Title:

The Middle East Respiratory Syndrome (MERS)

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SUMMARY/SYNOPSIS

The Middle East Respiratory Syndrome (MERS) is a novel lethal zoonotic disease of humans caused by the Middle East respiratory Syndrome coronavirus (MERS-CoV). Whilst MERS is endemic to the Middle East, travelers have exported MERS-CoV upon their return to their home countries. As of February 20th, 2019, there have been 2,358 cases of laboratory-confirmed MERS-CoV cases reported to the World Health Organization, including 856 deaths (35% mortality). The largest MERS outbreak outside the Middle East occurred in South Korea resulting in 186 MERS cases with 38 deaths was caused by a Korean businessman returning to Seoul. Since Millions of pilgrims visit Saudi Arabia each year from across the world, watchful surveillance and a high degree of clinical awareness of the possibility of MERS-CoV infection in turning travelers from the Middle East is important. A wide range of clinical manifestations of MERS have been recorded from mild to severe acute respiratory disease and death. The elderly, immunocompromised, and those with chronic co-morbid liver, lung and hepatic conditions have a high mortality rate. There is no specific treatment for MERS. Person to person spread cause Hospital and household outbreaks of MERS-CoV and thus improved compliance with internationally recommended infection control protocols and rapid implementation of infection control measures are required.

Keypoints

- **The Middle East Respiratory Syndrome (MERS) is a novel lethal zoonotic disease of humans endemic to The Middle East, caused by the Middle East respiratory Syndrome coronavirus (MERS-CoV).**
- **Humans are thought to acquire MERS-CoV though contact with camels or camel products**
- **MERS carries a 35% mortality rate. There is no specific treatment for MERS. Person to person spread causes hospital and household outbreaks of MERS-CoV**
- **Millions of visitors travel to Saudi Arabia each year from across the world, thus watchful surveillance and a high degree of clinical awareness and early diagnosis with rapid implementation of infection control measures in turning travelers is important**

Introduction

The Middle East Respiratory Syndrome coronavirus (MERS-CoV) is a new zoonotic human viral pathogen endemic to the Middle East.[1-3] It was identified in 2012 in a lung sample of a 60-year-old patient who had died of respiratory failure in Jeddah, Saudi Arabia.[4] The disease caused by MERS-CoV is named Middle East Respiratory Syndrome (MERS). MERS has remained on the radar of global public health authorities because of recurrent nosocomial and community outbreaks, and its association with severe disease and high mortality rates.[1-3] Intermittent sporadic cases, community clusters and nosocomial outbreaks of MERS-CoV have continued to occur in Saudi Arabia.[1] MERS-CoV remains on the WHO Blueprint list of priority pathogens[5] since it remains a persistent threat to global health security

Epidemic potential and global spread

Cases of MERS from outside the Middle East have been reported from all continents have been linked with travel to the Middle East.[1] Nosocomial outbreaks of MERS-CoV infection and account for about 40% of MERS-CoV cases globally. Large health care associated outbreaks of MERS-CoV have occurred in Saudi Arabia, United Arab Emirates, and the Republic of Korea.[6-10] From June 1 to July 31, 2015, MERS-CoV caused the largest outbreak outside the Arabian Peninsula in the Republic of Korea resulting in 186 confirmed MERS cases with 38 deaths.[7-9] This occurred when a Korean traveler returning from a trip to Qatar, UAE, Saudi Arabia and Bahrain, became ill with a respiratory illness and visited several hospitals before finally being diagnosed as having MERS-CoV infection on May 20, 2015 at Samsung Medical Center.[7-9] This resulted in 186 people, including 25 healthcare workers, contracting MERS-CoV infection. 181 out of 186 cases were associated with hospital associated transmission. This outbreak clearly illustrated the epidemic potential of MERS-CoV, spreading person to person.

Epidemiology

The number of MERS-CoV cases reported to the WHO have steadily increased since the first report of MERS-CoV in September 2012.[4] MERS-CoV cases continue to be reported from the community and hospitals across the Arabian Peninsula. As of February 24th, 2019, 2,358 cases of laboratory-confirmed MERS cases were reported to the World Health Organization. Of these there were 856 deaths (35% mortality).[1] (**Figure 1 - WHO World Map**). Approximately 80% of human cases have been reported by Saudi Arabia. 27 countries have reported cases of MERS.[11] Countries in or near the Arabian Peninsula which report MERS cases are Bahrain, Iran, Jordan, Kuwait, Lebanon, Oman, Qatar, Saudi Arabia, United Arab Emirates (UAE), and Yemen. Cases identified outside the Middle East are usually in travellers who were infected in the Middle East and then travelled to areas outside the Middle East. Countries outside the Arabian Peninsula which have reported travel-associated MERS cases are: Algeria, Austria, China, Egypt, France, Germany, Greece, Italy, Malaysia, Netherlands, Philippines, Republic of Korea, Thailand, Tunisia,

Turkey, United Kingdom, and United States of America.[1]

Source of Primary Human MERS-CoV infections

The exact mode of transmission of MERS-CoV to humans is not yet accurately defined. Epidemiological, genetic, and phenotypic studies indicate that dromedary camels appear to be the main intermediary reservoirs of MERS-CoV.[12-15] Camels are assumed to be intermediary host species for the MERS-CoV, although the exact source and the mode of transmission in many primary MERS cases remain unclear. Antibodies to MERS-CoV have been detected in serum and milk collected from 33 camels in Qatar, April 2014. In one study, active virus shedding in nasal secretions and in faeces was observed for 7 out of 12 camels.[13] MERS-CoV survives for prolonged periods in Camel's milk but viable virus became undetectable after pasteurization at 63C for 30 min.[16] MERS-CoV has been detected in camels from Kenya 792 out of 1,163 camels studies had ELISA seropositivity of which 11 camel nasal swabs were positive for MERS-CoV by reverse transcription-quantitative PCR.[17] A study of humans in Kenya has detected MERS-CoV ´neutralizing antibodies in persons living in rural areas, although no human MERS cases have been detected yet.[18]

The primary source of human MERS-CoV infections remains unknown. There are no definitive data on the epidemiological link between human MERS-CoV infections and bats. Only one fragment of MERS CoV with close matching to a human isolate of MERS-CoV was found in a study of over 1,000 samples from Taphozous bats.[19] Phylogenetic analysis of a MERS-related CoV identified from a *Neoromicia capensis* bat sampled in South Africa supports the hypothesis that bats are the evolutionary source of MERS-CoV but not a zoonotic reservoir.[20] To date no sustained human-to-human transmission has been documented, although tertiary and quarternary spread did occur in the Korean outbreak.[8-9]

Risk factors for primary MERS-CoV infection

Several independent risk factors for increased susceptibility to acquiring primary MERS-CoV infections have been identified: direct dromedary exposure in the fortnight before illness onset; direct physical contact with dromedary camels during the previous 6 months; diabetes mellitus, heart disease. Risk factors for MERS-CoV infection among camel workers include milking camels, contact with camels' waste, poor hand hygiene before and after animal tasks and training activities and workers with respiratory symptoms requiring overnight stay in hospital.[21] Viral RNA sequencing has confirmed camel to human transmission of MERS-CoV[22-24] after known exposure to the infected camels. Recent data suggests that whilst MERS-CoV is widespread among dromedary camels in the Middle East and Africa, zoonotic transmission of MERS-CoV from camels to humans is relatively uncommon, and human disease is not directly proportional to potential exposure. MERS-CoV does not transmit easily from person to person unless there is close contact, such as occurs when providing care to a patient in the household or nosocomial

setting when the diagnosis of MERS-CoV has not yet been recognized and there are lapses in instituting infection control measures.[2,3,6,7]

Clinical features

The symptoms, signs, laboratory, and imaging abnormalities associated with MERS-CoV infection are not MERS-specific and are like other respiratory tract infections.[2,3,7,26-28] (**Table 1**). The clinical manifestations of MERS-CoV infections range from asymptomatic infection to mild, moderate and severe disease, often complicated by severe pneumonia, Acute Respiratory Distress Syndrome (ARDS), septic shock, and multi-organ failure. The incubation period is between 2 to 14 days. Mild cases can have low-grade fever, chills, runny nose, dry cough, sore throat, and myalgia. Some patients have gastrointestinal symptoms such as nausea, vomiting and diarrhoea. Fever may be absent in up to 15% of hospitalized cases. Laboratory abnormalities include cytopenias and elevated transaminases (**Table 1**). Co-infections with other respiratory viruses and bacterial pathogens have been reported. Upto half of MERS cases can have acute kidney injury and one third of very ill patients have gastrointestinal symptoms.

Severe illness can cause respiratory failure that requires mechanical ventilation and support in an intensive care unit. Rapid progression to acute respiratory distress syndrome (ARDS) and multisystem disease and organ failure with a median of 2 days from hospitalization to intensive care unit (ICU) admission.[29,30] MERS-CoV infection appears to cause more severe disease in older people, people with weakened immune systems, and those with chronic diseases such as renal disease, cancer, chronic lung disease, and diabetes.[2,3]

Mortality and risk factors

A case study of 660 MERS patients in Saudi Arabia seen between Dec 2, 2014, and Nov 12, 2016 found that 3-day, 30-day, and overall mortality were 13.8%, 28.3%, and 29.8%.[31] Patients over the age of 60 were more likely to die (45.2% mortality) from their infections than were younger patients (20%). Patients with pre-existing medical co-morbidities tend to have more severe disease and higher mortality rates.

Factors associated with poor management outcomes (severe disease or death) in MERS patients include old age, male gender, comorbid pre-existing illnesses such as obesity, diabetes mellitus, heart and lung disease, and immuno-compromised states), low serum albumin, concomitant infections, positive plasma MERS-CoV RNA.[27-32] DPP4 receptors have been shown to be upregulated in the lungs of smokers and this may explain why patients with comorbid lung diseases are prone to sever illness.[33]

Making an early diagnosis of MERS-CoV infection

Many cases of MERS-CoV can be easily missed since the presentation is that of any community

acquired pneumonia or other respiratory illness caused by as influenza A and B respiratory syncytial virus, parainfluenza viruses, rhinoviruses, adenoviruses, enteroviruses (e.g. EVD68), human metapneumovirus, and endemic human coronaviruses (i.e. HCoV-HKU1, -OC43, -NL63, and -229E).[2] Most nosocomial outbreaks of MERS-CoV have been associated with a delay in diagnosis.

A history of travel to the Middle East is important for patients presenting in non-Middle Eastern countries with a febrile illness.[1,2,33,34]

Risk factors for nosocomial MERS-CoV outbreaks

Early and accurate diagnosis of MERS-CoV infection is important for the clinical management, instituting infection control and epidemiological control measures of MERS-CoV infections. Thus a high degree of clinical awareness of the possibility of MERS-CoV infection is required in all healthcare settings so that an accurate diagnosis can be made and infection control measures instituted as soon as the diagnosis is entertained clinically.[33,34]

Clinical samples for laboratory testing

Upper respiratory tract samples have yielded negative results in some symptomatic close contacts of confirmed cases, who later developed pneumonia and tested positive on lower respiratory specimens. For laboratory testing it is recommended by the World Health Organisation[35] that both upper respiratory tract specimens (nasopharyngeal and oropharyngeal) and lower respiratory tract specimens (sputum, tracheal aspirate or lavage) are collected whenever possible. Lower respiratory specimens have a higher diagnostic value than upper respiratory tract specimens for detecting MERS-CoV infection.[36] Sputum, endotracheal aspirate, or bronchoalveolar lavage be collected for MERS-CoV testing where possible. If patients do not have signs or symptoms of lower respiratory tract disease and the collection of lower tract specimens is not possible or clinically indicated, upper respiratory tract specimens such as a nasopharyngeal aspirate or combined nasopharyngeal and oropharyngeal swabs should be collected.

When taking nasopharyngeal and oropharyngeal specimens, dacron or rayon swabs specifically designed for collecting specimens for virology must be used. These swab kits should contain virus transport medium. The nasopharyngeal and oropharyngeal swabs should be placed in the same tube to increase the viral load.[35,36] A single negative test result does not exclude the diagnosis and repeat sampling and testing is strongly recommended. To confirm clearance of the virus, respiratory samples should be collected sequentially (every 2 to 4 days) over ensuing days until there are two consecutive negative results in clinically recovered persons. Specimens for MERS-CoV detection should reach the laboratory as soon as possible after collection and be delivered promptly to the laboratory shipped at 4°C if possible. When there is likely to be a delay of more than 72 hours in specimens reaching the laboratory, it is

recommended that the specimens are frozen at - 20°C or ideally -80°C and shipped on dry ice. It is important to avoid repeated freezing and thawing of specimens.[35,36]

Laboratory tests for MERS-CoV

Accurate laboratory molecular diagnostic tests are available using highly sensitive and specific real-time reverse transcription PCR (RT-PCR). Three rRT-PCR assays for routine detection of MERS-CoV have been developed targeting upstream of the E protein gene (upE) and the open reading frame 1b (ORF 1b), and ORF 1a. [35,36,37] The assay for the upE target is considered highly sensitive and is recommended for screening, with the ORF 1a assay considered of equal sensitivity. To date, these rRT-PCR assays have shown no cross-reactivity with other respiratory viruses including human coronaviruses and were suitable to detect all known MERS-CoV strains in humans and dromedary camels.

Laboratory confirmation of MERS-CoV infection[37] is obtained by detection of the virus by: (a) MERS-CoV specific nucleic acid amplification test (NAAT) with up to two separate targets and/or sequencing; or (b) virus isolation in tissue culture; or (c) serology on serum tested in a WHO collaborating center with established testing methods.[35,36] A case confirmed by serology requires demonstration of sero-conversion in 2 samples ideally taken at least 14 days apart, by a screening (ELISA, IFA) and a neutralization assay.

Serological tests such as ELISAs for MERS-CoV are being developed and refined for surveillance or investigational purposes.[36,38] An indirect ELISA has been developed for sero-epidemiological testing and surveillance purposes and requires evaluation in field studies.[39]

MERS-CoV testing must be performed in appropriately equipped biosafety laboratories by staff trained in the relevant technical and safety procedures. National or WHO guidelines on the laboratory biosafety should be followed in all circumstances.[40]

Clinical management of MERS cases

The management of MERS patients is largely symptomatic and supportive and aims to reduce the risk of complications such as secondary infections, renal and respiratory failure.[1-3] Seriously ill patients should receive intensive care.

Whilst a range of existing and developmental treatments may be useful[41] (**Table 3**), currently there are no specific treatments to treat MERS-CoV. A range of treatments such as lopinavir/ritonavir, pegulated IFN-α2a and ribavirin have been used empirically for serious cases of MERS but there is no accurate evidence base that any of them improve treatment outcomes. Treatment with either lopinavir/ritonavir or IFN-β1b in the marmoset model was associated with improved clinical, radiological, and pathologic outcomes with lower viral loads in comparisons with no treatment whereas mycophenolic acid alone increased viral loads and fatality.[42] Macrolide therapy is commonly started before the patient arrived in intensive care unit

in Saudi Arabia. A retrospective study of 136 MERS patients found that macrolide therapy is not associated with a reduction in mortality or improvement in MERS-CoV RNA clearance.[43]

Currently there is an ongoing randomized controlled trial (RCT) in progress in KSA comparing lopinavir/ritonavir, recombinant IFN-β1b and standard supportive care against placebo and standard supportive care in patients with lab-confirmed MERS requiring hospital admission.[44] Systemic corticosteroids were shown to delay viral clearance in critically ill patients with MERS-CoV infection.[30] A range of anti-MERS-CoV drugs and host-directed therapies are being considred as potential therapies for MERS-CoV.[41] Properly designed studies are needed to answer several knowledge gaps for us understand the disease pathogenesis, viral kinetics, mode of disease transmission, and the intermediary source of MERS in order to guide infection control prevention measures and treatment responses in MERS-CoV infection.

Infection control measures in hospitals when MERS-CoV infection is suspected.

The main infection prevention and control measures for managing patients with MERS are well documented from the SARS epidemic.[45] Early identification and isolation of suspected or confirmed cases and ongoing surveillance are key to preventing nosocomial spread. Droplet precaution (wearing a surgical mask within 1 m of the patient) and contact and droplet precautions (wearing gown, gloves, mask, eye protection on entering the room and removing them on leaving) when caring for patients with suspected MERS-CoV infection.[46] Healthcare workers (HCWs) should implement airborne precautions and wear a fit-tested particulate respirator (e.g., a US NIOSH-approved N95 filtering facepiece respirator [FFR] or a European EN-approved FFP2 or FFP3 filtering facepiece respirator) when performing aerosol-generating procedures for infected and potentially-infected patients. Avoiding aerosolizing procedures in crowded hospital emergency or inpatient medical wards which do not have adequate infection control measures in place may decrease MERS-CoV human-to-human spread and environmental contamination. It is also prudent to use higher levels of protection for HCWs who extended close contact with MERS patients and those who are exposed to aerosols from high-risk procedures.

Higher levels of ventilation (more air changes, higher air flow and velocity), greater effort to prevent air dispersion beyond the point of generation (enclosure, using capture ventilation) and higher levels of personal protective equipment (more coverage, more protective types of respiratory protection) are all necessary. To reduce room contamination in the hospital setting, the application of a minimum room ventilation rate of 12 air changes per hour in a single room or or at least 160 litres/second/patient in facilities with natural ventilation is recommended when caring for patients receiving mechanical ventilation and during aerosol-generating procedures.

Decreasing risk of transmission

Instituting appropriate infection control measures as soon as the diagnosis is considered is critical to preventing spread especially in hospitals. Since symptoms and signs of respiratory tract infections (RTIs) are non-specific, it is difficult to diagnose primary cases of patients with MERS-CoV infection. Infection prevention and control measures are important to prevent the spread of MERS-CoV within households, the community and in health care facilities. Guidelines and recommendations from global public health bodies are given in **Table 4**.

Transmission in hospitals

Human-to-human transmission occurs within communities, households and more strikingly within hospital settings. Health care associated outbreaks have occurred in several countries, with the largest outbreaks seen in Saudi Arabia, United Arab Emirates, and the Republic of Korea. Several outbreak studies have shown that MERS-CoV does not appear to transmit easily from person to person unless there is close contact, such as providing clinical care.[2,7,47-52] MERS-CoV has been identified in clinical specimens such as sputum, endotracheal aspirate, bronchoalveolar lavage; nasal or nasopharyngeal swabs, urine, faeces, blood and lung tissue.[2,3] The modes of MERS-CoV transmission through direct or indirect contact, airborne, droplet or ingestion have yet to be defined.

The upsurge in the number of human infections due to MERS-CoV over the past few years in healthcare facilities in the Middle East and South Korea [2,3,47-48] were related to low awareness for MERS-CoV infection resulting in nosocomial outbreaks involving existing hospitalized patients, outpatients, visitors and HCWs within healthcare facilities with over-crowding, lack of isolation room facilities, environmental contamination, and inadequate infection control measures without any significant change in the transmissibility of the virus. Health-care workers should always undertake standard precautions consistently with all patients with fever and symptoms of RTIs. Droplet precautions should be added to the standard precautions when providing care to these while contact precautions and eye protection should be included when caring for probable or confirmed cases of MERS-CoV. Airborne precautions are important when performing aerosol generating procedures.

Household transmission

Human to human transmission in the community or those living in large households and family compounds has been described.[50-54] An investigation of 280 household contacts of 26 index MERS-CoV-infected Saudi Arabian patients, with follow-up serologic analysis in 44 contacts performed in 2014 to determine the rate of 'silent or subclinical' secondary infection after exposure to primary cases of MERS-CoV infection, found there were 12 probable cases of secondary transmission (4%; 95% CI, 2 to 7).[51] There have been several reports of MERS-CoV carriage after exposure to patients with MERS. Apparently healthy household contacts have been found to have MERS-CoV in their upper respiratory tract. Low levels of MERS-CoV RNA have been detected in asymptomatic health care workers from nosocomial MERS-CoV

outbreaks in a Jeddah hospital [52] indicate. Of 79 relatives that were investigated after MERS-CoV infections affected an extended family in Saudi Arabia in 2014, 19(24%) were MERS-CoV positive; 11 were hospitalized, and 2 died.

Healthcare worker and community education

In MERS-CoV endemic countries where MERS-CoV cases can occur in the community and households, educational awareness of MERS-CoV and MERS prevention measures may reduce the risk of household transmission and prevent community clusters.[53,54] Regular hand washing before and after touching camels and avoiding contact with sick camels is advised. People should avoid drinking raw camel milk or camel urine or eating camel meat that has not been properly cooked. Persons who have diabetes, kidney disease chronic lung disease, cancer or are on immunosuppressive treatment are at high risk of developing severe MERS-CoV disease, thus they should avoid close contact with camels and bats.

WHO does not advise special screening for MERS-CoV at points of entry after return from the Middle East nor does it currently recommend the application of any travel or trade restrictions.[1] Persons with a history of travel from or to the Arabian Peninsula within 10 days of developing symptoms of an acute respiratory infection involving fever of 38°C or more, cough with radiologic pulmonary changes presentation should alert the physician to the possibility of MERS-CoV infection.[55]

MERS-CoV vaccines

No vaccines are yet available which can protect against MERS-CoV infection. There are several groups working on developing a vaccine using a variety of platforms and some have shown efficacy in animal models.[56]

CONCLUSIONS

MERS-CoV remains an important public health risk and possible consequences of further international spread could be serious in view of the patterns of nosocomial transmission within healthcare facilities. With 10 million pilgrims visiting Saudi Arabia each year from 182 countries to perform the Hajj and Umrah pilgrimages,[57] watchful surveillance by public health systems, and a high degree of clinical awareness of the possibility of MERS-CoV infection is essential.[58-60] Nosocomial transmission is often due to a delayed diagnosis of MERS-CoV infection in a patient shedding MERS-CoV in a crowded healthcare setting such as an inpatient ward, emergency department or renal dialysis unit. Early recognition of cases, improved compliance with internationally recommended infection control protocols and rapid implementation of infection control measures are required to prevent health care facility-associated outbreaks of MERS-CoV. Spread to countries with weak health systems and laboratory facilities unable to rapidly identify

an unexpected virus may result in hospital outbreaks or even an epidemic in the 182 countries from which Ramadan, Hajj and Umrah pilgrims originate.

AUTHOR DECLARATIONS

All authors have an academic interest in coronaviruses. We declare no conflicts of interest

AUTHOR ROLES

All authors contributed equally to writing this manuscript

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LEGENDS TO FIGURES AND TABLE

LEGEND TO FIGURE

Figure 1 (World Map): Geographic distribution of MERS reported to WHO (2012-2018)

LEGENDS TO TABLES

Table 1: Clinical and laboratory features of patient with MERS (compiled from xyz)

Table 2: Risk factors for nosocomial MERS-CoV outbreaks

Table 3: Potential treatments for Middle East respiratory syndrome Coronavirus (MERS-CoV) infection (adopted from refs)

Figure 1

Geographic distribution of MERS reported to WHO (2012-2018) (courtesy of WHO-EMRO)

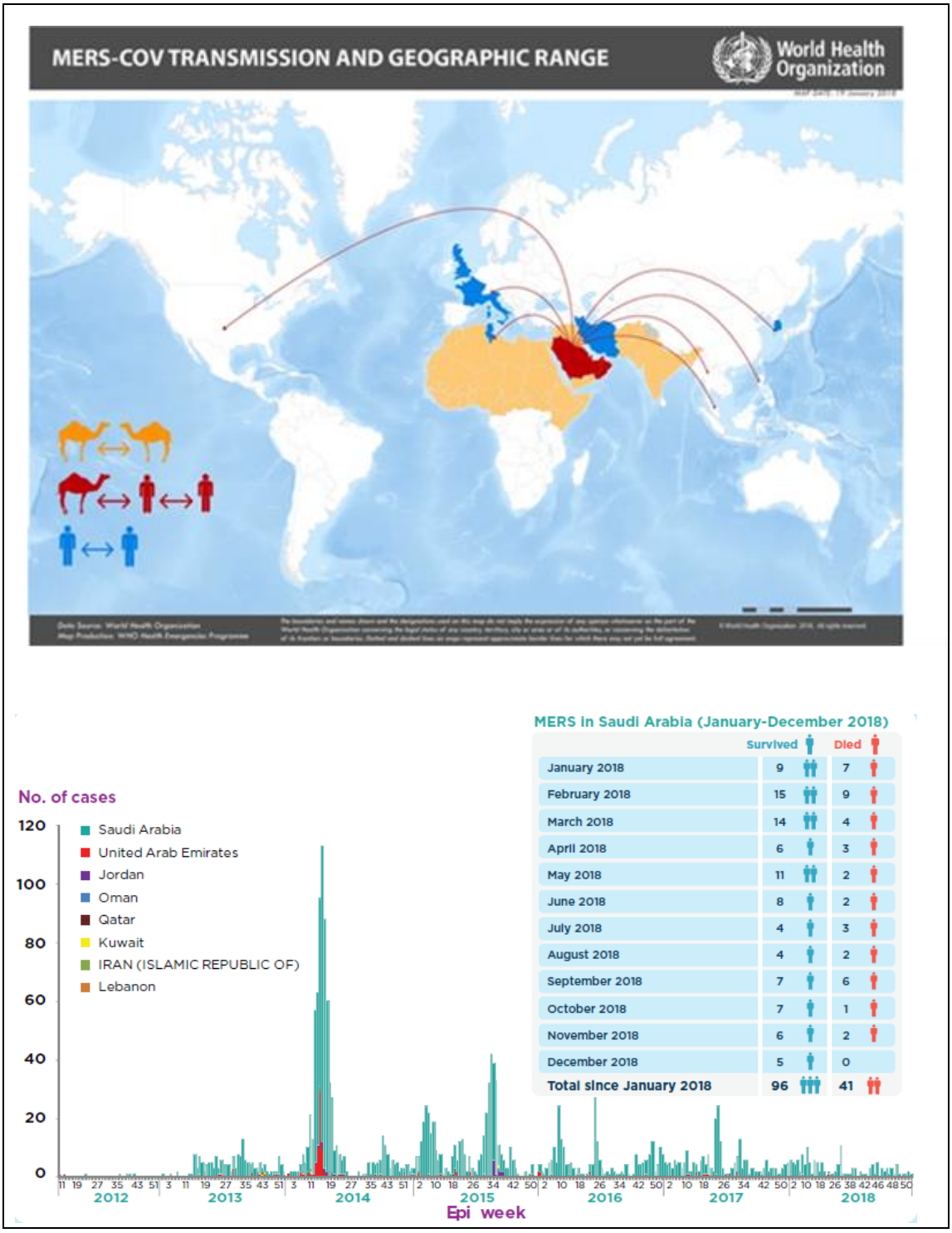

Table 1

Clinical and laboratory features of patient with MERS (compiled from references [1,2,3,7])

Clinical / Laboratory feature(s)	
Date of first MERS case (place) (retrospective analyses)	April 2012 (Zarqa, Jordan) June 2012 (Jeddah, KSA)
Incubation period	Mean: 5.2 days (95%CI:1.9-14.7) Range: 2-14 days
Age group	
Adults Children	Adults (98%) Children (2%)
Age (years): **Range, Median**	Range:1-94; Median: 50
Gender (M, F)	M: 64.5%, F: 35.5%
Presenting symptoms	**Estimated proportion of cases**
Fever > 38C	98%
Chills / rigors	87%
Cough -dry -productive	83% 56% 44%
Shortness of breath	72%
Myalgia	32%
Malaise	38%
Nausea	21%
Vomiting	21%
Diarrhoea	26%
Sore throat	14%
Haemoptysis	17%
Headache	11%
Rhinorrhoea	6%
Co-morbidities (eg obesity, diabetes, cardiac disease and lung disease)	76%
Laboratory results	
CXR and CT abnormalities	90-100%
Leukopenia (< 4.0 x 10^9/L)	14%
Lymphopenia (< 1.5 x 10^9/L)	32%
Thrombocytopenia <140 x 10^9 / L)	36%

Elevated LDH	48%
Elevated ALT	11%
Elevated AST	14%
Risk factors associated with poor outcome (severe disease or death)	Any immunocompromised state, comorbid illness, concomitant infections, low albumin, age ≥ 65 years
Mortality	
Case fatality rate (CFR)-overall	35%*
CFR in patients with co-morbidities	60%

Table 2.

Risk factors for nosocomial MERS-CoV outbreaks (References [1,2,3,7,8,47,51])

- Lack of awareness of the possibility of MERS in febrile patients presenting to healthcare facilities
- Overcrowded Emergency Departments where patients with MERS first present
- Exposure of Healthcare workers and other patients to symptomatic MERS patients
- Poor compliance with infection control measures: a). hand hygiene, b). droplet and contact precautions, c). inadequate environmental cleaning.
- Inadequate compliance with appropriate Personal Protective Equipment
- Lack of proper isolation room facilities
- Distance between beds <1metre
- Aerosol-generating procedures on MERS-patients
- Family or friends staying as caregivers in overcrowded healthcare facilities.
- Crowded inpatient wards including non-essential staff and visitors

Table 3.

Potential treatments for MERS (adopted from refs [2,41])

• ***Antivirals***

-ribavirin monotherapy# (±interferon)

-HIV protease inhibitors (lopinavir*, nelfinavir)

Repurposed drugs:

-cyclophilin inhibitors (ciclosporin, alisporivir)

-chloroquine (active *in vitro*)

-mycophenolic acid,

-nitazoxanide.

• ***Interferons****:

-Interferon alfa

-Interferon beta

Neutralizing Antibodies*:

-Convalescent plasma

-Polyclonal human immunoglobulin from transgenic cows

-Equine F(ab')2 antibody fragments

-Camel antibodies

-Anti-S monoclonal antibodies

• ***Recombinant human mannose-binding lectin***

• ***siRNA to key MERS-CoV genes***

*Treatment benefits likely to exceed risks

#Risks likely to exceed benefits