spread of MERS-CoV but we don't see these success stories being shared as case studies on the DON, which the researchers believe is an important platform for creating awareness and preparedness amongst member states. No vaccination for MERS-CoV has been successfully developed, studying immune correlates of protection and vaccine efficacy in camels (the single accepted host besides bats and humans recognized thus far) may reveal vulnerabilities of MERS-CoV that may be exploited for human vaccine strategies and for these further incentives for pharmaceutical companies should be considered by WHO and the member states. Because camels and bats are believed to be carriers of MERS-CoV and significant data points towards zoonotic transmission of the virus, local communities who come in contact with them should be taken into confidence before implementing the infection control techniques. Otherwise the whole activity can go in vain. Wildlife surveillance can be another important facet for monitoring MERS-CoV which WHO and Ministry of Health, across various affected countries could look up to and simultaneously regular updates regarding the same is posted on DON.

Conclusion

The researchers conclude that channels of communication between WHO and the various effected governments should be dynamically operated, so that any important development related to MERS-CoV, after due verification process, could be updated on the DON, for other affected parties to benefit from, which in turn, could stop further causalities due to this dreaded disease.

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Limitations of the Study

The research is based on secondary data only and there is scope for the future study based on primary data as well. Future researchers can take up further studies based on the above-mentioned limitation.

Conflict of Interest

The authors declare to have no financial or personal relationships that could inappropriately influence the research described.

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