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REVIEW ARTICLE
CURRENT SITUATION OF MIDDLE EAST RESPIRATORY SYNDROME (MERS)

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ABSTRACT

The Middle East Respiratory Syndrome (MERS) was first recorded in 2012 in Saudi Arabia, where infected people suffered from rapidly progressive acute respiratory distress after direct contact with infected dromedary camels, which act as reservoirs for this disease. Human cases reached 2617 infected and 947 deaths at the end of 2023. In this review article, different points have been discussed, such as epidemiology and recent diagnostic techniques, the current situation of MERS, especially in Egypt, and risk factors in addition to control and prevention. There have been 54 publications about MERS and Egypt in PubMed platform from 2013 until 2023. The highest numbers (10) were recorded in 2019, 2020, and 2021. To decrease the prevalence of MERS in humans, it is important to reduce the prevalence of the virus in camels. The aim of this article is to shed some light on the negative hazards of this serious disease, not only in humans but also the role of camels in this regard.

Keywords: Dromedary camel, MERS-CoV, Coronavirus, Risk factors

INTRODUCTION

Camels are essential in desert areas of the Middle East. Camels have been created with particular characteristics, especially their immune system. They have antibodies that are smaller than those of other animals, called ‘nanobodies’. They can cross tissues or even cells, which other antibodies cannot. They can also obstruct enzyme binding sites, resulting in camels' potent disease resistance (Food, 2013; Kandeel and Al-Mubarak, 2022). Consequentially, this strong immune system overcomes several infections, and camels become pathogen carriers that affect other mammals, including humans. They are considered the connecting ring of the microbiota between wildlife and humans. From literature about zoonotic pathogens transmitted by camels, they revealed that eight (36.4%) of the 22 works of literature included MERS, 5 (22.7%) brucellosis, 4 (18.2%) plague caused by *Yersinia pestis*, 3 (13.6%) camel pox, 1 (4.5%) hepatitis E, and 1 (4.5%) anthrax. In addition, several other zoonotic diseases have been recorded as transmitted by camels, such as Rift Valley fever, Q fever, toxoplasmosis, TB, and Crimean-Congo hemorrhagic fever. Camel meat, milk, and contacts, either direct or indirect, with camels are the main origin of infection (Khalafalla, 2023).

MERS-CoV was found to be transmitted from camels, which are considered intermediate hosts. In December 2023, the European Centre for Disease Prevention and Control reported two new MERS cases, one in Saudi Arabia and another in the United Arab Emirates, reaching 2,617 cases, of which 947 deaths, with the case fatality as high as 36.19% from the beginning of this disease in April 2012 (ECDC, 2023).

MERS-CoV was first recorded in 2012 in Saudi Arabia in humans in contact with dromedary camels suffering from rapidly progressive acute respiratory distress (Zaki et al., 2012; Groot et al., 2013; Memish et al., 2013). Then MERS-CoV was isolated from dromedary camels, bats, and humans with severe acute pneumonia syndromes. In humans, MERS-CoV causes infectivity that differs from without clinical signs to quickly acute progressive respiratory distress, which can lead to septic distress, multi-organs malfunction, and fatality (Chafekar et al., 2018). Sequencing of the first case was performed, and the virus was called human coronavirus EMC (HCoV-EMC), and the International Committee on Taxonomy of Viruses renamed it the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) (Aleanizy et al., 2017; Khan et al., 2013).

In this review article, MERS was discussed with different points, such as epidemiology and diagnosis, current situation especially in Egypt, and risk factors in addition to control and prevention to decrease the prevalence of MERS in humans.

CURRENT SITUATION

1. Epidemiology and Diagnosis.

1.1. Incidence

Recently, there has been an observed increase in infection seasonally in human MERS cases, particularly during the winter and early spring. Dromedary camels, being seasonal breeders, exhibit mating behavior primarily during the winter months (Davis et al., 2000; Ghonaim et al., 2023). The reproductive season for camels typically occurs between late October and late February. Studies have indicated an association between dromedary MERS-CoV camel infections and the calving season (Hemida et al., 2014; Wernery, 2014). For instance, in one camel herd, MERS-CoV infection was detected in November, with the infection peak occurring in late December, primarily affecting offspring (Hemida et al., 2014). Before the last days of February, the infection had been broken. Also, a study in Dubai discovered that virus spreading was more common in calves and of relatively short duration (Wernery et al., 2015).

Serological surveys indicated that MERS-CoV infection presented in dromedary camels in several areas of Asia, including Saudi Arabia, UAE, Oman, Qatar, and Jordan, as seroprevalence among adult dromedaries has consistently been over 90% (Reusken et al., 2013; Hemida et al., 2014; Nowotny and Kolodziejek, 2014). Similar high seroprevalence rates have been observed in dromedaries from African countries (Perera et al., 2013; Reusken et al., 2013; Corman et al., 2014). Generally, seropositives were greater in adult dromedaries when compared to juveniles. Studies on archived sera indicate that MERS-CoV has been present in camels in the Arabian Peninsula for at least three decades (Alagaili et al., 2014; Hemida et al., 2014; Meyer et al., 2014). Australia is the only region where dromedaries were tested as seronegative for MERS-CoV so far (Hemida et al., 2014). Non-dromedary camels were recorded as seropositive camels (Sikkema et al., 2019). Dromedary camels in 20 countries were MERS-CoV seropositive, and in

13 countries they were viral RNA positive (Sikkema et al., 2019). The results of recent studies reported that MERS-CoV has been present in dromedary camels in Asian and African countries. The greatest detected pooled seropositive was in West Asia (Islam et al., 2023).

1.2. Characteristics of MERS-CoV

MERS-CoV associates with beta-coronaviruses (β-CoV) lineage C, which are large, enveloped RNA viruses. Phylogenetically, the virus divided into three major clades, temporarily named clade A, B and C (Pallesen et al., 2017; Te et al., 2022).

The genome of coronaviruses is unsegmented single-stranded positive-sense RNA (27–32 kb). It is the greatest genome in RNA viruses. Polyadenylated at the 3' end is a characterization of MERS-CoV genomes. The positive-strand genomic RNA is infectious. The helical nucleocapsid is 9–11 nm in width. The viral structural proteins, which include a 50–60 KDa phosphorylated nucleocapsid (N) protein and a 20–35 KDa membrane glycoprotein (M), serve as matrix proteins that are surrounded by the envelope lipid bilayer with a diameter of 120–160 nm. There are 20-nm-long club-shaped protrusions (spike protein) that are presented on the external surface, making a solar shape (Brooks et al., 2013).

1.3. Transmission

Direct contact between animals is the most common means of viral transmission. Despite the first emerging MERS disease in 2012, the pathogen linked to dromedary camels was only reported in 2014 (Raj et al., 2014a). The main hosts of the ancestor MERS-CoV are bats, but they are thought to be involved in coexistent MERS-CoV epidemiology. Dromedary camels are believed to be intermediate reservoirs (Memish et al., 2013; Mohd et al., 2016). Bats have been implicated as the natural reservoirs of several mammalian coronaviruses (Lau et al., 2013).

Both the SARS-CoV and the HCoV-229E are believed to have originated from precursor viruses found in bats (Pfefferle et al., 2009; Drexler et al., 2014). In Saudi Arabia, there has been a report suggesting the detection of a short fragment of viral RNA in a *Taphozous perforates* bat identical to MERS-CoV that was isolated from camels and humans (Memish et al., 2013). However, this finding has not been confirmed. A coronavirus closely related to MERS-CoV but not identical was identified in *Neoromicia capensis* bats (Corman et al., 2014).

On the other hand, longitudinal serological examinations through 100 days of separated camel groups with previous individuals' histories of MERS-CoV infection proved the virus continued to pass in the herd even with no other animal contact (Abdelazim et al., 2023). Also, the infection of MERS-CoV in a closed camel herd with limited interaction with other animals was documented, making the origin of the virus entry unclear. Transmission through feed and truck is another potential mechanical route to consider. Human to human transmission is limited, and can occur by direct contact (Hemida et al., 2014).

1.4. Pathogenesis

In camels, MERS-CoV can produce no or mild symptoms, includes nasal discharge, lacrimation and mild fever in young animal. In human, the MERS CoV infects bodies occasionally, who are considered to be the terminal host (Dudas et al., 2018).

About receptors and attachment factors, MERS-CoV consumes a dipeptidyl peptidase 4 (DPP4) β-propellers as its receptor, which differs from SARS-CoV. The receptor binding domain (RBD) of MERS-CoV contains an accessory subdomain that functions as the receptor-binding motif (RBM). Despite the fact that the RBMs of MERS CoV are distinct from those of SARS CoV, the RBD core structures are remarkably analogous between them. In addition, domain A of the MERS-CoV spike protein could bind specifically to glycotopes of α2,3-sialic acids to help the virus efficiently bind to target cells (Wang et al., 2013; Li et al., 2017).

MERS-CoV reacts with the host's innate immune system to identify the virus by using pattern recognition receptors to identify pathogen-associated molecular configurations. On the other hand, the adaptive immune response plays a considerable role by becoming a stable host defense mechanism against pathogens in addition to reducing an autoimmune reflex response. In addition, other organs can be damaged by MERS-CoV infection. An excessive immune response may cause immunopathological damage (known as a cytokine storm) because the virus may motivate host immune responses. Cytokine storms may stimulate the infiltration of unneutralizing antiviral proteins, consequently enabling viral introduction into host cells, leading to an increased viral infection (Abdelrahman et al., 2020).

1.5. Clinical symptoms

Remarkably, MERS-CoV infects camels without any signs or sporadically mild lesions, especially in young. Clinical symptoms in human include high temperature; sore throat with cough; dumpiness of breathing; muscle weakness (myalgia); chest aching, sickness, and gastrointestinal signs, including watery diarrhea, nausea, and abdomen ache. A significant percentage of severely sick patients required machine-driven aeration. Remarkably, many of the stated secondary cases exhibited asymptomatic or slight respiratory signs (Assiri et al., 2013 Al-Tawfiq et al., 2014). Between human coronaviruses, MERS-CoV has the greatest rate of case fatality in humans (>35%). The outside Middle East region cases were believed that the infection was from the Middle East (Islam et al., 2019; WHO, 2022).

1.6. Diagnosis

It is important to follow the WHO guidelines for testing MERS-CoV (WHO, 2018). Testing should be conducted in biosafety laboratories that are appropriately equipped, and the staff performing the tests should be qualified in the appropriate safety procedures. Guidelines of the WHO on lab biosafety must be adhered to in all conditions (WHO, 2013). In the lab examination of MERS-CoV, clinical sample type and quality are crucial. It is recommended to analyze upper respiratory tract samples in addition to samples of the lower respiratory tract if possible (Memish et al., 2014; WHO, 2018). MERS-CoV RNA has been reported in other body fluids. However, the viral loads in these specimens are typically much lower than those in the respiratory tract. Therefore, respiratory specimens remain the primary focus for MERS-CoV diagnosis and surveillance (Bermingham et al., 2012; Alfaraj et al., 2019). The virus can be propagated through rhesus macaque kidney cells and African green monkeys (Banik et al., 2015; Durai et al., 2015). The cultivation time continues from 2 to 14 days (de Wit et al., 2013; Shirato et al., 2013).

One specific fast with high specificity assay for MERS-CoV detection is the reverse transcription loop-mediated isothermal amplification technique combined with a vertical flow visualization strip (RT-LAMP-VF). This assay targets the nucleocapsid gene of MERS-CoV and can provide detection within 35 minutes (Huang et al., 2018).

For routine detection of MERS-CoV, three real-time RT-PCR (rRT-qPCR) assays have been improved. These examine the upstream of the E gene (upE), as well as the open reading frames (ORFs) 1b and 1a. The upE assay is suggested for screening purposes, while the ORF1b assay is considered less sensitive than the ORF1a assay (WHO, 2018).

There are ongoing efforts to develop new diagnostic tests for MERS-CoV. The 2019 roadmap for MERS-CoV product development provides a comprehensive list of tests (Kelly-Cirino et al., 2019). Some of these tests aim to reduce the turnaround time from swab analysis to results (Frans et al., 2019; Hashem et al., 2019).

In addition to molecular assays, many serological assays are present for MERS-CoV examinations. These include ELISA, recombinant spike immunofluorescent assays, and spike pseudoparticle neutralization and microneutralization assays (Perera et al., 2013; Park et al., 2015; Hashem et al., 2019; Okba et al., 2019).

2. MERS Situation in Egypt

Egypt recently has been free from MERS. Attentions must be paid as Egypt has a characteristic geographical location between African and Asian countries, which reflects camel populations, as it is considered a collection of Arabian camels (from the Arab Peninsula) and African camels. Dromedaries in the Middle East have great seropositive rates of MERS-CoV antibodies. About 90% of the imported camels in Egypt were positive for MERS-CoV. In addition, a highly distinct Egyptian strain is designated clade C3 (Ali et al., 2017; Chu et al., 2014; El- Kafrawy et al., 2019) (Fig. (1)).

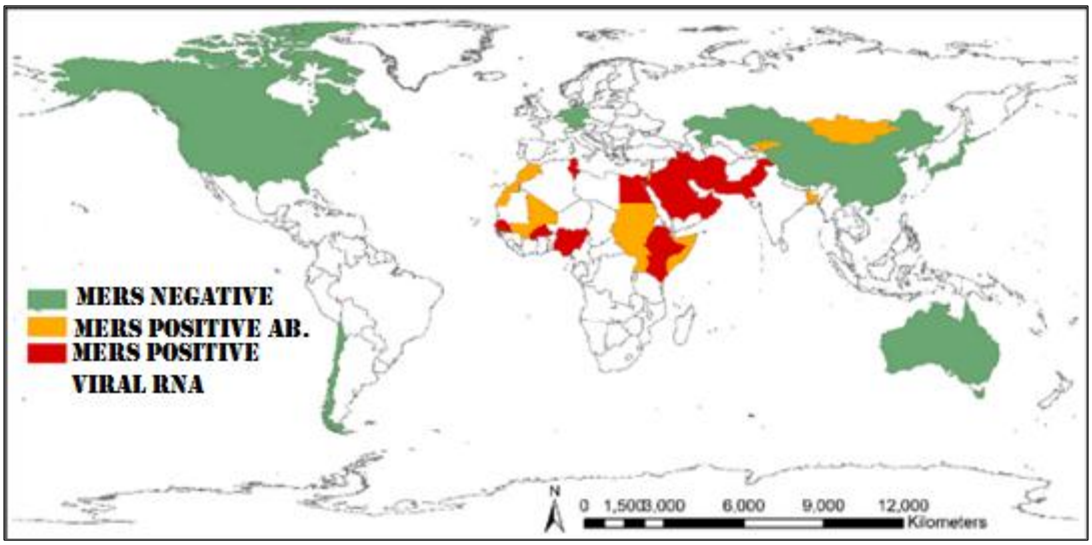

Fig. (1). World spreading of MERS-CoV in camels (Islam et al., 2023).

From the PubMed platform, there have been 54 publications about MERS in Egypt from 2013 untill 2023. The highest numbers of publications (10) were recorded in 2019, 2020, and 2021(Table (1) and Fig. (2)).

Table (1). Numbers of publications about MERS in Egypt distributed yearly from 2013 till now (pubmed, 2023).

Year	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Count	1	3	5	6	8	4	10	10	10	3	1

The first isolation of MERS CoV from a nasal swab of a dromedary camel in Egypt was recorded by Chu et al. (2013) who reported that the virus was genetically identical to that of human MERS CoV.

In 2016, Kandeil et al., (2016) isolated new MERS CoV from camels in Egypt. They found the new virus was identical to that isolated in 2014. Till now, there is no, MERS CoV isolated in Egypt.

In other domestic animals, Sheep in Egypt were reported as seropositive of low antibody titers without isolation of the viral RNA. It is clear that, the capability of MERS CoV to infect other animals with viral modifications may occur (Ali et al., 2017).

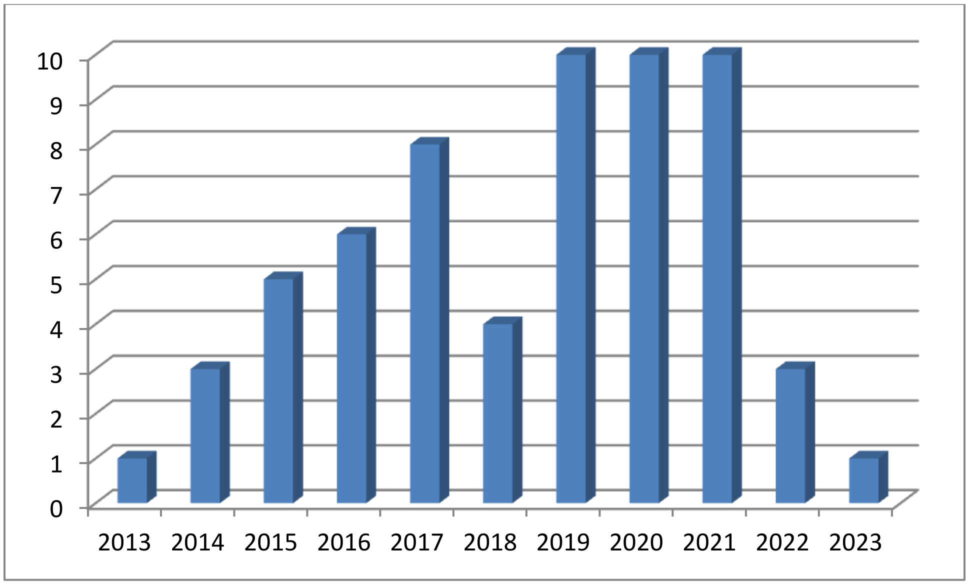

Fig. (2). MERS in Egypt Publications on the Pubmed platform from 2013 till now (PubMed, 2023)

3. MERS Risk Factors

Dromedary camels are included in the culture of people in Middle Eastern countries, where meat and camel milk are consumed (Ali et al., 2017). Dromedary camels and natural hosts are considered the main risk factors. Direct contact between animals is the most common means of viral transmission. Virus spreading was more common in calves and of relatively short duration particularly during the winter and early spring (Wernery et al., 2015).

The highest cases numbers is in Saudi Arabia, which has recorded ~80% of world human cases, in addition to healthcare workers and nurses, who were reported as more than 50% of these cases (Memish et al., 2013). Consequently, regular examination of MERS CoV in camels is very essential. Despite transmission rates between humans being lower in MERS-CoV than in SARS-CoV, it has a higher case fatality (34.4%) than SARS-CoV (9.6%) (Zumla et al., 2015).

MERS-CoV can survive on inanimate surfaces for a long period of time. The factors may be the types of surfaces, the titer of the virus, variations of MERS strains, deposition mode, humidity, temperature, and determination methods (Duan et al., 2003; van Doremalen et al., 2013). Many reports have illustrated that MERS-CoV can be present on dry surfaces for a period of time to induce infection. MERS-CoV surface viability was reported on steel and plastic after 48 h at 20°C with 40% relative humidity and about 24 h at 30°C with 30% relative humidity. But within 8 hours, viability decreased at about 30°C with 80% relative humidity The half-life of MERS-CoV was detected to be between ~0.5 and 1 h (van Doremalen et al., 2013).

4. Control and Prevention

The WHO has been working with healthcare workers and scientists in collaboration with the Food and Agriculture Organization of the United Nations (FAO), the World Organization for Animal Health (WOAH), and governments in affected countries to gather information for management tactics (Suwantarat and Apisarnthanarak, 2015). To decrease the prevalence of MERS in humans, it is important to reduce the prevalence of the virus in camels; especially there is no approved camel vaccination till now. Control imported camels' movements, regular herd screening and protective measurements must be taken. Restrictions on consuming raw camel milk or uncooked camel meat should be followed. No effective antiviral medication has been reported for MERS in vivo (Raj et al., 2014b). Kandeel et al. (2021) developed peptides structures as potent anti MERS CoV agents that inhibited cell- virus fusion in vitro. Recently natural antiviral nanoparticles were reported as moderately active in vitro against MERS CoV as Ginkgo biloba leaves extract and silver nanoparticles (El Shazly et al., 2023).

CONCLUSIONS

Research, training, surveillance, laboratory capability, education, and communication are key elements to control and prevent the spreading of hazards. Updating surveys of MERS-CoV between resident and imported camels especially in Egypt is mandatory. Scientific cooperation between nations is very important to control and prevent MERS.

REFERENCES

Abdelazim, M., Abdelkader, R., Ali, A., Shahein, M. A., Tadesse, Z., Saad, A., Mansour, A., Ali, S. F., Atea, M., Gardner, E., VonDobschuetz, S., Morzaria, S., Makonnen, Y., Lubroth, J., Sumption, K., ElMasry, I., Zakaria, T., Eid, S., Hatab, E. A., Hagag, N. M., … Guitian, J. 2023. A longitudinal study of Middle East respiratory syndrome coronavirus (MERS-CoV) in dromedary camels. *BMC veterinary research*, *19*(228) 1-11. https://doi.org/10.1186/s12917-023-03769-z

Abdelrahman, Zeinab, Li Mengyuan, Wang Xiaosheng, 2020. Comparative Review of SARS-CoV-2, SARS-CoV, MERS-CoV, and Influenza A Respiratory Viruses. Frontiers in Immunology, 11, 1-14.

Abdul Moneim, A. S. 2014. Middle East Respiratory Syndrome coronavirus (MERS COV): Evidence and speculations. Arch Virol., 159, 1575-1584.

Alagaili, A. N., Briese, T., Mishra, N., Kapoor, V., Sameroff, S. C., Burbelo, P. D., de Wit, E., Munster, V. J., Hensley, L. E., Zalmout, I. S., Kapoor, A., Epstein, J. H., Karesh, W. B., Daszak, P., Mohammed, O. B., & Lipkin, W. I. 2014. Middle East respiratory syndrome coronavirus infection in dromedary camels in Saudi Arabia. *mBio*, *5*(2), e00884-14. https://doi.org/10.1128/mBio.00884-14

Aleanizy, F.S., Mohmed, N., Alqahtani, F.Y., El Hadi, Mohamed R. A. 2017.The outbreak of Middle East respiratory syndrome coronavirus in Saudi Arabia: a retrospective study. *BMC Infect Dis*., **17** (23), 1-7. https://doi.org/10.1186/s12879-016-2137-3

Alfaraj, S. H., Al-Tawfiq, J. A., Memish, Z. A. 2019. Middle East Respiratory Syndrome coronavirus intermittent positive cases: implications for infection control. Am. J. Infect Control, 47, 290–93.

Ali, M., El-Shesheny, R., Kandeil, A., et al. 2017. Cross-sectional surveillance of Middle East respiratory syndrome coronavirus (MERS-CoV) in dromedary camels and other mammals in Egypt, August 2015 to January 2016. Euro Surveill., 22(11).

Al-Tawfiq, J. A., Hinedi, K, Ghandour, J., et al. 2014. Middle East respiratory syndrome coronavirus: a case-control study of hospitalized patients. Clin Infect Dis., 59,160-165.

Assiri A, Al-Tawfiq JA, Al-Rabeeah AA, et al. Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease from Saudi Arabia: a descriptive study. Lancet Infect Dis 2013;13,752–761.

Banik, G. R., Khandaker, H., Rashid, 2015. Middle East respiratory syndrome coronavirus “MERS-CoV”: current knowledge gaps. Paediatr Respir Rev. 16, 197-202.

Bermingham, A., Chand, M. A., Brown CS, et al. 2012. Severe respiratory illness caused by a novel coronavirus, in a patient transferred to the United Kingdom from the Middle East. Euro Surveill., 17, 20290.

Brooks, G.F., Jawetz, E., Melnick, J.L., Adelberg, E.A., Carroll, K. C., Butel, Janet S, Morse, S.A., Mietzner, T.A., 2013. Coronaviruses In: Jawetz, Melnick & Adelberg's Medical Microbiology (26th Ed.). New York, McGraw-Hill., pp. 165-173.

CDC. CDC laboratory testing for Middle East respiratory syndrome coronavirus (MERS-CoV). https://www.cdc.gov/coronavirus/mers/ lab/lab-testing.html (accessed Feb 21, 2020).

Chafekar, A., Chafekar, B.C. Fielding 2018. MERS-CoV: understanding the latest human coronavirus threat, Viruses 10. https://doi.org/10.3390/v10020093.

Chu, D. K. W., Poon, L. L. M., Gomaa, M. M., Shehata, M. M., Perera, RAPM, Abu Zeid, D., et al. 2014. MERS coronaviruses in dromedary camels, Egypt. Emerg Infect Dis., 20,1049–53. https://doi.org/10.3201/eid2006.140299

Corman, V. M., J. Jores, B. Meyer, M. Younan, A. Liljander, M. Y. Said, I. Gluecks, E. Lattwein, B. J. Bosch, J. F. Drexler, S. Bornstein, C. Drosten, M. A. Muller 2014. Antibodies against MERS coronavirus in dromedary camels, Kenya, 1992–2013. Emerg. Infect. Dis. 20, 1319–1322.

Davis, E., B. R. Rush, J. Cox, B. DeBey, S. Kapil, 2000. Neonatal enterocolitis associated with coronavirus infection in a foal: a case report. J. Vet. Diagn. Invest. 12, 153–156.

de Wit E, Rasmussen, AL Falzarano, D., et al., 2013. Middle East respiratory syndrome coronavirus (MERS-COV) causes transient lower respiratory tract infection in rhesus macaques. Proc Natl Acad Sci USA. 110,16598-16603.

Drexler, J. F., V. M. Corman, C. Drosten, 2014. Ecology, evolution, and classification of bat coronaviruses in the aftermath of SARS. Antiviral Res. 101, 45–56.

Duan, S. M., Zhao, X. S., Wen, R. F., Huang, J. J., Pi, GH, Zhang, S. X., et al. 2003. Stability of SARS coronavirus in human specimens and environment and its sensitivity to heating and UV irradiation. Biomed Environ Sci. 16, 246–55.

Dudas, G. Dudas, L.M. Carvalho, A. Rambaut, T. Bedford, 2018. MERS-CoV spillover at the camel-human interface. eLife. 7. https://doi.org/10.7554/eLife.31257 e31257.

Durai, P. V., Batool, M., Shah, M., Choi, S., 2015. Experimental & molecular medicine, Middle East respiratory syndrome coronavirus: transmission, virology and therapeutic targeting to aid in outbreak control. Exp Mol Med. 47,e181.

ECDC, 2023. European Centre for Disease Prevention and Control. https://www.ecdc.europa.eu/en

El-Kafrawy, S. A., Corman, V. M., Tolah, A. M., et al. 2019. Enzootic patterns of Middle East respiratory syndrome coronavirus in imported African and local Arabian dromedary camels: a prospective genomic study. Lancet Planet Health. 3(12), e521–e528.

Elshazly, E.H.; Nasr, A.; Elnosary, M.E.; Gouda, G.A.; Mohamed, H.; Song, Y. 2023.Identifying the Anti-MERS-CoV and Anti-HcoV-229E Potential Drugs from the Ginkgo biloba Leaves Extract and Its Eco-Friendly Synthesis of Silver Nanoparticles. Molecules. 28, 1375. https://doi.org/10.3390/ molecules28031375

Frans, G., Beuselinck, K., Peeters, B., et al. 2019. Migrating a lab-developed MERS-CoV real-time PCR to 3 "sample to result" systems: experiences on optimization and validation. Diagn Microbiol Infect Dis. 94, 349–54.

Food, J. M. 2013. Immunity and charismatic camel. Lab Anim., 42, 159 https://doi.org/10.1038/laban.290

Ghonaim, Ahmed, H., Mai G. Hopo, Noha H. Ghonaim, Yunbo Jiang, Qigai He, and Wentao Li., 2023. The Epidemiology of Circulating Rotavirus Associated with Diarrhea in Egyptian Kids and Calves: A Review. Zoonoses. 3(1). https://doi: 10.15212/zoonoses-2023-0004.

Groot, R.J., De Groot, S.C. Baker, R.S. Baric, C.S. Brown, C. Drosten, L. Enjuanes, R.A. M. Fouchier, M. Galiano, A.E. Gorbalenya, Z.A. Memish, et al. 2013. Middle East respiratory syndrome coronavirus (MERS-CoV): announcement of the coronavirus study group, J. Virol. 87, 7790–7792, https://doi.org/10.1128/JVI.01244- 13.

Hashem, A. M., Al-Amri, S. S., Al-Subhi, T. L., et al. 2019. Development and validation of different indirect ELISAS for MERS-CoV serological testing. J Immunol Methods. 466, 41–46.

Hemida, M. G., D. K. Chu, L. L. Poon, R. A. Perera, M. A. Alhammadi, H. Y. Ng, L. Y. Siu, Y. Guan, A. Alnaeem, Peiris, M. 2014. MERS coronavirus in dromedary camel herd, Saudi Arabia. Emerg. Infect. Dis. 20, 1231–1234.

Huang, P., Wang, H., Cao, Z., et al. 2018. A rapid and specific assay for the detection of MERS-CoV. Front Microbiol. 9, 1101.

Islam, M.M., Hamida Khanom, Elmoubashar Farag, Zarin Tasnim Mim, Pragalathan Naidoo, Zilungile Lynette Mkhize-Kwitshana, Markos Tibbo, Ariful Islam, Ricardo J. Soares Magalhaes, Mohammad Mahmudul, H. 2023. Global patterns of Middle East respiratory syndrome coronavirus (MERS-CoV) prevalence and seroprevalence in camels: A systematic review and meta-analysis, One Health. 16.

Islam, S. J. Ferdous, M.K. Rahman, S. Akter, M. Hassan, Islam, A. 2019. Reference values for hematological and serum biochemical parameters of dromedary camel (*Camelus dromedarius*) in SubTropical climate of Bangladesh, Adv. Anim. Vet. Sci. 7, 232–237, https://doi.org/10.17582/journal.aavs/2019/7.4.232.237.

Kandeel, M. and Al-Mubarak, A.I.A. 2022. Camel viral diseases: Current diagnostic, therapeutic, and preventive strategies. Front. Vet. Sci. 9:915475. doi: 10.3389/fvets.2022.915475

Kandeel, M., Yamamoto, M., Park, B. K., Al-Taher, A., Watanabe, A., Gohda, J., Kawaguchi, Y., Oh-hashi, K., Kwon, H., Inoue, J. 2021. Discovery of New Potent anti-MERS CoV Fusion Inhibitors. Front. Pharmacol. 12, 685161. doi: 10.3389/fphar.2021.685161

Kandeil, A., Shehata, M. M., El Shesheny, R., Gomaa, M. R., Ali, M. A., & Kayali, G. 2016. Complete Genome Sequence of Middle East Respiratory Syndrome Coronavirus Isolated from a Dromedary Camel in Egypt. Genome announcements, 4(2), e00309-16. https://doi.org/10.1128/genomeA.00309-16

Kelly-Cirino, C, Mazzola, L. T., Chua, A., Oxenford, C. J., Van Kerkhove, M. D. 2019. An updated roadmap for MERS-CoV research and product development: focus on diagnostics. BMJ Glob Health. 4, e001105.

Khalafalla, A. I., 2023. Zoonotic diseases are transmitted from the camels. Frontiers in veterinary science. 10, 1244833. https://doi.org/10.3389/fvets.2023.1244833

Khan G. A. 2013. Novel coronavirus capable of lethal human infections an emerging picture. Virol J. 10,66.

Lau, S. K., K. S. Li, A. K. Tsang, C. S. Lam, S. Ahmed, H. Chen, K. H. Chan, P. C. Woo, Yuen, K. Y. 2013. Genetic characterization of Betacoronavirus lineage C viruses in bats reveals marked sequence divergence in the spike protein of Pipistrellus bat coronavirus HKU5 in Japanese pipistrelle: implications for the origin of the novel Middle East respiratory syndrome coronavirus. J. Virol. 87, 8638–8650.

Li, W., Hulswit, R. J. G., Widjaja, I., Raj, V. S., McBride, R., Peng, W., Widagdo, W., Tortorici, M. A., van Dieren, B., Lang, Y., van Lent, J. W. M., Paulson, J. C., de Haan, C. A. M., de Groot, R. J., van Kuppeveld, F. J. M., Haagmans, B. L., & Bosch, B. J., 2017. Identification of sialic acid-binding function for the Middle East respiratory syndrome coronavirus spike glycoprotein. Proceedings of the National Academy of Sciences of the United States of America. 114(40), E8508–E8517. https://doi.org/10.1073/pnas.1712592114

Memish, Z. A., Al-Tawfiq, J. A., Makhdoom, H. Q., et al. 2014. Respiratory tract samples, viral load, and genome fraction yield in patients with the Middle East respiratory syndrome. J Infect Dis. 210, 1590–1594.

Memish, Z. A., N. Mishra, K. J. Olival, S. F. Fagbo, V. Kapoor, J. H. Epstein, R. Alhakeem, A. Durosinloun, M. Al Asmari, A. Islam, A. Kapoor, T. Briese, P. Daszak, A. A. Al Rabeeah, Lipkin, W. I. 2013, the Middle East respiratory syndrome coronavirus in bats, Saudi Arabia. Emerg Infect Dis. 19(11), 1819-23. https://doi.org/10.3201/eid1911.131172

Meyer , B., Müller, M. A., Corman, V. M., Reusken, C. B., Ritz , D., Godeke, G. J., et al., 2014. Antibodies against MERS coronavirus in dromedary camels, United Arab Emirates, 2003 and 2013. Emerg Infect Dis. 20(4), 552-9. https://doi.org/1 0.3201/eid2004.131746 PMID: 24655412

Mohd, H.A. Mohd, J.A. Al-Tawfiq, Memish, Z. A. 2016. Middle East respiratory syndrome coronavirus (MERS-CoV) origin and animal reservoir, Virol. J. 13, 87. https://doi.org/10.1186/s12985-016-0544-0.

Nowotny, N., and J. Kolodziejek, 2014. Middle East respiratory syndrome coronavirus (MERS-CoV) in dromedary camels, Oman, 2013. Euro. Surveill. 19, 20781.

Okba, N. M. A., Raj, V. S., Widjaja, I., et al., 2019. Sensitive and specific detection of low-level antibody responses in mild Middle East respiratory syndrome coronavirus infections. Emerg Infect Dis. 25, 1868–77

Pallesen, J., N. Wang, K.S. Corbett, D. Wrapp, R.N. Kirchdoerfer, H.L. Turner, C. A. Cottrell, M.M. Becker, L. Wang, W. Shi. et al. 2017. Immunogenicity and structures of a rationally designed perfusion MERS-CoV spike antigen, Proc. Natl. Acad. Sci. U. S. A. 114, E7348–E7357, https://doi.org/10.1073/pnas.1707304114.

Park, S. W., Perera, R. A., Choe, P. G. et al. 2015. Comparison of serological assays in human Middle East respiratory syndrome (MERS)- coronavirus infection. Euro Surveill. 20, 1–5.

Perera, R. A., P. Wang, M. R. Gomaa, R. El-Shesheny, A. Kandeil, O. Bagato, L. Y. Siu, M. M. Shehata, A. S. Kayed, Y. Moatasim, M. Li, L. L. Poon, Y. Guan, R. J. Webby, M. A. Ali, J. S. Peiris, Kayali, G. 2013. Seroepidemiology for MERS coronavirus using microneutralization and pseudoparticle virus neutralization assays reveals a high prevalence of antibodies in dromedary camels in Egypt. Euro. Surveill. 18, Pii=20574.

Pfefferle, S., S. Oppong, J. F. Drexler, F. Gloza-Rausch, A. Ipsen, A. Seebens, M. A. Muller, A. Annan, P. Vallo, Y. Adu-Sarkodie, T. F. Kruppa, and C. Drosten, 2009. Distant relatives of severe acute respiratory syndrome coronavirus and close relatives of human coronavirus 229E in bats, Ghana. Emerg. Infect. Dis. 15, 1377–1384.

Pubmed. 2023. MERS Camel in Egypt. https://pubmed.ncbi.nlm.nih.gov/?term=MERS+Camel+Egypt

Raj, V. S., Farag, E. A., Reusken, C. B., Lamers, M. M., Pas, S. D., Voermans, J., Smits, S. L., Osterhaus, A. D., Al-Mawlawi, N., Al-Romaihi, H. E., AlHajri, M. M., El-Sayed, A. M., Mohran, K. A., Ghobashy, H., Alhajri, F., Al-Thani, M., Al-Marri, S. A., El-Maghraby, M. M., Koopmans, M. P., Haagmans, B. L., 2014a. Isolation of MERS coronavirus from a dromedary camel, Qatar, 2014. Emerging infectious diseases. 20(8), 1339–1342. https://doi.org/10.3201/eid2008.140663

Raj, V. S., Osterhaus, A. D., Fouchier, R. A., Haagmans, B. L. 2014b. MERS: emergence of a novel human coronavirus. Current opinion in virology, 5, 58–62. https://doi.org/10.1016/j.coviro.2014.01.010

Reusken, C. B., M. Ababneh, V. S. Raj, B. Meyer, A. Eljarah, S. Abutarbush, G. J. Godeke, T. M. Bestebroer, I. Zutt, M. A. Muller, B. J. Bosch, P. J. Rottier, A. D. Osterhaus, C. Drosten, B. L. Haagmans, Koopmans M. P. 2013. Middle East Respiratory Syndrome coronavirus (MERS-CoV) serology in major livestock species in an affected region in Jordan, June to September 2013. Euro. Surveill. 18, 20662.

Shirato, K., Kawase, M., Matsuyama, S. 2013. Middle East respiratory syndrome coronavirus infection mediated by the transmembrane serine protease TMPRSS2. J. Virol. 87,12552-12561.

Sikkema, R.S., Sikkema, E., Farag, M., Islam, M., Atta, C., Reusken, M.M., Al-Hajri, M.P., Koopmans, G. 2019. Global status of Middle East respiratory syndrome coronavirus in dromedary camels: a systematic review, Epidemiol. Infect. 147, e84, https://doi.org/10.1017/s095026881800345x.

Suwantarat, N. and Apisarnthanarak, A. 2015. Risks to healthcare workers with emerging diseases: lessons from MERS-CoV, Ebola, SARS, and avian flu. Curr Opin Infect Dis. 28, 349–61. https://doi: 10.1097/QCO.0000000000000183

Te, N., Rodon, J., Pérez, M., Segalés, J., Vergara-Alert, J., Bensaid, A. 2022. Enhanced replication fitness of MERS-CoV clade B over clade A strains in camelids explains the dominance of clade B strains in the Arabian Peninsula. Emerging microbes & infections, 11(1), 260–274. https://doi.org/10.1080/22221751.2021.2019559

van Doremalen, N., Bushmaker, T., Munster, V. J. 2013. Stability of Middle East respiratory syndrome coronavirus (MERS-CoV) under different environmental conditions. Euro Surveill. 18, 20590. https://doi: 10.2807/1560-7917.ES2013.18.38.20590

Wang, N., Shi,X., Jiang, L., Zhang, S., Wang, D., Tong, P., et al. 2013. Structure of MERS-CoV spike receptor-binding domain complexed with human receptor DPP4. Cell Res. 23, 986–93. https://doi: 10.1038/cr.2013.92

Wernery, U. 2014. Zoonoses in the Arabian Peninsula. Saudi Med. J. 35, 1455–1462.

Wernery, U., V. M. Corman, E. Y. Wong, A. K. Tsang, D. Muth, S. K. Lau, K. Khazanehdari, F. Zirkel, M. Ali, P. Nagy, J. Juhasz, R. Wernery, S. Joseph, G. Syriac, S. K. Elizabeth, N. A. Patteril, P. C. Woo, and C. Drosten, 2015. Acute middle East respiratory syndrome coronavirus infection in livestock Dromedaries, Dubai. Emerg. Infect. Dis. 21, 1019–1022.

WHO, 2013. Laboratory BioRisk management for laboratories handling human specimens suspected of confirmed to contain novel coronavirus: interim recommendations 2013. https://www.who.int/csr/disease/coronavirus_infections/Biosafety_ InterimRecommendations_NovelCoronavirus_19Feb13.pdf?ua=1 (accessed Oct 3, 2019).

WHO, 2018. Laboratory testing for Middle East respiratory syndrome coronavirus. https://apps.who.int/iris/bitstream/ handle/10665/259952/WHO-MERS-LAB-15.1-Rev1-2018-eng. pdf?sequence=1 (accessed Oct 3, 2019).

WHO, 2022. World Health Organization, Middle East respiratory syndrome: Global summary and assessment of risk, Available online, https://www.who.int/publications/i/it em/WHO-MERS-RA-2022.1, 16 November 2022 (accessed on 28 April 2023).

Zaki, A.M., Zaki, S., Van Boheemen, T.M., Bestebroer, A.D., Osterhaus, R.A., Fouchier, 2012. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia, N. Engl. J. Med. 367, 1814–1820. https://doi.org/10.1056/ NEJMoa1211721.

Zumla, A., Hui, D. S., Perlman, S., 2015. Middle East respiratory syndrome. Lancet. 386, 995–1007. https://doi: 10.1016/S0140-6736(15)60454-8

مقالة علمية: الوضع الحالي لمتلازمة الشرق الاوسط التنفسية

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الملخص العربي

مما لاشك فيه أن مرض متلازمة الشرق الاوسط التنفسية له من الخطورة الكثير، حيث سبب أضرارا صحية كبيرة للجنس البشري وهو مرض فيروسي مشترك ينتقل عن طريق الابل في منطقة الشرق الاوسط، لذا عكف كثير من العلماء والباحثين على دراسة مسببه الفيروسي والكثير من خصائص هذا المرض العضال، ولما كان الجمل أحد مسببات نقل هذا المرض للانسان فإننا فى هذه المقالة العلمية نميط اللثام عن وبائية هذا المرض و دور الابل في نقله.

بدأ اكتشاف هذا المرض في المملكة العربية السعودية في سنة 2012، ووصل عدد الحالات المصابة في البشر حتى نهاية عام 2023 الى 2617 حالة مسببا التهابات رئوية حادة مصحوب بأعراض تنفسية شديدة قد تصل الى الوفاة وعدد الوفيات من هذا المرض 947 حالة حتى نهاية عام 2023. اما في الابل المصابة بالفيروس فتكون غير مصحوبة بأعراض مرضية اوفي بعض الحالات تكون اعراض تنفسية خفيفة، وتستطيع الابل نقل العدوى للانسان من خلال الاتصال المباشر او الغير مباشر.

ومن خلال هذه المقالة العلمية يتم الاشارة الى بعض النقاط الهامة لهذا المرض مثل التشخيص المعملي الحديث بالاضافة الى الوضع الحالي له خصوصا في مصر حيث لم يثبت عزل الحمض النووي للفيروس من مصر في الابل في السنوات السبع الاخيرة. لكن يجب اليقظة الدائمة والمتابعة الدورية والتحليلات المعملية المستمرة خصوصا للابل الوافدة الى مصر وذلك لمنع انتشار هذا المرض الخطير وتجنب مخاطره والوقاية منه.

الكلمات الدالة: الابل – متلازمة الشرق الاوسط التنفسية – المخاطر - الوقاية