

Summary report on the

Virtual meeting on Middle East respiratory syndrome (MERS)

WHO-EM/CSR/514/E

Virtual meeting
16 August 2021



REGIONAL OFFICE FOR THE

World Health
Organization

Eastern Mediterranean

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1. Introduction

Middle East respiratory syndrome (MERS) is a viral respiratory disease caused by the Middle East respiratory syndrome coronavirus (MERS-CoV), a zoonotic virus that has repeatedly entered the human population via direct or indirect contact with infected dromedary camels. Populations in close contact with dromedaries (e.g. farmers, abattoir workers, shepherds, dromedary owners) and health care workers caring for patients with MERS-coV are believed to be at higher risk of infection. Healthy adults infected with MERS-CoV tend to have mild subclinical or asymptomatic infections. To date, limited human-to-human transmission has occurred between close contacts of confirmed cases in household settings. Non-sustained human-to-human transmission, mainly in health care settings, continues to occur due to inadequate and/or incomplete compliance with infection prevention and control (IPC) measures and delay in triage or isolation of suspected MERS-CoV cases.

A total of 2578 laboratory-confirmed cases of MERS, including 887 associated deaths, have been reported globally; a case–fatality rate (CFR) of 34%. The majority of these cases have been reported from Saudi Arabia (2178 cases, including 850 related deaths, with a CFR of 37%). In total, cases have been reported from 27 countries in the Middle East, North Africa, Europe, the United States of America and Asia. Since 2012, 12 countries from the World Health Organization (WHO) Eastern Mediterranean Region have reported MERS cases. Males above the age of 60 with underlying medical conditions, such as diabetes, hypertension and renal failure, are at a higher risk of severe disease, including death.

Overall, the epidemiology, transmission patterns, clinical presentation of MERS patients and viral characteristics reported since the last MERS-CoV update are consistent with the past patterns described in

previous WHO risk assessments. The risk of exported cases to areas outside of the Middle East due to travel remains significant.

While there have been significant improvements in surveillance for MERS, especially in the Middle East, early identification in the community and in health care systems, compliance with IPC measures and contact follow-up remain major challenges for MERS outbreak prevention and control. MERS-specific therapeutics and vaccines are in development and some clinical trials have begun. WHO, through the WHO R&D Blueprint, is developing clinical trial protocols to evaluate therapeutics and vaccines for MERS. Lessons learnt from MERS readiness and preparedness paved the way for developing a comprehensive infrastructure for the COVID-19 pandemic response. Vigilance is still needed regarding MERS and it should be regarded as a priority threat necessitating national, regional and international collaboration under the umbrella of the One Health approach.

Against this background, the WHO Regional Office for the Eastern Mediterranean held a virtual meeting on 16 August 2021 to review the MERS situation in the Eastern Mediterranean Region in the context of the ongoing COVID-19 pandemic, including MERS surveillance in humans, the impact of MERS on COVID-19 pandemic preparedness and response activities, lessons learned from countries in prevention and control of MERS, and progress in research and development for diagnostics, therapeutics and vaccine production.

The meeting was attended by participants from the ministries of health of Oman, Qatar, Saudi Arabia and the United Arab Emirates, as well as from the Erasmus Medical Center, Food and Agriculture Organization of the United Nations (FAO), Hong Kong University, United States Centers for Disease Control and Prevention (CDC), WHO

headquarters, WHO Regional Office for the Eastern Mediterranean and World Organisation for Animal Health (OIE).

The objectives of the meeting were to:

- review the MERS situation in the Eastern Mediterranean Region and globally, particularly within the context of the COVID-19 pandemic and its impact on MERS surveillance, preparedness and response activities;
- review available scientific knowledge and priority activities necessary to prevent, manage and control the disease;
- review and share lessons learned and best practices in control and prevention of MERS;
- identify critical needs for technical guidance and research to support updating of the WHO roadmap for MERS-CoV research and product development for diagnostics, therapeutics and vaccines and the broader public health research agenda; and
- review and propose updates on previous recommendations on preparedness and response to the disease, using the latest scientific evidence.

Dr Wasiq Khan, team leader for the Infectious Hazard Prevention and Preparedness (IHP) programme at the WHO Regional Office, inaugurated the meeting by thanking country participants and partners for their continued work and stressed the importance of ongoing collaboration under the One Health approach. Dr Abdinasir Abubakar, manager of the regional IHP programme, noted that although countries were currently focused on the response to the COVID-19 pandemic, it remained important to be vigilant regarding MERS, which remained a public health threat.

Dr Richard Brennan, director of the regional WHO Health Emergencies Programme, highlighted how the work done for the response to MERS

had been an asset in the response to COVID-19. Dr Maria Van Kerkhove, head of emerging diseases at WHO headquarters, also observed how the preparedness and readiness activities done for MERS, including guidelines and standard operating procedures, whether for surveillance or IPC, had provided the foundations of the response to COVID-19. She urged colleagues and partners to remain vigilant regarding MERS and to strengthen capacities and collaboration using the One Health approach.

Dr Abdallah Assiri, from Saudi Arabia, noted the country's collaboration with WHO and how it had used the established infrastructure for MERS in the early response to COVID-19. He pointed to the importance of learning and benefiting from the response to COVID-19, especially for vaccine development and case management.

2. Summary of discussions

MERS surveillance in humans

Dr Amgad ElKohly, WHO Regional Office, gave a brief epidemiological summary of MERS cases in humans since 2012 to date, with the biggest outbreak detected in early 2014 in Saudi Arabia. In total, 2578 confirmed cases have been identified, with a 34% CFR, with the majority in Saudi Arabia (84%). The CFR has been decreasing in Saudi Arabia since 2012, reaching its lowest levels in 2019 (25%). In 2020 and 2021, it increased to 35% and 36%, respectively, although there was a decrease in confirmed cases to under 10 cases per week, possibly due to the COVID-19 pandemic and the resulting shift in focus of health providers to COVID-19 diagnosis.

The CFR in primary cases is higher, mainly because most secondary cases are from health care settings and are mostly young. The age group 50–59 years continues to be at the highest risk for acquiring infection

in primary cases, while the age group 30–39 years is most at risk for secondary cases. The CFR in health care workers is 20% compared to a CFR of 40% in non-health care workers; moreover, the CFR in patients with comorbidities is 46% compared to 10% in patients without comorbidities. From 2014 to 2021, community-acquired cases exceeded hospital-acquired cases except in 2015. In terms of gender, 70% of cases are males, who have a higher CFR than females (40% and 30%, respectively). In Saudi Arabia, from 2013 to 2021, 78% of cases were in non-health care workers.

Impact of COVID-19 pandemic on MERS surveillance in humans in Saudi Arabia

Dr Emad Al Mohammedy, WHO Collaborating Centre for MERS, stressed that the progress made in human surveillance due to MERS had paved the way for a rapid and efficient response to the COVID-19 pandemic in Saudi Arabia. During the pandemic, the country had reported a dramatic decrease in diagnosis of MERS cases, with even suspected cases decreasing by 50%. The CFR remains higher in primary cases. The pandemic had a negative impact on MERS surveillance due to changes in health care-seeking behaviours and resource limitations and shifting priorities in health care delivery.

However, positive impacts included enhanced laboratory capacity, the creation of efficient specimen tracking systems, a focus on timely reporting and reducing human error, and the useful experience gained in contact tracing, including the use of smartphone applications, and in risk communication with the public using tailored messages via several tools. Moreover, the trained staff will be ready for any future outbreaks and over 200 guidance documents, standard operating procedures and protocols had been produced for the public and health facilities.

MERS surveillance/studies in animals

Dr Amal Mansour, FAO, described a USAID-funded project for MERS surveillance in animals in Egypt, Ethiopia, Jordan and Kenya that has been running since 2015. Technical and logistical support has focused on improving surveillance data and analysis, specimen handling and transportation, the camel value chain and building national laboratory capacities through developing guidelines and testing protocols, training staff on MERS-CoV screening tests, and the provision of consumables, reagents, kits, etc. Surveillance studies include abattoir-based surveillance, longitudinal surveillance and cross-sectional surveillance. Specimens are tested for both serology and RT-PCR, with cross-sectional surveillance yielding high seroprevalence rates (50–90%), although for RT-PCR testing only 0–7% of case were positive. Sequencing of MERS RNA revealed three different subtypes (clades A, B and C).

Recent regional research

Dr Lubna AlAriqi, WHO Regional Office, highlighted recent research in the Eastern Mediterranean Region, published between 2019 and 2021, focused on a better understanding of how humans become infected from animal or environmental sources in the community and the identification of risk factors for infection from humans or the environment in occupational settings and health care settings. The main objectives of this research are to prevent human infections and reduce severe illness and death, and the five main areas of focus are: virus origin and characteristics; epidemiology and transmission; clinical management and infection and prevention and control; product development and implementation; and the impact of interventions and operational research.

WHO support to MERS studies in countries across the Region has led to 80 published studies (of which 25 used WHO protocols). During the COVID-19 pandemic, research attention and resources have been diverted to research related to the new virus, although interest has been sparked in research on other coronaviruses and zoonotic diseases. Studies in the Region on MERS continue to progress, particularly in MERS-affected countries, including serologic studies to assess the magnitude of transmission and identify exposure risk factors, mainly in asymptomatic infection. However, large, including multi-county, studies remain limited, highlighting a need for more collaborative research among affected countries.

Update on MERS vaccine development

Dr Naif Al Harbi, King Abdullah International Medical Research Center (KAIMRC), outlined the work done in the development of a MERS vaccine for humans and camels. There are three leading candidates using the spike protein, with differences in platform (viral or DNA vector). Trials for one of the three vaccine candidates (ChAdOx1-MERS), done so far on rodents and primates, have shown significant antibody response. Studies using the same candidate vaccine have been conducted on camels: it was found to be safe and induced a higher antibody response in camels with previous exposure (pre-existing immunity). However, further studies are needed before conclusions can be reached on the vaccine's efficacy.

As for a human vaccine, a phase 1 clinical trial has begun as part of a collaboration between Saudi Arabia and Oxford University, UK. Two sub-phases have been conducted: phase 1a to determine safety and immunogenicity of the candidate vaccine in UK healthy adult volunteers; and phase 1b to determine the safety and immunogenicity of the candidate vaccine in healthy adult volunteers in MERS-endemic

areas. Preliminary results show a promising response. Phase 2 is in the planning phase.

The lack of a commercial market so far means that MERS vaccine development (whether human or animal) has been mainly academic in nature. Moreover, there are no clear regulations for manufacturing vaccine for camels; if manufactured, success would only be possible if there are governmental subsidies and regional uptake and buy-in from endemic countries. Furthermore, Saudi Arabia does not have a facility to stockpile vaccines and would rely on the stockpile of the Coalition for Epidemic Preparedness Innovations (CEPI) emergency use.

Leveraging MERS capacities for responding to COVID-19

Dr Rebecca Grant, WHO headquarters, introduced WHO's global MERS workplan, highlighting its three objectives to: 1) strengthen surveillance in endemic countries to be able to early detect suspected cases of high-threat respiratory pathogen infections, such as MERS; 2) improve country abilities to respond to respiratory pathogen infections; and 3) accelerate public health research, product development and improve evidence-based MERS guidance. MERS-related capacities have been leveraged for the COVID-19 response in laboratory and diagnostics, including in developing sequencing capacity, as well as in IPC, clinical management, mathematical modelling and technical guidance, mainly for IPC in health care facilities.

Detection of MERS-CoV during circulation of SARS-CoV-2 and influenza

Dr Claire Midgley, CDC, noted that the COVID-19 pandemic raised important questions about who should be tested for MERS and what tests or algorithms should be followed. MERS identification is very crucial to prevent onward transmission and contain any possible

outbreak, and several respiratory testing kits and algorithms have been used by laboratories to rule out MERS during the pandemic. Symptoms of MERS are of a wide spectrum, ranging from mild to severe and death. The CFR for MERS is 34%, but this is probably an overestimate as many cases with mild symptoms will have been mistaken for other respiratory infections. Health care workers constitute 17% of MERS cases, suggesting low compliance with IPC measures, and delays in identifying index cases, given the non-specific clinical presentation. High-risk wards for MERS transmission in health care facilities include inpatient wards, emergency departments and dialysis units. Severely ill patients with high viral loads are superspreaders, but more knowledge is needed on the transmission risk from asymptomatic or mild cases. It is important not to focus solely on clinical presentation when detecting and testing MERS cases, but to look at epidemiological risk factors, represented by travel history, close contact with known MERS-positive case, contacts with camels and health care exposure.

Infection prevention and control

Dr Maha Talaat, WHO Regional Office, noted the important role played by IPC in preparedness for and response to emerging infectious diseases. Loose measures or breeches in IPC measures in health care setting can result in large outbreaks, such as in the case of MERS, with 17% of cases being health care workers. Outbreaks caused by coronaviruses in health care settings had underlined the need for IPC programmes and increased support for them by political and public health leaders. WHO has produced several guidelines on the core components of IPC programmes, with a focus on preventing health care-associated infections (HAIs). Challenges include competing priorities and limited availability of accredited IPC training courses, IPC recognition/career paths, data on the burden of HAIs, and surveillance and microbiology laboratory capacity, mainly in low- and middle-income countries.

Country experiences and lessons learned

Dr Mohammad Qashgari, Public Health Authority of Saudi Arabia, described how Saudi Arabia has been developing its IPC tools and programmes through a process of continuous monitoring and evaluation since the initial MERS outbreaks in its health-care settings, and has developed a MERS/COVID-19 preparedness tool and an auditing programme that all hospitals need to meet the standards of. Every hospital has to have an IPC department staffed by trained and qualified personnel and the establishment of respiratory triage in all hospitals has been mandated to minimize the risk of early disease transmission inside hospital wards. Moreover, guidelines for COVID-19 have been tailored from the SOPs developed for MERS on how to identify suspected cases, isolate cases in negative pressure (isolation) rooms, collect nasopharyngeal specimens in negative pressure rooms, transport patients to designated wards, and disinfect and clean.

Dr Amina Al Jardani, Central Public Health Laboratories of Oman, noted that since Oman's first MERS case was detected in 2013, 24 cases and eight deaths (CFR 33%) had been reported in the country, with no nosocomial infections until 2019, when there were outbreaks in two hospitals. The notification of suspected cases is mandated and done electronically, and testing of specimens is done in the national reference laboratory, recognized by WHO as the national influenza centre (NIC) in 2009. Within the national acute respiratory infection system (NARI) there are two surveillance systems for severe acute respiratory infections (SARI) and for influenza-like illness (ILI). The NARI aims to monitor SARI/ILI activities, identify circulating viruses in the community, provide timely feedback and useful information to the public health authorities, detect unusual and unexpected events, share virus isolates with WHO collaborating centres, and identify antiviral drug resistance mutations. Oman uses several testing algorithms for

influenza and SARS-CoV2, and the NIC conducts molecular testing, virus isolation and genomic sequencing. To be able to focus on MERS testing at the NIC during the pandemic, decentralized testing has been allowed for SARS-CoV-2. Training and awareness-raising on MERS for clinicians and laboratories has resulted in the number of reported suspected MERS cases increasing from 453 in 2020 to 947 in 2021. While MERS infection is rare and sporadic in Oman, the threat of MERS and other respiratory pathogens remains high, necessitating vigilance.

Dr Elmoubasher Farag, Ministry of Public Health in Qatar, explained that the cultural and economic importance of camel owning, racing and trading in Qatar had presented huge challenges to convincing camel owners of the risk from MERS. However, this was overcome by adopting the One Health approach through strong collaboration between the health ministry and animal health department, community participation and involvement, and strengthened human and animal laboratory diagnostic capacities. During outbreaks, teams from both departments are deployed to investigate human cases and collect specimens from suspected cases and camels. As a result of this approach, recommendations have been made to test camels regularly at slaughterhouses, racing tracks and ports of entry to Qatar. The main factors behind this success story have been international guidance, the development of national MERS competencies and leadership at all levels. Challenges include stigma, convincing camel owners and community members of the risks in the absence of disease symptoms in infected camels, and limited technical guidance in the animal sector. For emerging infections at the human/animal interface, many factors can increase the risk of spillover, including intensified closed camel farming, poor biosafety measures in farms, sociocultural factors, camel reproduction practices, and camel movements and importation.

Dr Salama Almuhaire, Director of Veterinary Laboratories Division, Abu Dhabi Food Control Authority, outlined the shared responsibility and strong coordination between human and animal departments under the One Health approach adopted in the United Arab Emirates, including through two-way information-sharing. Lessons learnt from the response to MERS regarding business continuity planning, emergency preparedness and response, capacity-building, and sustainable implementation of the One Health approach were leveraged for the COVID-19 response. At national level, the United Arab Emirates succeeded in establishing a multidisciplinary laboratory network committee to harmonize testing algorithms and exchange knowledge and information. As a result of this collaboration, specimens from animals are collected based on human notifications. At the international level, the United Arab Emirates has been collaborating with OIE to develop international guidance for testing human specimens in veterinary laboratories and has published an article in the OIE Bulletin on the use of lessons learnt from MERS in the response to COVID-19.

Update by CDC

Dr Aron Hall, CDC, in his update explained that in mild cases of MERS, virus shedding remains for up to one week as opposed to 2–3 weeks in severely ill patients, which has a major impact on IPC in health-care settings, and noted that patients with chronic diseases have an increased risk of death. He described outbreaks in health-care settings where transmission, mainly in emergency rooms, inpatient wards and dialysis units. Immediate contact tracing and repeat testing are believed to be major factors in the control of transmission in health-care settings, with delays in identification of suspected cases leading to delays in implementation of control measures. A study in the United Arab Emirates on risk factors for sero-positivity among farm workers, found significantly increased risk of infection where the occupation is camel

salesperson, where there is contact with camel waste and where a person has diabetes. However, there remains a knowledge gap for cases with no recognized exposure, and therefore a need for further research to understand differences in transmission sources, as well as dynamics outside the Arabian peninsula. Despite changes in priorities due to the COVID-19 pandemic, there is a need to sustain MERS surveillance and case management and to reassess the performance of MERS serologic essays for cross-reactivity.

Remarks by the Hong Kong University

Dr Leo Poon, the Hong Kong University, described studies on the differences in MERS lineages in different geographical areas, demonstrating that clades A and B are found in Saudi Arabia, while clade C is found in Africa, with some deletions when comparing the lineages. Differences are found in spike proteins among the three clades, with clade C having less ability to replicate in human lung tissue in vitro compared to clades A and B, which may partly explain why there are not yet any MERS cases among humans in Africa despite the high seropositivity in camels. This does not mean that clade C does not infect humans, because studies have shown considerable T-cell responses in workers dealing with camels in Africa. There is a need for further genetic characterization of clade C viruses and determination of the potential risk of infection in humans. There remains much to be learnt about MERS, both biologically and epidemiologically, and MERS-CoV in camels needs to be closely monitored as the virus is continuously mutating. There is a need to remain vigilant and control the threat of zoonotic diseases, including MERS, but the world is better equipped than ever as a result of the solid infrastructure built during the COVID-19 pandemic.

Remarks by the Erasmus Medical Centre

Dr Bart Haagmans, Erasmus Medical Centre, described the progress of clinical trials for MVA-MERS-S vaccine. The trial is funded by CEPI and is being conducted on 160 healthy volunteers in Hamburg and Rotterdam. So far, sera from positive COVID-19 patients have showed neutralizing effects in MERS patients, which is promising. However, there are differences in the MERS immune responses in SARS-CoV2 seropositive and seronegative individuals. Phase 2 of the trial is currently in preparation. There remains a need to compare the tropism, pathogenesis and transmission of different MERS viruses in different geographical areas, using organoids and animal studies in camelids.

Remarks by OIE

Dr Gounalan Pavade, OIE, described the ad hoc group on MERS that was held in January 2019 where there had been discussion on an updated case definition for reporting MERS-CoV infection in dromedary camels to OIE. It was stated during the meeting that the virus was widely circulating in some populations of dromedary camels, resulting in high seroprevalence, and that serological evidence was therefore not useful in determining active infection or positive cases in camels. It was agreed that MERS met the criteria for consideration for inclusion as an OIE-listed disease, and in May 2021, the General Assembly of OIE included MERS as a notifiable disease on the OIE list. OIE has published standards related to MERS, including terrestrial codes and in its terrestrial manual, and OIE's reference laboratory for MERS provides scientific and technical advice on diagnosis and control of the disease in collaboration with the United Arab Emirates central veterinary research laboratory. OIE is also developing a chapter for its manual on infection of dromedary camels with MERS-CoV to provide guidance on facilitating the safe trade of camels and their products and

highlighting the importance of surveillance in dromedary camels for the prevention and control of human disease.

3. Conclusion

Dr Khan thanked colleagues, partners and country representatives for their participation and emphasized the importance of continued and sustained investment in both animal and human research, and the need to remain vigilant. He noted the opportunities presented by the response to COVID-19, such as the lessons learnt in vaccine development and information-sharing, and the strong collaboration between partners, and stressed the need to adopt a One Health approach.

Dr Abubakar concluded by highlighting the need to integrate work on MERS and COVID-19, the lessons learnt from COVID-19 on vaccine development during emergencies, and the need for collaboration between veterinary and human laboratories.



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