International Journal of Community Medicine and Public Health
Alaenazi M et al. Int J Community Med Public Health. 2018 Feb;5(2):405-410
http://www.ijcmph.com
pISSN 2394-6032 | eISSN 2394-6040

DOI: http://dx.doi.org/10.18203/2394-6040.ijcmph20180042

Review Article

Emerging infectious diseases: MERS-COV, the new *Betacoronavirus* pandemic

Mohammed Alaenazi[1]*, Hmoud Algarni[2], Saeed Alqahtani[2], Raed Aldahmeshi[3], Sabah Almutairi[4], Alaa Alaskar[1]

Department of Dentistry, [1]Ar'ar dental Center, Ar'ar, [3]King Saud Medical City, Riyadh, Saudi Arabia
College of Dentistry, [2]Aljouf University, Aljouf, [4]Qassim University, Qassim, Saudi Arabia

Received: 20 December 2017
Accepted: 09 January 2018

***Correspondence:**
Dr. Mohammed Alaenazi,
E-mail: zoor77@hotmail.com

ABSTRACT

Both the recent MERS-CoV and the past SARS-CoV indicate that new pathogens would probably emerge. Because it is not possible to predict when or where a new epidemic would occur, this continues to be a challenging issue for physicians and healthcare organizations. Furthermore, there are prophylactic vaccines or effective treatment for these infections and little is known about the origin and the zoonotic transmission of MERS-CoV which hinders the progress of its spread to humans. MERS-CoV is highly pathogenic, exhibiting high fatality rate than the former human corona virus SARS and can obviously be transmitted through several routes, with higher incidence in compromised healthcare settings. Currently, efforts to manage MERS-CoV spared should be directed towards developing educational programs, targeting the public and more importantly health care providers. For one major concern, this infection has and still could pose potential to spread rapidly across the globe, especially during religious mass gathering originating from a MERS-CoV hot spot (i.e., Hajj). Continued epidemiologic surveillance and vigilance remains crucial to compact this virus, or any future mutation.

Keywords: *Betacoronavirus*, Emerging pandemic, MERS-CoV

INTRODUCTION

London witnessed a horrific cholera outbreak in 1854. Physicians then called it "bad air" and they took an action by supporting the sale of flowers. Not, as one might expect helpful to the 600 or so who died. However, a doctor mapped out the victims and this was the very first epidemiological study. He found a cluster of cases around a water pump, which he then took of the handle, bringing the outbreak to an end.[1]

Since then and long before, mankind was defenceless against these epidemics which in some events wiped-out complete civilizations, and were described, at certain time, by historians as apocalyptic. Not until the introduction of the germ theory, human race was set for extinction. The association of a specific microorganism, as to be the cause of a wide range of infectious diseases, have led to an enormous leap in compacting these diseases, especially with the discovery of vaccines and eventually the development of antimicrobial agents.[2] Since then and after the Second World War, with the wide spread of antibiotics, containing smallpox, and discovery of a treatment for tuberculosis, confidence had settled in among the general. It was believed that "war against infectious diseases has been won".[3] This assurance came crashing down when a new pandemic - acquired immune deficiency syndrome (AIDS)- begin to emerge in 1981. This emerging infection believed to be surpassing both the 1918 flu pandemic and the Black

Death of the 14th-century, each of which had a death toll of 50 million people, placing infectious diseases back at every health origination agenda.[4]

Besides AIDS, infections such as SARS, West Nile, Ebola and variant of Creutzfeldt-Jacob disease (vCJD) have been classified as new emerging infectious diseases in the past decades. Where "newly emerged infectious diseases" defined as "those whose incidence in humans has increased within the past two decades or threatens to increase in the near future" And are originating from unknown agent to affect humans for the first time. Other diseases such as malaria and tuberculosis, were thought to be contained in the past with vaccines, have now developed and "re-emerged".[5]

These infections have a heavy global burden, mainly when they become epidemics or pandemics. They generally have a high mortality rate and spread across countries very rapidly causing panic and fear. It is estimated that more than 15 million people all over the planet lose their life's directly because of infectious disease, and millions more due to the complications of chronic ones.[14] A case in pointis the first pandemic to emerge in the twenty-first century; severe acute respiratory syndrome (SARS). This infection, caused by a new *Coronavirus*, reported to be having its first outbreak in China, spreading across three continents, infecting more than 8000 and causing 812 deaths within 8 months. What's more, these types of infections pose security and economic challenges were 10-30 billion $ estimated to be lost in Asia because of SARS.[6]

This paper provides an overview of a more recently emerging infections caused by corona virus; Middle East respiratory syndrome coronavirus (MERS-CoV).

THE NEWLY EMERGED *BETACORONAVIRUS*

History intends to repeat itself with emerging infections. Since identifying *Betacoronavirus* (betaCoVs) to be the etiological agent behind the SARS epidemic in 2003, a novel coronavirus has been detected in a Saudi Arabian patient a decade later.[7] Since its discovery in 2012, this novel CoV was renamed MERS-CoV (Middle East respiratory syndrome coronavirus) on the basis of its geographical outbreak spread with virtually all cases originating from, or had a history of travel to, the Middle East.[8]

As of December, 2nd 2016, this emerging infection managed to spread across countries in the Middle East, North Africa, Europe, the United States of America, and Asia. Resulting in 1888 case which were confirmed by laboratory investigations, 80% (1504 cases) were reported by Saudi authorities alone, causing a total of 670 individuals to lose their life.[9]

VIROLOGY OF MERS-CORONAVIRUS AND ITS ORIGIN

Middle East respiratory syndrome coronavirus represents with a large single-stranded, positive-sense, RNA genome. The coronavirus is divided into four genera of which both SARS and MERS coronaviruses belong to the genus β *Betacoronaviruses* (betaCoVs), were they are further sub grouped into lineages B and C, respectively. Upon infection, MERS-CoV binds to Dipeptidyl peptidase 4 (DPP4) receptor, found on non- ciliated human bronchial epithelial cells, as it also binds to nonhuman primate or other animals having the same DPP4 receptor.[10]

MERS-CoV is zoonotic pathogen originating from an animal, which is believed to be passed from a natural host, most likely bats, to an intermediate animal host before infecting humans.[11]

Bats as an origin for MERS-CoV

Since identifying MERS-CoV, bats were suspected to be the origin of this pathogen as they are known to be the host for multiple corona viruses.[12] On the account of phylogenetic resemblance of MERS-CoV to both bat CoV-HKU4 and -HKU5, initial investigations were driven towards bats as the plausible source.[13] To support this theory, several Virologic studies were carried out to show some of the coronavirus RNA sequences having a close resemblance to MERS-CoV sequence. A survey of bats faecal samples, around were the index Saudi patient lived, were tested by PCR. In which, only a fragment of a single 190-nucleotide MERS-CoV RNA sequence was detected to be a 100% match to the clone obtained from the same patient, suggesting that Egyptian tomb bat might be the source of this virus. A more recent report of a novel beta-coronavirus obtained from bats in South Africa, implies that MERS coronavirus predecessors may perhaps exist in the Old-World bats.[13] However, all the evidence advocating that bats play a role in the transmutation of MERS-CoV are lacking and yet to be established.

Camels as an intermediate host to MERS-CoV

Since its unusual to have human contact with bats, and the fact that MERS-CoV cases had no history of such contact, several domestic animals were investigated as they might be a direct source of MERS-CoV transmission.[12] A serological study provided a conclusive evidence connecting camels (one-humped dromedaries) to MERS-CoV to which a specific antibody to this virus was found only among these creatures. Additionally, these neutralizing antibodies were found across the Middle East and Africa,[14] as they were also detected in archived camel secretion samples from Saudi Arabia and the UAE dating back to the 1990s.[15] These discoveries, indicate that MERS-CoV was previously spread among camels long before it was recognized as a human

infection, and probably circulating in countries were MERS-CoV cases haven't been identified yet. Furthermore, several MERS-CoV cases were directly linked to camels, on the basis of highly identical genome sequences, recovered from human cases who were in close contact with the animal.[16] These results indicate a strong evidence supporting a zoonotic transmission of MERS-CoV to humans via camels. However, these results remained controversial because many reported cases had no contact with camels.[17] Nevertheless, a sero-epidemiological survey on a representative sample of Saudi population found that; individuals who were exposed to camels, on a regular basis, have significantly higher numbers of MERS-CoV antibodies than the rest. This study, predict that those individuals (young men) were infected with MERS-CoV, sometime during their life but didn't develop symptoms, and might be responsible for spreading the virus among people without previous contact.[18]

EPIDEMIOLOGY AND MODE OF MERS-CoV TRANSMISSION

In June 2012, a 60-year-old male from Saudi Arabia was hospitalized with pneumonia, progressing to renal and respiratory failure, leading to death. At that time MERS-CoV was isolated from the patient sputum, and was reported September of the same year.[19] Shortly after, another report of a patient in Qatar, who was returning from Saudi Arabia, describing the same symptoms and almost exact strain of the virus.[20] In Jordan, after the announcement of the first reported MERS case, health care personnel of an intensive care unit (ICU) were retested, fallowing an outbreak of acute respiratory illnesses in April 2012, revealing two cases to be positive for MERS.[21] Since that time, majority of the cases took place in the middle east, specifically Saudi Arabia with serval reports from almost all around the world.

MAJOR OUTBREAKS AND CLUSTERS

One of the noteworthy, was in Al- Ahsa, Saudi Arabia, April 2013. A cluster of 43 MERS-CoV cases were directly linked to the same hospital indicating a human to human transmission. Two healthcare personnel were confirmed cases and three family members were identified through contact tracing survey.[22] This outbreak was contained after implementing simple infection control measures, as a later genotyping report suggest that several introductions of the virus had occurred. Another significant healthcare-associated outbreak of MERS-CoV was in Jeddah, Saudi Arabia between February and April 2014, were 14 hospitals held a total of 128 MERS-CoV cases, of which 60% were healthcare-associated infections involving 39 healthcare personnel.[23]

Apart from MERS-CoV outbreaks in the Middle East, a cluster reported in the UK February 2013. A UK resident, returning from Saudi Arabia developed fever and severe respiratory illness and was tasted later to be positive for MERS-CoV. After infecting tow family members, he died in March the same year. In France, May 2013, a patient was reported to be infected with MERS-CoV after his recent return from Dubai UAE. Before dying, the virus managed to infect a second patient sharing the same room as him, indicating a human to human transmission.[19] The largest MERS-CoV outbreak outside the Middle East occurred in South Korea in 2015, resulting in a total number of 186 cases with 36 deaths.[24] The index case, male late sixty, was returning from Bahrain after visiting multiple countries (Saudi Arabia, Qatar, and UAE). The patient developed symptoms to which he attended various hospitals, resulting in an outbreak affecting five health care facilities escalating to involve 67 more by June 19, 2015.[25]

CAMEL TO HUMAN TRANSMISSION

While camels were identified as a source of infection in some cases abovementioned, the mode of transmission is yet to be confirmed. Droplet transmission form a MERS-CoV infected camels, argued to be the most likely route of a direct transmission. This assumption is supported by multiple reports indicating that MERS-CoV have been detected more frequently in nasal secretions of infected camels.[26] Other indirect routes, that might implicate this kind of transmission have been reported through consumption of unpasteurized camel milk or raw meat contaminated with MERS-CoV. As a result, the World Health Organization (WHO) issued a statement advising to avoid eating meat, that is not thoroughly cooked, or consuming raw camel milk or urine.[27]

HUMAN TO HUMAN TRANSMISSION

Given that majority of MERS confirmed secondary cases had no contact with camels, transmission of the virus via this animal have been doubted. Thus, the possibility of a person to person transmission was and still is more likely to happen, or even through another intermediate host. This can be observed throughout the major outbreaks abovementioned, taking place in healthcare settings over different geographical regions. A worth mentioning example, is the MERS-CoV outbreak of South Korea, when a single patient managed to infect more than 70 other individuals while being cared for in an emergency room for three days, representing a clear role of a "superspreader".[28]

Spread of the virus highly presumed to be thru droplet and close contact of an infected MERS-CoV individual. To witch, the US Center for Disease Control and Prevention (CDC) urged the use appropriate personal protective equipment (PPE) to prevent the transmission among both patients and healthcare providers.79Other potential ways of MERS-CoV spread have been suggested through air borne transmission and/or fomite transmission. This is proven by the fact that the virus is able to be sustained for a long period of time, potentially

contaminating an occupied room by a symptomatic MERS case.[29]

However, the fact is MERS-CoV transmission reported to be sporadic, limited to no more than one other individual, requiring long and close contact of a symptomatic MERS-CoV Case. Moreover, the virus has not been self-sustaining, occurring in clusters and more often healthcare settings.[30]

CLINICAL PRESENTATION AND DIAGNOSIS

The severity and outcome of MERS infection appeared to be heterogenetic, as the majority of the MERS-CoV cases are elderly males with median age of 56 years.[31] Besides age, underlying medical conditions (comorbidities)and immune-compromised patients, were apparently relative to the high severity of this infections. While respiratory symptoms have been reported in almost all the cases, some showed gastrointestinal symptoms, and more than half developed acute renal injury. This high rate of comorbidities need to be revised carefully, since diabetes is a common chronic disease in Saudi Arabia, with one of the outbreaks taking place in a haemodialysis unit.[32] Another possibility explaining the common reports of acute renal failure in MERS patients is the high presence of DPP4 in the renal cells to which MERS-CoV binds, causing a direct injury to the kidneys.[33] Mild and asymptomatic infections have been reported among healthcare personnel, patients contacts, and less frequently in children.[34]

SIGNS AND SYMPTOMS OF MERS-CoV

Clinical features of MERS-CoV are wide, saying that the infection could present without symptoms to mild respiratory symptoms to severe respiratory distress with or without multi-organ failure resulting in death. Early symptoms are mild were patients present with an influenza-like illness such as, fever, dry cough, sore throat, and myalgia, followed by rapid progression to pneumonia within several days. Furthermore, gastrointestinal symptoms (loss of appetite, nausea, abdominal pain, diarrhoea), disseminated intravascular coagulopathy, pericarditis and chest pain has been reported. It is noteworthy to mention that immune-compromised patients, believed to stand at a high risk of contracting this virus, as there is no prognostic sign to differentiate between MERS-CoV and a community-acquired pneumonia in hospital sittings.[35]

DEFINITION OF MERS-CoV CASES AND LABORATORY DIAGNOSTICS

MERS-CoV infection cases has been classified in to confirmed, probable, and suspected cases by the WHO, CDC, and the Ministry of Health of Saudi Arabia. To which, a probable MERS-CoV case is defined as; any patient presenting with an acute respiratory distress syndrome (ARDS) who had a direct contact with a confirmed MERS-CoV case and laboratory confirmation wasn't available or inconclusive. Where a MERS-CoV confirmed laboratory case, is considered a definite MERS patient irrespective of clinical signs and symptoms. A Suspected case, anyone who develop fever and pneumonia or ARDS and have a travel history to, or came in contact with another traveller (devolving the same symptoms), from countries in or near the Arabian Peninsula within two weeks prior to symptoms onset. This is based on the incubation period of the virus, which could range between 2-14 days.

Real-time reverse transcriptase polymerase chain reaction (qRT-PCR) assay has been used and set as a standard diagnostic tool to confirm MERS-CoV infection. The recommendation, is to obtain multiple samples from patient serum, upper respiratory tract, and particularly the lower respiratory tract where detection of MERS-CoV have found to be sensitive.[36] Serologic assays have been created to detect MERS coronavirus, while they are useful to diagnose a "probable" case, they need to be taken twice (14 days apart) with a neutralizing assay to confirm MERS-CoV infection.[37]

PREVENTION AND MANAGEMENT OF MERS

While the fact that patterns of MERS transmission haven't change, owning it to multiple introductions from animals to humans, the majority of MERS cases are nosocomial infections. This type of transmission is readily observed over the outbreaks and clusters above-named. Breach of infection control and overcrowding, especially in emergency departments were a common feature in MERS secondary spread.

The most important measure for controlling MERS-CoV infection is containing the transmission through early diagnosis and prompt intra-hospital isolation. The CDC, WHO, Public Health England, and the Saudi Ministry of Health have set recommendation to prevent spread of MERS, which of most importance are:

I) Taking airborne and contact precautions when managing a confirmed MERS case, by mounting PPE such as disposable gowns, gloves, eye protection, and an N-95 respirator. Along with these precautions, treatment procedures generating aerosols (intubation or endotracheal aspiration), should be performed in a negative pressure room allowing at least six air changes per hour. For one thing, this virus was reported to survive on surfaces longer than any other human coronaviruses.[38]

II) Utilizing a hospital-based triage with appropriate ventilation to isolate confirmed or suspected MERS patients, along with health care providers taking immense care through proper hand hygiene, especially upon changing PPE between patients. Furthermore, any individual who is showing signs or suspected of acquiring MERS should have elective procedures postpone and emergency ones preformed in hospital-based clinics under the abovementioned

precautions. These recommendations have been proven to be effective in controlling hospital outbreaks in affected countries.

THERAPEUTIC OPTIONS

Till date, there are no approved proper treatment or vaccine for MERS-CoV. The challenge of devolving a pathogen specific intervention, in a relatively short time, has been a major difficulty. Management of this infection largely depends on diagnostic improvement, organs function preservation, and attention to prevent complications. Nevertheless, existing antiviral agents used on similar viruses before, such as; interferon, ribavirin, and lopinavir were the first approach. While combined therapy of ribavirin and interferon showed some promising results, the clinical outcome reports were inconsistent. Another approach was to screen large number of existing drugs to serve as a candidate antiviral against MERS-CoV. Among those drugs are cyclosporine A, chloroquine, nationwide, mycophenolic acid, immunoglobulins, and SARS-CoV convalescent, which there is no clinical data to support use of these drugs as they are still in vitro stage.[39]

The most promising approach is the development of antibodies specifically targeting MERS coronaviruses, as the high potential therapeutic of these antibodies was observed during the SARS outbreak. Among those, m336, a highly potent neutralizing monoclonal antibody against MERS-CoV, which has the greatest potential to serve as a drug and vaccine. While others, in an effort to develop a vaccine, involves extracting antibodies from a MERS-CoV survivor or seropositive camels.[40] However, these antibodies need time and investment, as they still to be evaluated in animal models.

CONCLUDING REMARKS

The recent epidemic MERS-CoV and the past outbreak of SARS-CoV, clearly demonstrate that new pathogens will emerge. As they are accelerated by globalization there is really no way to know when or where they might occur.

What is more, there are no effective treatments or vaccines against these infections. Additionally, little is known about the zoonotic transmission of MERS-CoV, or even its origin, which hinder the progress of containing its spread to humans. MERS-CoV is highly pathogenic, exhibiting high fatality rate than the former human corona virus SARS. (36 vs. 10%), and can be obviously transmitted through several routes, with higher incidence in compromised healthcare settings.

For now, efforts to manage MERS-CoV spared should be directed towards developing educational programs, targeting the public and more importantly health care providers. For one major concern, this infection has and still could pose potential to spread rapidly across the globe, especially during religious mass gathering originating from a MERS-CoV hot spot (i.e., Hajj). Continued epidemiologic surveillance and vigilance remains crucial to compact this virus, or any future mutation.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Eyler JM. The changing assessments of John Snow's and William Farr's cholera studies. Soz Praventivmed. 2001;46(4):225-32.
2. Mooney G. Spreading germs: diseases, theories, and medical practice in Britain, 1865-1900 by Michael Worboys, book review. Hist Philos Life Sci. 2002;24(2):327-8.
3. Fauci AS. Infectious Diseases: Considerations for the 21st Century. Clin Infect Dis. 2001;32(5):675-85.
4. Johnson NPAS, Mueller J. Updating the accounts: global mortality of the 1918-1920 "Spanish" Influenza Pandemic. Bull Hist Med. 2002;76(1):105-15.
5. Morens DM, Folkers GK, Fauci AS. The challenge of emerging and re-emerging infectious diseases. Nature. 2004;430(6996):242-9.
6. WHO. World Health Statistics. 2007: 2007.
7. Ksiazek TG, Erdman D, Goldsmith CS. A novel coronavirus associated with severe acute respiratory syndrome. N Engl J Med. 2003;348(20):1953-66.
8. Banik GR, Khandaker G, Rashid H. Middle East Respiratory Syndrome Coronavirus "MERS-CoV": Current Knowledge Gaps. Paediatr Respir Rev. 2015;16(3):197-202.
9. Pavli A, Tsiodras S, Maltezou HC. Middle East respiratory syndrome coronavirus (MERS-CoV): Prevention in travelers. Travel Med Infect Dis. 2014;12(6):602-8.
10. Meyer B, García-Bocanegra I, Wernery U, Wernery R, Sieberg A, Müller MA, et al. Serologic assessment of possibility for MERS-CoV infection in equids. Emerg Infect Dis. 2015;21(1):181-2.
11. Al-Tawfiq JA, Memish ZA. Middle East respiratory syndrome coronavirus: Transmission and phylogenetic evolution. Trends Microbiol. 2014;22(10):573-9.
12. AlBarrak AM, Stephens GM, Hewson R, Memish ZA. Recovery from severe novel coronavirus infection. Saudi Med J. 2012;33(12):1265-9.
13. Lelli D, Papetti A, Sabelli C, Rosti E, Moreno A, Boniotti MB. Detection of coronaviruses in bats of various species in Italy. Viruses. 2013;5(11):2679-89.
14. Alagaili AN, Briese T, Mishra N, Kapoor V, Sameroff SS, Burbelo PD, et al. Middle east respiratory syndrome coronavirus infection in dromedary camels in Saudi Arabia. MBio. 2014;5(2):e01002-14.
15. Hemida MG, Perera RA, Al Jassim RA, Kayali G, Siu LY, Wang P, et al. Seroepidemiology of middle east respiratory syndrome (MERS) coronavirus in

Saudi Arabia (1993) and Australia (2014) and characterisation of assay specificity. Euro Surveill. 2014;19(23):20828.
16. Azhar EI, El-Kafrawy SA, Farraj SA, Hassan AM, Al-Saeed MS, Hashem AM, et al. Evidence for Camel-to-Human Transmission of MERS Coronavirus. N Engl J Med. 2014;370(26):2499-505.
17. Han H-J, Yu H, Yu X-J. Evidence for zoonotic origins of Middle East respiratory syndrome coronavirus. J Gen Virol. 2016;97(2):274-80.
18. Hemida MG, Perera RA, Wang P, Alhammadi MA, Siu LY, Li M, et al. Middle east respiratory syndrome (MERS) coronavirus seroprevalence in domestic livestock in Saudi Arabia, 2010 to 2013. Euro Surveill. 2013;18(50):20659.
19. Guery B, Poissy J, El Mansouf L, Séjourné C, Ettahar N, Lemaire X, et al. Clinical features and viral diagnosis of two cases of infection with Middle East Respiratory Syndrome coronavirus: A report of nosocomial transmission. Lancet. 2013;381(9885):2265-72.
20. Lim PL, Lee TH, Rowe EK. Middle east respiratory syndrome coronavirus (MERS CoV): Update 2013. Curr Infect Dis Rep. 2013;15(4):295-8.
21. Hijawi B, Abdallat M, Sayaydeh A. Novel coronavirus infections in Jordan, April 2012: Epidemiological findings from a retrospective investigation. East Mediterr Heal J. 2013;19(1):12-8.
22. Assiri A, McGeer A, Perl TM. Hospital outbreak of Middle East respiratory syndrome coronavirus. N Engl J Med. 2013;369(5):407-16.
23. Oboho IK, Tomczyk SM, Al-Asmari AM. 2014 MERS-CoV Outbreak in Jeddah — A Link to Health Care Facilities. N Engl J Med. 2015;372(9):846-54.
24. Cowling BJ, Park M, Fang VJ, Wu P, Leung GM, Wu JT, et al. Preliminary epidemiological assessment of MERS-CoV outbreak in South Korea, may to june 2015. Euro Surveill. 2015;20(25):1-7.
25. World Health Organization. Middle East respiratory syndrome coronavirus (MERS-CoV): summary and risk assessment of current situation in the Republic of Korea and China. Available at: http://www.who.int/emergencies/mers-cov/mers-cov- republic-of-korea-and-china-risk-assessment-19-june-2015.pdf?ua =1. Accessed on 19 June 2015.
26. Khalafalla AI, Lu X, Al-Mubarak AIA, Dalab AHS, Al-Busadah KAS, Erdman DD, et al. MERS-CoV in upper respiratory tract and lungs of dromedary camels, Saudi Arabia, 2013–2014. Emerg Infect Dis. 2015;21(7):1153-8.
27. Reusken CBEM, Raj VS, Koopmans MP, Haagmans BL. Cross host transmission in the emergence of MERS coronavirus. Curr Opin Virol. 2016;16:55-62.
28. Park HY, Lee EJ, Ryu YW. Epidemiological investigation of MERS-CoV spread in a single hospital in South Korea, may to june 2015. Euro Surveill. 2015;20(25):1-5.
29. van Doremalen N, Bushmaker T, Munster VJ. Stability of Middle East respiratory syndrome coronavirus (MERS-CoV) under different environmental conditions. Euro Surveill. 2013;18(38):1-4.
30. Drosten C, Meyer B, Müller MA. Transmission of MERS-Coronavirus in Household Contacts. N Engl J Med. 2014;371(9):828-35.
31. Al-Tawfiq JA, Omrani AS, Memish ZA. Middle East respiratory syndrome coronavirus: current situation and travel-associated concerns. Front Med. 2016;10(2):111-9.
32. Shalhoub S, Farahat F, Al-Jiffri A. IFN-α2a or IFN-β1a in combination with ribavirin to treat Middle East respiratory syndrome coronavirus pneumonia: A retrospective study. J Antimicrob Chemother. 2015;70(7):2129-32.
33. Lambeir A-M, Durinx C, Scharpé S, De Meester I. Dipeptidyl-Peptidase IV from Bench to Bedside: An Update on Structural Properties, Functions, and Clinical Aspects of the Enzyme DPP IV. Crit Rev Clin Lab Sci. 2003;40(3):209-94.
34. Al-Tawfiq JA. Middle east respiratory syndrome-coronavirus infection: An overview. J Infect Public Health. 2013;6(5):319-22.
35. Arabi YM, Arifi AA, Balkhy HH. Clinical course and outcomes of critically ill patients with middle east respiratory syndrome coronavirus infection. Ann Intern Med. 2014;160(6):389-97.
36. Memish ZA, Al-Tawfiq JA, Makhdoom HQ. Respiratory tract samples, viral load, and genome fraction yield in patients with middle east respiratory syndrome. J Infect Dis. 2014;210(10):1590-1594.
37. Perera RA, Wang P, Gomaa MR. Seroepidemiology for MERS coronavirus using microneutralisation and pseudoparticle virus neutralisation assays reveal a high prevalence of antibody in dromedary camels in Egypt, June 2013. Euro Surveill. 2013;18(36):205.
38. Otter JA, Donskey C, Yezli S, Douthwaite S, Goldenberg SD, Weber DJ et al. Transmission of SARS and MERS coronaviruses and influenza virus in healthcare settings: The possible role of dry surface contamination. J Hosp Infect. 2016;92(3):235-50.
39. de Wilde AH, Raj VS, Oudshoorn D. MERS-coronavirus replication induces severe in vitro cytopathology and is strongly inhibited by cyclosporin A or interferon-α treatment. J Gen Virol. 2013;94(8):1749-60.
40. Corti D, Zhao J, Pedotti M. Prophylactic and postexposure efficacy of a potent human monoclonal antibody against MERS coronavirus. Proc Natl Acad Sci. 2015;112(33):10473-8.

Cite this article as: Alaenazi M, Algarni H, Alqahtani S, Aldahmeshi R, Almutairi S, Alaskar A. Emerging infectious diseases: MERS-COV, the new *Betacoronavirus* pandemic. Int J Community Med Public Health 2018;5:405-10.