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Middle East Acute Respiratory Syndrome: A Sworn Enemy of Public Health

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Abstract Zoonotic diseases, both newly emerging and re-emerging, are major causes of morbidity and mortality across all demographic groups. Globally, about one billion people are affected with zoonotic infections annually. Middle East Respiratory Syndrome (MERS), caused by the MERS coronavirus (MERS-CoV), is a notable emerging zoonotic respiratory disease that was initially reported in Saudi Arabia in 2012. Afterwards, instances were recorded from 27 nations, resulting in 2,609 infections and 939 deaths overall as of February 2024, with the majority of cases coming from Saudi Arabia. As the only known animal reservoir for MERS-CoV, dromedary camels are essential to the survival of the virus and possible spread as they secrete the virus through bodily fluids, especially nasal and rectal discharges. Although there is proof of direct zoonotic transmission from camels to people, further research is necessary to determine whether camel milk and meat play a part in the transmission chain. Human-to-human transmission has a long history and continues to be a concern for public health, particularly in those with comorbid conditions. The affected persons exhibit signs of fever, headache, chills, dyspnea, and nonproductive cough. The laboratory help is imperative to make an unequivocal diagnosis of disease. This review emphasizes the need for integrated ways to combat MERS-CoV and emphasizes the implementation of a One Health-based prevention and control strategy as a means of mitigating this persistent danger.

Keywords: *camel, middle east respiratory syndrome, one health, public health, viral zoonosis*

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1. Introduction

Zoonotic diseases are described as infections that come from animals, their secretions, contaminated food, or habitats [1]. These diseases include both established and emerging infectious diseases (EIDs). Several biological, socio-demographic, and environmental factors influence the complex geographic distribution of zoonoses, both developing and re-emerging zoonoses [2]. A number of viral zoonotic diseases, including COVID-19, Avian Influenza, Monkeypox, Middle East Respiratory Syndrome (MERS), Nipah virus, Zika fever, Hendra virus disease, Swine Influenza, Contagious Ecthyma, and Hantavirus disease, have become noticeably more prevalent in recent years in a number of different parts of the world [3,4,5,6].

One of the most important newly discovered zoonotic viral respiratory infections is MERS, which is caused by the MERS coronavirus (MERS-CoV) [7]. Since its discovery in Saudi Arabia, MERS has had a significant impact on world health. As of April 2024, there had been 2,613 laboratory-confirmed cases with 941 associated deaths at a case- fatality ratio (CFR) of 36%. The majority of these cases were reported from Saudi Arabia, with 2204 cases and 860 related deaths (CFR) of 39% [8,9]. Human-to-human transmission has been documented in home and healthcare settings, despite the fact that the majority of cases in the Region that have been confirmed thus far have been irregular and have an unknown source of infection. [10]. The rapid viral transmission of this disease has been greatly aided by geographical dispersion. Following a primary respiratory disease outbreak in the Middle East, MERS-CoV subsequently spread to different parts of the world namely Europe, Africa, Asia, and North America. Among them, the outbreak of 2015 in South Korea was the largest epidemic outside of the Middle East [7].

It is thought that the virus originated from bats, and that dromedary camels served as intermediary hosts for amplification before spreading to humans. Moreover, nearly similar MERS-CoV strains have been recovered from camels and humans with epidemiological links, demonstrating inter-transmission, most likely from camels to humans [11,12]. Aerosols released into the atmosphere by infected patients are the means by which

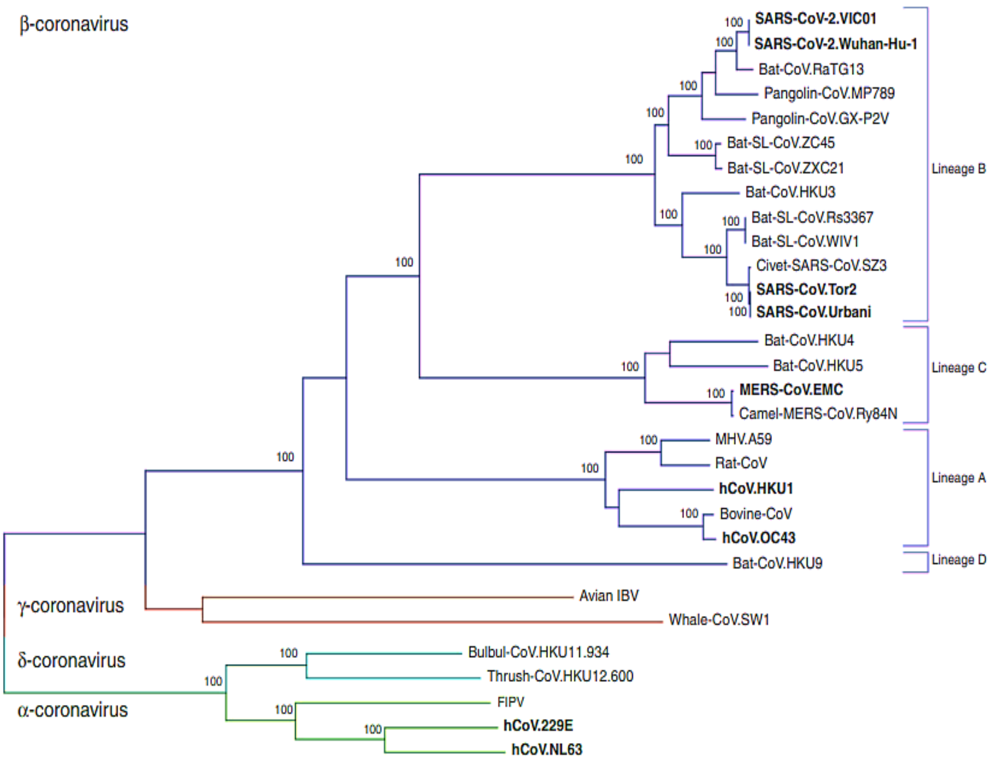
MERS-CoV propagates [13]. Furthermore, there is ample evidence of camel-to-human and human-to-human transfers, which usually occur through close contact with infected people [14]. It is yet unknown, meanwhile, how camel milk and meat may contribute to the spread of MERS-CoV. According to WHO (2024), outbreaks typically occur in healthcare settings and primarily impact elderly patients or those with comorbid diseases. The case fatality rate for confirmed cases is roughly 36% with the median time from the onset of symptoms to death being 11.5 days [15,16]. A significant relationship was found between the calving season and dromedary MERS-CoV infections [17]. It was observed that MERS incidences frequently rise in the winter and early spring, when dromedary camels calving occurs.

MERS-CoV infection can cause mild to severe acute respiratory distress syndrome (ARDS). Common clinical symptoms include fever with chills, headache, dyspnea, and nonproductive cough. The epidemiology and mechanisms of transmission of MERS-CoV have a substantial impact on the morbidity and mortality caused by the disease. Since there are presently no effective vaccinations or antiviral treatments for MERS-CoV, the virus poses a serious threat to public health. It is crucial to understand the One Health idea, which emphasises the connection between environmental, animal, and human health. Reducing animal overcrowding, identifying and quarantining active shedders, wearing personal protective equipment, avoiding the ingestion of raw milk or contaminated food, and regularly conducting monitoring are all effective methods for preventing the spread of MERS-CoV. This review calls attention to the growing zoonotic threat posed by MERS-CoV, highlighting its importance for public health and promoting One Health-based preventive and control measures.

2. Epidemiology of the Disease

2.1. Etiology

A class of viruses known as Coronaviruses can infect animals and humans with respiratory diseases [7]. Coronaviruses are divided into four main genera based on phylogenetic analyses: Alpha, Beta, Gamma, and Delta. Both Alpha and Beta coronaviruses are mostly found in animals, including humans. Notable examples of Alpha coronaviruses include HCoV-NL63 (Human Coronavirus NL63) and HCoV-229E, whereas Beta coronaviruses include OC43, Human Coronavirus HKU1, SARS-CoV, MERS-CoV, and SARS-CoV-2. On the other hand, only animals can contract Gamma and Delta coronaviruses [18]. Middle East Respiratory Syndrome (MERS) is caused by the MERS coronavirus (MERS-CoV), a member of the Beta coronavirus lineage C (Figure 1). Coronaviruses have the largest RNA genomes (27 to 32 kb) among the RNA viruses [19]. Replicase polyprotein open reading frames (ORF) 1a and 1b, envelope protein (E), spike proteins (S), membrane proteins (M), nucleocapsid (N), and five nonstructural proteins (ORF 3, 4a, 4b, 5, and 8b) are among the proteins encoded by the roughly 29 kilobases long MERS-CoV genome. These proteins are being studied as possible therapeutic targets in recent research [20].



Source: [21]

Figure 1. Phylogenetic relationships between lineage A, B, C, and D Coronaviruses

2.2. Reservoir and Susceptible Host

Humans and a wide range of animal species, such as cats, mice, pigs, bats, chickens, and cattle can contract coronaviruses [22]. Nevertheless, they hardly ever infect humans across the species barrier. Studies revealed that animals in the *Camelidae* family-more especially, llamas, dromedaries, and alpacas are vulnerable to MERS-CoV infection [23]. The CoV strains discovered in camels and humans are almost the same, indicating that dromedary camels were crucial in the development of MERS-CoV. It is known that bats serve as reservoir hosts for coronaviruses, and the genetic resemblance between human MERS-CoV and bat coronaviruses emphasises the zoonotic genesis of the latter [24].

2.3. Occurrence and Distribution of MERS-Cov

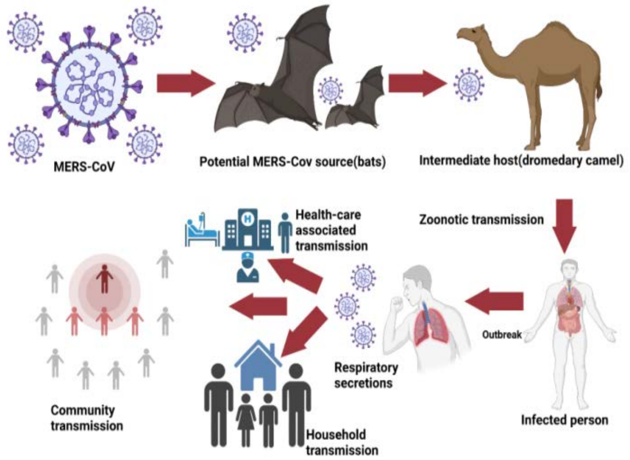
Before the Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) first appeared in China in 2002, coronaviruses were thought to be of low pathogenicity to humans. The outbreak led to a global pandemic that resulted in 8,273 cases and 774 deaths in less than a year [15]. After then, a new viral respiratory disease known as Middle East Respiratory Syndrome Coronavirus (MERS-CoV) surfaced as a potential zoonotic hazard. The year 2012 saw the discovery of MERS-CoV in Saudi Arabia [25,26]. Following its isolation from humans, dromedary camels, and bats, epidemiological research suggested that it might spread by person-to-person contact and a pandemic was imminent [22]. MERS-CoV was detected in 27 countries between 2012 and 2024; 2,613 cases and a 36% death rate were recorded [19]. It was noticed that most of the incidents happened in Saudi Arabia and on the Arabian Peninsula [14]. In the Middle East, MERS-CoV triggered respiratory sickness outbreaks that later extended to Europe, Africa, Asia, and North America. In 2015, the Republic of Korea saw notable outbreaks in hospital settings as a result of this virus [28].

It is concerning to note that the frequency of human MERS cases rises with the seasons, particularly in the winter and early spring when dromedary camels are mating. Research has indicated a connection between the calving season and MERS-CoV infections in camels [29]. High levels of MERS-CoV seropositivity were found in dromedary camels throughout several African nations, as evidenced by 94% of adult dromedaries in Nigeria and 93% and 97% of juvenile and adult camels in Ethiopia, respectively, according to serological surveys. The fact that MERS-CoV has been subtly spreading among camels in the Arabian Peninsula for at least 30 years [29,30] raises concerns because it suggests that the virus existed even before 2012. In Egypt, Tunisia, and Senegal, serological investigations on domestic animals exposed to camels produced antibodies against MERS-CoV [31]. Additionally, research indicates that dromedary camels served as intermediate hosts for human infections of MERS-CoV, which most likely originated from the bats [11].

2.4. Route of Infection and Transmission

MERS-CoV predominantly affects the respiratory system of humans, infecting different kinds of lung cells [32]. According to research done on ex vivo human lung tissue, the virus specifically infects endothelial cells of pulmonary arteries as well as bronchial, bronchiolar, and alveolar epithelial cells that express Dipeptidyl Peptidase 4 (DPP4) [32,33]. Furthermore, MERS-CoV has been found in stool samples from clinical patients, indicating that the human intestinal tract is a potential source of infection[34]. This has been demonstrated by primary intestinal epithelial cells, small intestine explants, and organoids [35].

The primary means of transmission is direct contact with diseased animals, especially dromedary camels. There is strong evidence in favour of transmission occurring through both direct and indirect contacts with infected animals [1]. There is also a risk associated with consuming tainted milk and meat [19]. Bat-to-human transmission is seen as possible and may happen through intermediary hosts or direct contact [36]. Close contact, shared medical equipment, and respiratory droplets are the main ways by which illnesses spread from person to person. This is especially true in healthcare settings, where reports of infection clusters in hospitals spanning multiple is observed. There are reports of travellers who have contracted the virus, spreading the virus to neighbouring nations [37].



Source: [8]

Figure 2. Route of infection and the method by which zoonotic MERS-CoV is transmitted

2.5. Clinical Features

It is mentioned that MERS-CoV usually takes five to six days to incubate before symptoms appear [37,38]. However, symptoms usually appear 14 days after infection. Severe respiratory sickness, severe respiratory syndrome, and even mortality is among the symptom severity ranges reported by the World Health Organisation (2024). Frequent symptoms of the respiratory system include fever, chills, headache, dyspnea, and nonproductive cough. Pneumonia is a common consequence. Additionally, vomiting and diarrhoea are examples of gastrointestinal symptoms that could happen [39]. It has been demonstrated that dromedary camels expel MERS-CoV in their faeces, milk, and possibly even in their nasal fluids. Despite the lack of well-documented clinical characteristics, a study carried out in Saudi Arabia demonstrated that spontaneously infected dromedary camels displayed nasal and lachrymal discharge. The upper and lower respiratory tracts are the main locations of viral replication in camels, as confirmed by the positive virus tests on samples taken from these discharges [17].

3. Diagnosis

The primary obstacle associated with MERS-CoV infection is the lack of distinct clinical characteristics that allow for a differential diagnosis with other viral respiratory illnesses [18]. Sputum, swabs, blood, tissue samples (including lung tissue), and serum collection are examples of standard diagnostic procedures [14]. Reverse Transcription-Polymerase Chain Reaction (RT-PCR) is a highly successful molecular approach for identifying cases of MERS-CoV, especially in respiratory samples. Targeting the nucleocapsid (N) gene or the RNA-dependent RNA polymerase (RdRp) gene to amplify MERS-CoV sequences, RT-PCR is essential for early diagnosis and the application of quarantine measures [40]. In order to confirm the diagnosis, molecular approaches are combined with serological testing, such as Enzyme-Linked Immunosorbent Assay (ELISA), Immunofluorescence Assays (IFA), and Virus Neutralisation Assays (VNA). Commercial reagents or particular monoclonal antibodies are used as capture agents in these serological tests for MERS-CoV detection [36].

4. Public Health Importance of Mers-Cov

Severe respiratory illness is brought on by MERS-CoV, especially in people who are receiving immunosuppressive medication, have comorbid diseases, such as diabetes, hypertension, heart disease, kidney disease, cancer, chronic lung disease, or renal disease [41]. MERS-CoV infection is more common in people who interact closely with camels, such as farm workers, abattoir employees, and veterinarians [28]. Healthcare systems face difficulties with diagnosis, treatment, and prevention during outbreaks, especially because vague symptoms make it difficult to make a primary diagnosis of MERS-CoV infections. Thirty percent of confirmed cases include healthcare workers, who are disproportionately impacted; many infections are hospital-acquired [42].

A past history of travel to high-risk nations and smoking are two important other risk factors for serious illness. There may be risks associated with ancient practices throughout the Middle East, North Africa, and Asia that involve consuming camel urine for its alleged therapeutic benefits for conditions like cancer, diabetes, infectious disorders, and hair and skin issues. Although there isn't any information available about MERS-CoV being found in camel urine, the virus has been found in human urine samples [41], which raises the possibility that consuming camel urine increases the risk of infection. Additionally, outbreaks have a major impact on mental health. According to a study on the mental health of patients during quarantine, 6.4% of the 1,656 patients had regular episodes of rage and 7.6% of them showed signs of worry [43].

Table 1. General Features of Middle East Respiratory Syndrome Coronavirus

Feature	Comment	Source
Classification	beta-CoV, lineage C	[7]
Natural reservoir	Probably bats	[44]
Intermediate host	Dromedary camels	[11]
First identified location	Saudi Arabia in 2012	[25]
Reported country	27	[19]
Incubation period	Approximately 5 days (2-14)	[28]
Transmission	Aerosol droplets, inhalation, and ingestion of camel milk and meat	[13,45]
Case fatality	36%	[19]
Clinical symptoms	Fever, Cough, Chills Sore throat, Dyspnea, Pneumonia Diarrhea, and vomiting	[39,19]
Public health importance	People with comorbidities	[19]
Prevention and control strategies	Hand hygiene, wearing PPE (Personal Protective Equipment), isolating and quarantining those at risk, regular surveillance	[8,46]

5. One Health-Based Prevention and Control Strategies

Understanding the complex interrelationships between people, animals, and the environment requires an understanding of the notion of "One Health" [47]. Additionally, the establishment or strengthening of surveillance systems, which include early warning systems that promptly detect epidemics of national and international public health concerns—is essential for monitoring possible zoonotic risks [44]. The holistic approach recognises a clear correlation between the well-being of humans and the health of animals and their surroundings. In order to prevent the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) from spreading from camels to humans, the following measures are crucial.

5.1. Reducing Overcrowding

Preventing overcrowding is crucial to stopping the spread of viruses, especially among those who are actively shedding the virus. Important actions for quarantine include reducing the number of animals in each pen and identifying animals that are actively shedding the virus [21].

5.2. Abattoirs and Personal Hygiene

The risk of viral transmission to humans can be decreased by placing animal slaughterhouses distant from areas with high population density. Enforcing strict cleaning procedures for animal biological waste at slaughterhouses is essential to stopping the spread of viruses. It is imperative that healthcare personnel receive sufficient resources, training, and periodic policy inspections. In a surveillance study conducted in 2016 in a healthcare system in South Korea among healthcare workers, the seroprevalence of MERS-CoV IgG was greater in those who did not wear the proper protective equipment [11]. Therefore, ensuring the usage of proper personal protective equipment (PPE) by personnel being in close contact with camels can greatly lower the risk of transmission [8,21,48].

5.3. Food safety and Community Education

In MERS-CoV endemic locations, educating people about the virus and preventive measures is essential for lowering the risk of transmission within households and communities. It is advised to stay away from raw milk and tainted food until it has been thoroughly cleaned, peeled, or cooked in order to prevent illness. Due to their increased risk of developing a severe MERS-CoV sickness, people with illnesses like diabetes, cancer, chronic lung disorders, or those undergoing immunosuppressive therapy should stay away from bats and camels [46].

5.4. Surveillance

Monitoring and containing the spread of MERS-CoV in the population requires regular observation, especially during the camel reproductive season.

5.5. Diminishing the Shedding of Virus Through Vaccination

The debate over vaccinating humans and camels against MERS-CoV is intricate. Camels serve as a reservoir for the virus and transmission may not be stopped by natural immunity [42]. Nonetheless, immunization has shown to be successful in reducing the MERS-CoV outbreak. It was reported that experimental vaccination candidates have exhibited effectiveness in eliciting strong neutralizing antibodies in dromedary camels and alpacas [49]. Immunizing young camels, particularly those under two years old, could dramatically lower the amount of virus that naive animals shed [31]. However, Pan-CoV based on m-RNA and other novel vaccine platforms can be adopted for minimizing the shedding of CoV and for prevention of CoV outbreaks and pandemics in animals [50].The danger of human infection could be significantly reduced by reducing the amount of virus shedding in camels, highlighting the potential of vaccination as a prophylactic approach.

6. Conclusion

National and international institutions have been paying close attention to the rise of viral zoonoses, which has led to the development of strategic controls over them to protect public health. There have been occasional instances of diseases since MERS-CoV was identified in 2012; the virus is still common amongst dromedary camels in the Middle East and Africa, and it probably will be for years to come. Affected nations have to prioritise funding for research, surveillance, and vaccine development due to the ongoing threat. Bats are the main hosts of the virus and help it spread to camels, which puts humans at danger. With every viral evolution, rates of disease and mortality rise, indicating a gradual increase in pathogenicity. Although diagnostic techniques based on genetic and serological methods have demonstrated potential, successful preventative measures require a thorough understanding of the routes of transmission. Because camels are repositories for human infection, it is crucial to find effective vaccinations for both humans and camels. Developing focused control measures, prioritising research into animal transmission, and educating healthcare professionals about MERS-CoV are essential steps in controlling and lessening the effects of this zoonotic virus.

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Conflict of Interest

The authors have no competing interests.

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Contribution of Authors

All the authors made significant contributions to the preparation of the manuscript.

List of Abbreviations

ARDS - Acute Respiratory Distress Syndrome
E - Envelope protein
EIDs - Emerging Infectious Diseases
ELISA - Enzyme-Linked Immunosorbent Assay
CoV - Coronavirus
DPP4 - Dipeptidyl Peptidase 4
HCoV - Human Coronavirus
HKU1 - Human Coronavirus HKU1
NL63 - Human Coronavirus NL63
IFA - Immunofluorescence Assay
M - Membrane protein
MERS - Middle East Respiratory Syndrome
MERS-CoV - Middle East Respiratory Syndrome Coronavirus
N - Nucleocapsid
ORF - Open Reading Frame
PPE - Personal Protective Equipment
RT-PCR - Reverse Transcription Polymerase Chain Reaction
RdRp - RNA-dependent RNA Polymerase
SARS-CoV - Severe Acute Respiratory Syndrome Coronavirus

SARS-CoV-2 - Severe Acute Respiratory Syndrome Coronavirus 2
VNA – Virus Neutralization Assay
WHO - World Health Organization

References

[1] Memish, Z. A., Al-Tawfiq, J. A., Makhdoom, H. Q., Assiri, A., Alhakeem, R. F., Albarrak, A., ... and Zumla, A. Respiratory tract samples, viral load, and genome fraction yield in patients with Middle East respiratory syndrome. *J.Infect.Dis.*, Nov.2014, 210(10), 1590-1594.

[2] Pal, M. and Gutama, K.P..Emergence of monkey pox pose a challenge to public health. *Am.J.Microbiol.Res.*, June 2022,10 (2): 55-58.

[3] Meyer, B., Müller, M. A., Corman, V. M., Reusken, C. B., Ritz, D., Godeke, G. J., ... and Drosten, C. Antibodies against MERS coronavirus in dromedary camels, United Arab Emirates, 2003 and 2013. *Emerg.Infect.Dis*., April 2014. 20(4), 552.

[4] Oboho, I. K., Tomczyk, S. M., Al-Asmari, A. M., Banjar, A. A., Al-Mugti, H., Aloraini, M. S., ... and Madani, T. A. 2014 MERS-CoV outbreak in Jeddah—a link to health care facilities, *N.Engl.J.Med*. Feb 2015, *372*(9), 846-854.

[5] Pal, M and Gutama, K.P. Clinical manifestations, diagnosis and treatment and prevention of Coronavirus disease 2019 (COVID-2019). *MOJ Biol. Med.*, October 2021, 6: 165-167.

[6] Pal, M. and Gutama, K.P .Hantavirus disease: An emerging and re-emerging viral disease of public health concern. *Am.J.Public Health Res.*, Feb 2024, 12(1): 19-22.

[7] Perlman, S., and Netland, J.. Coronaviruses post-SARS: update on replication and pathogenesis. *Nat.rev.microbiol.*, 2009, 7(6), 439-450.

[8] Qureshi, A., Bashir, S., Abbas, S., Arshad, M., Rehman, A., Yousaf, S., ... and Tahir, S. Middle East respiratory syndrome (MERS): an overview. *Zoonosis*, Sept. 2023, 3, 465-476.

[9] World Health Organization, MERS situation update, Available online, *https://www.emro.who.int/health-topics/mers-cov/mers-outbreaks.h*, April 2024 (Accessed on 18 June, 2024).

[10] WHO World Health Organization, Middle East respiratory syndrome coronavirus (MERS-CoV) MERS-CoV: efforts to unravel the mystery continued throughout 2013, Available at: https://www.who.int/health-topics/middle-east-respiratory-syndrome-coronavirus-mers#tab=tab_1 (Accessed on 23 June, 2024).

[11] Kim, C. J., Choi, W. S., Jung, Y., Kiem, S., Seol, H. Y., Woo, H. J., ... and Choi, H. J. Surveillance of the Middle East respiratory syndrome (MERS) coronavirus (CoV) infection in healthcare workers after contact with confirmed MERS patients: incidence and risk factors of MERS-CoV seropositivity. *Clin Microbiol Infect*, October 2016, 22(10), 880-886.

[12] Omrani, A. S., Al-Tawfiq, J. A., and Memish, Z. A. Middle East respiratory syndrome coronavirus (MERS-CoV): animal to human interaction. *Pathogens and global health*, December 2015, 109(8), 354-362.

[13] Destoumieux-Garzon, D., Mavingui, P., Boetsch, G., Boissier, J., Darriet, F., Duboz, P., ... and Voituron, Y. The one health concept: 10 years old and a long road ahead. F*ront. Vet. Sci.*, Feb 2018, 5, 14.

[14] Lee, S. M., Kang, W. S., Cho, A. R., Kim, T., and Park, J. K. Psychological impact of the 2015 MERS outbreak on hospital workers and quarantined hemodialysis patients. *Compr. Psychiatry*, Oct.2018, 87, 123-127.

[15] Chafekar, A., and Fielding, B. C. MERS-CoV: understanding the latest human coronavirus threat. *Viruses*, Feb. 2018, 10(2), 93.

[16] World Health Organization, 16 February 2024. Disease Outbreak News; Middle East respiratory syndrome coronavirus – Saudi Arabia, Available at: https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON506 (Accessed on 18 June, 2024).

[17] Hemida, M. G., Chu, D. K., Poon, L. L., Perera, R. A., Alhammadi, M. A., Ng, H. Y., ... and Peiris, M. MERS coronavirus in dromedary camel herd, Saudi Arabia. *Emerg. Infect. Dis.*, July 2014, 20(7), 1231.

[18] Bleibtreu, A., Bertine, M., Bertin, C., Houhou-Fidouh, N. and Visseaux, B.Focus on Middle East respiratory syndrome coronavirus (MERS-CoV). *Medecine et Maladies Infectieuses*, 2020, 50(3), 243-251.

[19] Abdi, F., and Javanshir, S. Identification of flavonoids as potent inhibitors against MERS-CoV 3C-like protease. *Coronaviruses*, July 2022, 3(1), 9-17.

[20] Rabaan, A.A., Al-Ahmed, S.H., Haque, S., Sah, R., Tiwari, R., Malik, Y.S., Dhama, K., Yatoo, M.I., Bonilla-Aldana, D.K. and Rodriguez-Morales, A.J. SARS-CoV-2, SARS-CoV, and MERS-COV: a comparative overview. *Infez Med*, 28(2), 174-184, 2020.

[21] Gartner, M. J., and Subbarao, K.. The threat of zoonotic coronaviruses. *Microbiol. Aust.*, 2016, 42(1), 4-9.

[22] Pal, M. Public health concern due to emerging and re-emerging zoonoses. *Int.J.Livest.Res* , 2015,2: 56-62.

[23] Chan, J. F., Sridhar, S., Yip, C. C., Lau, S. K., and Woo, P. C. The role of laboratory diagnostics in emerging viral infections: the example of the Middle East respiratory syndrome epidemic. *Sci. J. Microbiol.*, Feb. 2017, *55*, 172-182.

[24] Alsafi, R. T. Lessons from SARS-CoV, MERS-CoV, and SARS-CoV-2 infections: what we know so far. *Can. J. Infect. Dis. Med. Microbiol*, 2022,

[25] Zaki, A. M., Van Boheemen, S., Bestebroer, T. M., Osterhaus, A. D., and Fouchier, R. A. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. *N.Engl J. Med.* Nov. 2012, 367(19), 1814-1820,

[26] Wani, N Munshi, Z.H. and Ganai, W.A.. Middle East Respiratory Syndrome (MERS): The Emerging Zoonoses. *Asian J Anim Vet Adv*. 2015,10: 843-851,

[27] Pereyaslov, D., Rosin, P., Palm, D., Zeller, H., Gross, D., Brown, C. S., and Struelens, M. J.. Laboratory capability and surveillance testing for Middle East respiratory syndrome coronavirus infection in the WHO European Region, June 2013. *Eurosurveillance*, October 2014, 19(40), 20923.

[28] Cunha, C. B., and Opal, S. M. Middle East respiratory syndrome (MERS) A new zoonotic viral pneumonia. *Virulence*, August 2014, *5*(6), 650-654.

[29] Hemida, M. G. Middle East respiratory syndrome coronavirus and the one health concept. *Peer J*, Aug 2019, *7*, e7556.

[30] Mann, R., Perisetti, A., Gajendran, M., Gandhi, Z., Umapathy, C., and Goyal, H. Clinical characteristics, diagnosis, and treatment of major coronavirus outbreaks. *Front Med*, Nov.2020, 7, 581521,

[31] Hemida, M. G., and Alnaeem, A. Some One Health based control strategies for the Middle East respiratory syndrome coronavirus. *One Health*, Aug 2019, *8*, 100102.

[32] Widagdo, W., Sooksawasdi Na Ayudhya, S., Hundie, G. B., and Haagmans, B.. Host determinants of MERS-CoV transmission and pathogenesis. *Viruses*, March 2019. 11(3), 280.

[33] Pal, M. Emergence of Zika fever poses a public health concern. Blog Posted on 18th November by Science Range Publications, November, 2018.

[34] Zhou, J., Li, C., Zhao, G., Chu, H., Wang, D., Yan, H. H. N., ... and Yuen, K. Y. Human intestinal tract serves as an alternative infection route for Middle East respiratory syndrome coronavirus. *Science advances*, 3(11), eaao4966, Nov. 2017.

[35] WHO. 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, (accessed on 28 April 2023), 2022.

[36] Breban, R., Riou, J., and Fontanet, A. Interhuman transmissibility of Middle East respiratory syndrome coronavirus: estimation of pandemic risk. *The Lancet*, July 2013, 382(9893), 694-699.

[37] Assiri, A., McGeer, A., Perl, T. M., Price, C. S., Al Rabeeah, A. A., Cummings, D. A., ... and Memish, Z. A. Hospital outbreak of Middle East respiratory syndrome coronavirus. *N Engl J Med*, 2013, 369(5), 407-416.

[38] De Wit, E., Van Doremalen, N., Falzarano, D., and Munster, V. J. SARS and MERS: recent insights into emerging coronaviruses. *Nat. Rev. Microbiol.*, Aug 2016, 14(8), 523-534.

[39] Khalafalla, A. I., Al-Mubarak, A. I., Dalab, A. H., Al-Busadah, K. A., and Erdman, D. D. MERS-CoV in upper respiratory tract and lungs of dromedary camels, Saudi Arabia, 2013–2014. *Emerg. Infect. Dis*, July 2015, 21(7), 1153.

[40] Pal, M. and Mahendra, R. Swine flu: A highly infectious viral zoonosis. *Ethiopian Int. Multidiscip. Res. J.*, January 2015,2: 51-53.

[41] Ali, M. A., Shehata, M. M., Gomaa, M. R., Kandeil, A., El-Shesheny, R., Kayed, A. S., ... and Kayali, G. Systematic, active

surveillance for Middle East respiratory syndrome coronavirus in camels in Egypt. *Emerg. Microbes and Infect.*, Jan 2017,6(1), 1-7.

[42] Masood, N., Malik, S. S., Raja, M. N., Mubarik, S., and Yu, C. Unraveling the epidemiology, geographical distribution, and genomic evolution of potentially lethal coronaviruses (SARS, MERS, and SARS CoV-2). *Front.Cell.Infect.Microbiol.*, August 2020. 10, 499,

[43] Kandeil, A., Gomaa, M., Shehata, M., El-Taweel, A., Kayed, A. E., Abiadh, A., ... and Kayali, G. Middle East respiratory syndrome coronavirus infection in non-camelid domestic mammals. *Emerg. Microbes and Infect.*, 2019, 8(1), 103-108.

[44] Pal, M., Tariku F., Upadhyay D., and Zende R., "Current Innovations in the Diagnosis and Immunization of Emerging and Re-Emerging Zoonoses." *Am. J. Epidemiol*, 2024, 12(2): 23-28.

[45] Seys, L. J., Widagdo, W., Verhamme, F. M., Kleinjan, A., Janssens, W., Joos, G. F., ... and Brusselle, G. G. DPP4, the Middle East respiratory syndrome coronavirus receptor, is upregulated in lungs of smokers and chronic obstructive pulmonary disease patients. *Clinl.Infect. Dis.* Jan. 2018, *66(1)*, 45-53.

[46] Aldohyan, M., Al-Rawashdeh, N., Sakr, F. M., Rahman, S., Alfarhan, A. I., and Salam, M. The perceived effectiveness of MERS-CoV educational programs and knowledge transfer among primary healthcare workers: a cross-sectional survey. *BMC Infect. Dis.*, March 2019, 19, 1-9.

[47] David, D., Rotenberg, D., Khinich, E., Erster, O., Bardenstein, S., van Straten, M., ... and Davidson, I. Middle East respiratory syndrome coronavirus specific antibodies in naturally exposed Israeli llamas, alpacas and camels. *One Health*, 2018, *5*, 65-68.

[48] Behnke, M., Valik, J. K., Gubbels, S., Teixeira, D., Kristensen, B., Abbas, M., ... and Tängdén, T. Information technology aspects of large-scale implementation of automated surveillance of healthcare-associated infections. *Clin Microbiol Infect*, 2021, 27, S29-S39.

[49] Adney, D. R., Wang, L., Van Doremalen, N., Shi, W., Zhang, Y., Kong, W. P., ... and Munster, V. J.. Efficacy of an adjuvanted Middle East respiratory syndrome coronavirus spike protein vaccine in dromedary camels and alpacas. *Viruses*, March 2019,11(3), 212.

[50] Tai, W., Zhang, X., Yang, Y., Zhu, J., and Du, L. Advances in mRNA and other vaccines against MERS-CoV. *Transl.Res*. Nov. 2022 ,242, 20-37.