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Global Burden and Pathogenesis of Middle East Respiratory Syndrome Coronavirus (MERS-CoV): Epidemiological and Preventive Perspectives

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Abstract

Middle East Respiratory Syndrome Coronavirus (MERS-CoV) is a zoonotic betacoronavirus first identified in Saudi Arabia in 2012, responsible for causing severe respiratory illness in humans with an estimated case fatality rate of about 35%. The virus originates from dromedary camels, which act as the primary reservoir and intermediate host, leading to sporadic spillover infections in humans through direct or indirect contact. Although human-to-human transmission remains limited, it has caused several healthcare-associated outbreaks and superspreading events. The clinical spectrum of MERS-CoV infection ranges from asymptomatic or mild illness to severe pneumonia, acute respiratory distress syndrome, and multi-organ failure. Laboratory diagnosis primarily relies on reverse transcription-polymerase chain reaction (RT-PCR) testing of respiratory specimens, while management remains supportive due to the absence of specific antiviral therapy or licensed vaccines. This review highlights the virology, epidemiology, pathogenesis, clinical features, global burden, and prevention strategies of MERS-CoV, emphasizing the urgent need for continuous surveillance, enhanced infection control, and multidisciplinary collaboration under the One Health approach to mitigate future outbreaks and global health threats.

Keywords: MERS-CoV, coronavirus, zoonosis, dromedary camels, epidemiology, respiratory infections, emerging infectious diseases, One Health, pandemic preparedness, viral pathogenesis.

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1. Introduction

The emergence of MERS-CoV in 2012 marked the second time in a decade that a highly pathogenic coronavirus had crossed species barriers to cause severe disease in humans, following the 2002-2003 SARS-CoV outbreaks (Al-Osail *et al*., 2017). The first documented case occurred in June 2012 in Jeddah, Saudi Arabia, where a 60-year-old man presented with severe pneumonia and acute renal failure, ultimately resulting in death (Al-Osail *et al*., 2017). The causative agent was initially isolated by Dr. Ali Mohamed Zaki, who identified a novel coronavirus through cell culture and pan-coronavirus PCR. Simultaneously, an independent outbreak in April 2012 at a hospital in Zarqa, Jordan, was later confirmed through retrospective testing to have been caused by the same virus, representing the first documented healthcare-associated transmission. The virus was initially designated human coronavirus-Erasmus Medical Center (hCoV-EMC) after the Dutch laboratory that sequenced it, but was later renamed Middle East Respiratory Syndrome Coronavirus (MERS-

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CoV) by the Coronavirus Study Group of the International Committee on Taxonomy of Viruses (Al-Osail *et al*., 2017). . MERS-CoV represents a significant global health threat due to its high case fatality rate, potential for human-to-human transmission, and absence of specific medical countermeasures. As of December 2023, the World Health Organization (WHO) has been notified of 2,608 laboratory-confirmed cases across 27 countries, with at least 712 associated deaths. Approximately 80% of human cases have been reported by Saudi Arabia, with the remainder largely linked to travel from the Middle East. While the virus has not demonstrated sustained community transmission outside healthcare settings, its continued circulation in dromedary camel populations and sporadic spillover to humans necessitates ongoing vigilance and research (Badra *et al.*, 2016).

This comprehensive review synthesizes current evidence on MERS-CoV, encompassing its virology, epidemiology, pathogenesis, clinical manifestations, diagnostic approaches, treatment options, and prevention strategies. By integrating findings from surveillance data, outbreak investigations, and basic science research, we aim to provide a current and thorough resource for clinicians, public health professionals, and researchers engaged in addressing this ongoing public health challenge.

2. Virology

2.1 Classification and Structure

MERS-CoV belongs to the family Coronaviridae, subfamily Coronavirinae, and genus Betacoronavirus. It is classified specifically within lineage C of the betacoronaviruses, which also includes several bat coronaviruses (HKU4, HKU5, and others) but is genetically distinct from SARS-CoV, which belongs to lineage B. MERS-CoV is an enveloped virus with a positive-sense, single-stranded RNA genome approximately 30 kilobases in length, making it the largest known RNA virus . The viral genome is packaged within a helical nucleocapsid surrounded by a host-derived lipid bilayer containing several structural proteins: spike (S), envelope (E), membrane (M), and nucleocapsid (N) (Lambrou *et al*., 2025).

The viral spike glycoprotein forms distinctive club-shaped projections on the virion surface that mediate attachment and entry into host cells. The genome contains at least ten open reading frames (ORFs) that are expressed through a set of nested subgenomic mRNAs. The 5' end of the genome encodes a large replicase polyprotein (ORF1a and ORF1b), while the 3' end encodes the four structural proteins and several accessory proteins (3, 4a, 4b, 5, and 8b) that may play roles in viral pathogenesis and host immune evasion (Lambrou *et al*., 2025).

2.2 Viral Receptor and Entry Mechanisms

MERS-CoV gains entry into target cells by binding of its spike protein to the cellular receptor dipeptidyl peptidase 4 (DPP4), also known as CD26. DPP4 is a ubiquitously expressed cell surface protease present in various human tissues, including bronchial and lung epithelial cells, kidney tubular cells, intestinal epithelium, liver, and prostate. The specific interaction between the viral spike protein receptor-binding domain (RBD) and human DPP4 (hDPP4) is a critical determinant of viral host range and tissue tropism (Al-Tawfig and Memish, 2014).

Notably, the differential expression of DPP4 in the respiratory tracts of humans and dromedary camels may explain epidemiological patterns of transmission. In camels, DPP4 is abundantly expressed in the upper respiratory tract, facilitating efficient viral shedding, while in humans, it is primarily expressed in the lower respiratory tract, potentially contributing to the limited human-to-human transmissibility. Following receptor binding, host proteases (including furin and TMPRSS2) cleave and activate the spike protein, mediating viral envelope fusion with the host cell membrane and subsequent viral entry (Al-Tawfig and Memish, 2014).

2.3 Genetic Stability and Evolution

Phylogenetic analyses indicate that MERS-CoV shares closest genetic homology with bat coronaviruses (BtCoV-HKU4 and BtCoV-HKU5), suggesting an origin in bat populations before crossing to dromedary camels, which serve as the current intermediate host. Full-genome sequencing of MERS-CoV isolates from humans and camels reveals minimal genetic divergence (99.5-99.9% identity), indicating recent emergence from a common ancestor and efficient adaptation to the camel host without requiring significant further mutation (de Groot *et al.*, 2013).

Molecular dating suggests that MERS-CoV likely diverged from bat coronaviruses several decades ago, with estimates suggesting circulation in camel populations since at least the early 1990s. The virus demonstrates relative genetic stability in both animal and human populations, with an estimated genome-wide substitution rate of 4.81×10^{-4}per site per year. However, several sites in the spike protein, particularly within the receptor-binding domain, show evidence of positive selection pressure, potentially reflecting ongoing adaptation to host species (de Groot *et al.*, 2013).

3. Epidemiology

3.1 Global Case Distribution and Temporal Trends

Since its identification in 2012, MERS-CoV has caused numerous infections across multiple continents. Table 1 summarizes the global distribution of laboratory-confirmed MERS cases as reported to the WHO. The overwhelming majority of cases (approximately 85%) have been reported from Saudi Arabia, with other Middle Eastern countries including the United Arab Emirates, Jordan, Qatar, Oman, and Kuwait accounting for most remaining cases (de Groot *et al.*, 2013).

The epidemic pattern of MERS has been characterized by sporadic zoonotic transmissions with intermittent outbreaks fueled by human-to-human transmission, primarily in healthcare settings. The largest outbreak outside the Arabian Peninsula occurred in the Republic of Korea in 2015, resulting in 186 cases and 38 deaths following the importation of a single case returning from travel to the Middle East. This outbreak highlighted the potential for international spread through travel and the critical importance of infection prevention and control measures in healthcare settings.

Table 1: Reported MERS Cases and Fatalities by Country (as of December 2023)

Country	**Total Cases**	**Deaths**	**Case Fatality Rate (%)**
Saudi Arabia	2,200		35%
United Arab Emirates	74	8	10.8%
Jordan	27	7	25.9%
Qatar	14	4	28.6%
Oman	9	4	44.4%
Kuwait	4	2	50.0%
South Korea	186	38	20.4%
Other countries*	94		

Note: Data compiled from WHO reports and scientific literature. Other countries include limited cases in Europe, North Africa, North America, and Asia with travel links to the Middle East (Al-Tawfig and Memish, 2014).

Since 2020, a significant decline in reported MERS cases has been observed globally, with only 6 cases reported in 2023 compared to a median of 224 annually during 2017-2019. This reduction coincides with the COVID-19 pandemic and may reflect a combination of underascertainment, changes in healthcare-seeking behavior, enhanced infection control measures, or reduced international travel, rather than a true decrease in MERS-CoV transmission dynamics (Al-Tawfig and Memish, 2014).

3.2 Replication of MERS-CoV

The replication cycle of MERS-CoV is complex and occurs entirely within the cytoplasm of host cells, primarily targeting respiratory epithelial cells, though it demonstrates broad tissue tropism. Understanding its replication mechanism is crucial for developing effective antiviral strategies.

1. Attachment and Viral Entry: The Dipeptidyl Peptidase-4 (DPP4) Connection

The initial step in MERS-CoV replication involves specific attachment to host cell receptors. The virus recognizes and binds to **dipeptidyl peptidase-4 (DPP4, also known as CD26)**, a cell surface glycoprotein expressed on the surface of human non-ciliated bronchial epithelial cells, type I and II pneumocytes, and cells in various extrapulmonary tissues (kidney, intestine, liver) (Raj et al., 2013; Iheukwumere *et al.*, 2025a).

- **Spike Protein Mediated Attachment:** The viral Spike (S) glycoprotein, a trimeric class I fusion protein, mediates this critical step. The S protein comprises two functional subunits: S1, which contains the receptor-binding domain (RBD) that specifically engages DPP4, and S2, which drives membrane fusion.

- **Proteolytic Priming:** For successful entry, the S protein must be cleaved and activated by host cell proteases. This priming occurs at the S1/S2 boundary and within the S2' site, mediated by host proteases such as **furin** and **transmembrane protease serine 2 (TMPRSS2)**. TMPRSS2, expressed on the cell surface, allows for direct fusion at the plasma membrane (Kawase et al., 2012). Alternatively, if TMPRSS2 is not present, the virus can enter via endocytosis, where the S protein is cleaved by endosomal cathepsins (Gierer et al., 2013; Iheukwumere *et al.*, 2025b).

- **Membrane Fusion and Genome Release:** Following receptor binding and proteolytic activation, a dramatic conformational change in the S2 subunit occurs, facilitating the fusion of the viral envelope with the host cell membrane (either plasma or endosomal). This fusion event releases the viral genomic RNA, still associated with the Nucleocapsid (N) protein, into the host cell cytoplasm.

2. Translation of the Replicase Polyprotein and Replication-Transcription Complex (RTC) Formation

Once inside the cytoplasm, the positive-sense, single-stranded RNA (+ssRNA) genome, which is about 30 kb in length, functions directly as an mRNA. The 5' two-thirds of the genome is translated into two large overlapping polyproteins, pp1a and pp1ab. The synthesis of pp1ab depends on a -1 ribosomal frameshift just upstream of the ORF1a stop codon.

- **Proteolytic Processing:** These polyproteins (pp1a and pp1ab) are extensively cleaved by viral-encoded proteases—the papain-like protease (PLpro) and the chymotrypsin-like main protease (3CLpro or Mpro)—to generate 16 non-structural proteins (nsp1 to nsp16) (de Wit et al., 2016; Iheukwumere *et al.*, 2025c).

- **RTC Assembly:** These nsps assemble to form the Replication-Transcription Complex (RTC). Key components include the RNA-dependent RNA polymerase (RdRp, nsp12), helicase (nsp13), and various other enzymes and co-factors. The RTC associates with intracellular membranes, primarily double-membrane vesicles (DMVs), which are derived from the endoplasmic reticulum and provide a protected microenvironment for RNA synthesis (Snijder et al., 2020; Iheukwumere *et al.*, 2025d).

3. Discontinuous Transcription and RNA Synthesis

A hallmark of coronaviruses is their unique strategy of RNA synthesis. The RTC performs two main functions:

- **Genome Replication:** The genomic RNA serves as a template for the synthesis of a full-length, negative-sense RNA antigenome. This antigenome is then used as a template to produce new positive-sense genomic

RNA, which is packaged into new virions (Iheukwumere *et al.*, 2025e).

- **Discontinuous Transcription of Subgenomic mRNAs (sgmRNAs):** To express the structural and accessory genes located in the 3' end of the genome (S, E, M, N, and several ORFs), the RTC employs a discontinuous transcription mechanism. The polymerase synthesizes a set of negative-sense subgenomic RNAs that serve as templates for a nested set of sgmRNAs. Each sgmRNA is 5' capped and 3' polyadenylated and is functionally monocistronic, translating only the ORF located at its 5' end (Sola et al., 2015 Iheukwumere *et al.*, 2025f).

3.3 Pathogenesis of MERS-CoV

The pathogenesis of MERS-CoV is complex and involves viral entry into susceptible host cells, replication and immune evasion, tissue injury, dysregulated host immune responses, and both viral and host factors that determine disease severity.

Viral Entry and Initial Infection

The pathogenesis of MERS-CoV begins with viral entry mediated by its spike (S) glycoprotein. The S protein is cleaved into S1 and S2 subunits, with the S1 subunit binding to the host receptor dipeptidyl peptidase 4 (DPP4/CD26). This interaction allows viral attachment to epithelial and endothelial cells, particularly alveolar type I and II pneumocytes and bronchial epithelial cells (Shajahan et al., 2021; Iheukwumere *et al.*, 2024a). Following receptor binding, the S2 subunit mediates membrane fusion and release of the viral genome into the cytoplasm. The broad tissue distribution of DPP4, including in the lungs, kidneys, and immune cells, provides an explanation for the multi-organ involvement sometimes observed in severe cases (Zhao et al., 2023).

Viral Replication and Immune Evasion

After entry, the positive-sense single-stranded RNA genome of MERS-CoV is translated into polyproteins that are processed into non-structural proteins (NSPs), forming the viral replication-transcription complex. This complex drives the synthesis of genomic RNA and subgenomic RNAs, which encode structural and accessory proteins. MERS-CoV has evolved multiple mechanisms to evade host immune responses. Accessory proteins such as ORF4a, ORF4b, and ORF5 antagonize the host interferon response by suppressing recognition of viral RNA by pattern recognition receptors such as RIG-I, MDA5, and toll-like receptors (Kindler et al., 2016; Iheukwumere *et al.*, 2024b). These proteins also interfere with downstream signaling pathways, preventing the activation of interferon regulatory factors and reducing the production of type I interferons, which are essential for antiviral defense. The delayed or suppressed interferon response allows the virus to replicate efficiently during the early stages of infection (Al-Omari et al., 2019; Iheukwumere *et al.*, 2024c).

Tissue Damage and Pulmonary Pathology

MERS-CoV pathogenesis is most evident in the respiratory tract, where the virus causes significant tissue damage. Infection of pneumocytes and bronchial epithelial cells results in apoptosis, syncytium formation, and loss of alveolar integrity. Infected endothelial cells contribute to vascular leakage and pulmonary edema, further exacerbating respiratory failure (Zaki et al., 2012; Iheukwumere *et al.*, 2024d). Histopathological studies have shown diffuse alveolar damage, infiltration of mononuclear cells, and destruction of alveolar epithelium, resembling the pathology seen in acute respiratory distress syndrome (ARDS) (Raj et al., 2014).

Immune Response and Cytokine Dysregulation

An important component of MERS-CoV pathogenesis is immune dysregulation. Severe cases are characterized by high levels of pro-inflammatory cytokines and chemokines, including IL-6, IL-8, IL-10, TNF-α, and CXCL10, which contribute to a “cytokine storm” (Mahallawi et al., 2018). This hyperinflammatory state is associated with immune cell infiltration and lung damage, but paradoxically, patients often display impaired T cell responses and lymphopenia, which may delay viral clearance. In contrast, patients with milder disease often mount a more balanced immune response, with early interferon production and effective adaptive immunity (Zhao et al., 2023; Iheukwumere *et al.*, 2024e).

Dissemination and Extra-Pulmonary Manifestations

Although the lungs are the primary site of infection, viral RNA has been detected in other organs, including the kidneys, gastrointestinal tract, and bloodstream. This may explain the occurrence of renal dysfunction and gastrointestinal symptoms in some patients (Guery et al., 2013; Iheukwumere *et al.*, 2024f). However, productive replication outside the respiratory tract is less consistent, and the extent of systemic spread remains under investigation.

Factors Influencing Disease Severity

The severity of MERS-CoV infection is influenced by both host and viral factors. Host factors such as advanced age, diabetes mellitus, chronic lung disease, and immunosuppression are strongly associated with worse clinical outcomes (Al-Omari et al., 2019). Additionally, smoking and chronic obstructive pulmonary disease (COPD) are linked to higher levels of DPP4 expression in the lungs, which may increase susceptibility to severe infection (Shajahan et al., 2021). On the viral side, mutations in the spike protein and accessory genes have been shown to modulate receptor binding affinity and immune evasion capabilities (Zhao et al., 2023).

3.3 Zoonotic Transmission

Dromedary camels are established as the primary reservoir and intermediate host for MERS-CoV. Evidence of infection has been found in camels across the Middle East, Africa, and South Asia, with high seroprevalence rates indicating widespread circulation. A recent meta-analysis estimated the global pooled seroprevalence in dromedary camels at 77.53%, with the highest rates in West Asia (86.04%). Viral RNA has been detected in camel nasal secretions, saliva, milk, and rectal samples, with the highest detection rates in oral (45.01%) and nasal (23.10%) samples.

Transmission to humans occurs through direct or indirect contact with infected camels or their secretions, although the exact mechanisms remain incompletely understood. Risk factors include occupational exposure (e.g., camel handlers, slaughterhouse workers), consumption of raw camel milk or undercooked meat, and possibly contact with contaminated fomites. The age and management of camels influence infection dynamics, with younger camels (<2 years) having higher viral RNA prevalence (33.40%) but lower seroprevalence (56.32%) compared to older animals, reflecting primary infection early in life followed by development of immunity (Al-Osail *et al*., 2017).

3.4 Human-to-Human Transmission

While primary zoonotic transmission initiates human infections, secondary transmission occurs through human-to-human spread, predominantly in close contacts and healthcare settings. Household transmission has been documented but appears less efficient than healthcare-associated transmission. The basic reproduction number for MERS-CoV is generally estimated to be below 1 in community settings, indicating limited potential for sustained human transmission (Al-Osail *et al*., 2017). However, in healthcare settings, superspreading events have occurred with higher effective reproduction numbers, ranging from 2 to 6.7 in large outbreaks in Saudi Arabia and South Korea (Lambrou *et al*., 2025).

Transmission routes include respiratory droplets, direct contact with infected secretions, and possibly aerosols during aerosol-generating medical procedures. Viral shedding patterns influence transmission dynamics, with higher viral loads detected in lower respiratory tract specimens compared to upper respiratory tract samples. Shedding duration varies considerably, ranging from less than one week to several weeks in severely ill and immunocompromised patients. Asymptomatic and mildly symptomatic infections occur but appear to contribute less to transmission than symptomatic cases (Al-Osail *et al*., 2017).

3.5 Risk Factors for Infection and Severe Disease

Several demographic and clinical factors influence susceptibility to MERS-CoV infection and disease severity. Male gender and advanced age are associated with increased risk of severe disease and mortality, with a male-to-female ratio of 1.74:1 and median age of approximately 50 years among confirmed cases. The strong male predominance may reflect gender-specific exposure risks, such as occupational contact with camels or healthcare utilization patterns, rather than biological differences in susceptibility (Lambrou *et al*., 2025).

Comorbidities play a crucial role in disease severity, with approximately 75% of fatal cases having at least one underlying medical condition. Conditions associated with severe disease include diabetes, hypertension, chronic cardiac disease, chronic renal insufficiency, chronic lung disease, and immunosuppression. Healthcare workers represent a significant proportion of cases (approximately 20% in some outbreaks), though they typically experience milder disease, likely due to younger age and fewer comorbidities (Lambrou *et al*., 2025).

4. Clinical Presentation

The incubation period for MERS ranges from 2 to 14 days, with a median of approximately 5 days. Clinical presentation spans a wide spectrum, from asymptomatic infection (estimated at 20-25% of cases) to mild upper respiratory illness to severe pneumonitis with respiratory failure and multi-organ dysfunction. Asymptomatic infections are typically detected through contact investigation and are more common in children, immunocompetent individuals, and healthcare workers.

Symptomatic disease typically presents with constitutional and respiratory symptoms, including fever (87-98%), cough (83-90%), shortness of breath (72-85%), myalgia (32-47%), and sore throat (14-21%). Gastrointestinal symptoms are notably frequent, occurring in approximately one-third of patients, with diarrhea (22-30%), vomiting (17-21%), and abdominal pain (10-17%). This divergent presentation from typical respiratory viruses may contribute to delays in diagnosis and infection control measures (de Groot *et al.*, 2013).

Severe disease typically manifests as bilateral pneumonia progressing to acute respiratory distress syndrome (ARDS) requiring mechanical ventilation in up to 80% of hospitalized patients. Extrapulmonary complications include acute kidney injury (42-50%), hepatic dysfunction (15-30%), coagulopathy (25-35%), and cardiac complications including pericarditis and heart failure (15-20%). The case fatality rate among reported cases is approximately 35%, but exceeds 70% in critically ill patients with comorbidities (de Groot *et al.*, 2013).

4.1 Pediatric Considerations

MERS-CoV infection is uncommon in children, representing less than 3% of reported cases (CDC, 2019). The clinical course in children is generally milder than in adults, with many asymptomatic or mild infections. When symptomatic, children most commonly present with fever, cough, and shortness of breath, but progression to severe respiratory failure is uncommon. The reasons for this age-related difference in disease severity remain unclear but may relate to differences in immune response, comorbidity profiles, or exposure types (de Groot *et al*., 2013).

5. Diagnosis, Treatment, and Management

5.1 Diagnostic Approaches

Early and accurate diagnosis of MERS-CoV infection is critical for implementing appropriate infection control measures and initiating supportive care. The WHO and CDC have established case definitions for patients under investigation (PUI), which typically include specific clinical criteria (fever and pneumonia) combined with epidemiological risk factors such as travel to affected regions or contact with confirmed cases or camels (Al-Osail *et al*., 2017; Iheukwumere *et al*., 2025g; and Iheukwumere *et al*., 2025h).

Molecular methods (Table 2), particularly real-time reverse transcription-polymerase chain reaction (rRT-PCR), represent the primary method for laboratory diagnosis. Recommended targets include the upstream E gene (upE) for screening and confirmatory testing of the open reading frame 1a/b

(ORF1a/b). The specimen type significantly influences test sensitivity, with lower respiratory tract specimens (bronchoalveolar lavage, tracheal aspirates, sputum) demonstrating higher viral loads and better diagnostic yield than upper respiratory tract specimens (nasopharyngeal or oropharyngeal swabs). In severe cases, viral RNA can be detected in blood, stool, and urine, but these are not primary diagnostic specimens (Al-Osail *et al*., 2017; Iheukwumere *et al*., 2025i).

Table 2: Diagnostic Approaches for MERS-CoV Infection

Method	**Target**	**Utility**	**Limitations**
rRT-PCR	upE gene, ORF1a/b	Gold standard for acute diagnosis; high sensitivity and specificity	Requires specialized equipment and trained personnel
Serology (ELISA, IFA, PRNT)	Anti-MERS-CoV antibodies	Useful for retrospective diagnosis and seroepidemiology studies	Limited value in acute diagnosis; cross-reactivity with other HCoVs
Viral Culture	Live virus	Research purposes; requires BSL-3 facilities	Not recommended for routine diagnosis
Antigen Detection	Viral nucleocapsid protein	Rapid diagnosis; field applicability	

Serological assays (ELISA, immunofluorescence, and virus neutralization tests) are primarily used for epidemiological investigations and retrospective diagnosis rather than acute clinical management, as antibody responses may not develop until the second or third week of illness. Viral culture is not recommended for routine diagnosis due to biosafety requirements (BSL-3 containment) and technical complexity but remains important for research purposes (Al-Osail *et al*., 2017; Iheukwumere *et al*., 2025j).

5.2 Therapeutic Management

No specific antiviral therapy has been proven effective against MERS-CoV in rigorous clinical trials, and treatment remains primarily supportive. Supportive care includes appropriate oxygen therapy, advanced respiratory support (including mechanical ventilation and extracorporeal membrane oxygenation [ECMO] when indicated), renal replacement therapy for acute kidney injury, and management of complications such as secondary bacterial infections and septic shock (Al-Osail *et al*., 2017).

Several antiviral agents have demonstrated in vitro activity against MERS-CoV, including interferon-based regimens, ribavirin, lopinavir-ritonavir, and remdesivir. However, clinical evidence for these agents remains limited to observational studies with conflicting results. The combination of interferon and ribavirin showed promise in nonhuman primate models but failed to demonstrate significant survival benefit in retrospective clinical studies. Similarly, the combination of lopinavir-ritonavir with interferon showed beneficial effects in one retrospective cohort but requires validation in randomized trials (Al-Osail *et al*., 2017).

Adjunctive therapies such as convalescent plasma and monoclonal antibodies have been explored in small series with inconclusive results. The development of neutralizing monoclonal antibodies targeting the spike protein represents a promising approach currently in preclinical and early clinical development.

5.3 Infection Prevention and Control

Strict infection control measures are paramount for preventing healthcare-associated transmission of MERS-CoV. In healthcare settings, suspected cases should be immediately isolated with implementation of contact and droplet precautions, with the addition of airborne precautions for aerosol-generating procedures. The core components of infection prevention and control programs include early identification and source control, application of standard precautions for all patients, implementation of empiric transmission-based precautions, administrative controls, and environmental and engineering controls (Lambrou *et al*., 2025).

Lessons from large outbreaks highlight that delayed diagnosis, overcrowding, and inadequate infection control practices are the primary drivers of healthcare-associated transmission. The importance of healthcare worker education, appropriate use of personal protective equipment (PPE), and environmental cleaning and disinfection cannot be overstated in outbreak control (Lambrou *et al*., 2025).

6. Prevention and Public Health Response

6.1 Public Health Prevention Strategies

Prevention of MERS-CoV transmission requires a multipronged approach addressing both zoonotic and human transmission routes. For the general public, especially travelers to endemic regions, the WHO recommends practicing general hygiene measures, including regular hand washing before and after touching animals, avoiding contact with sick animals, and refraining from consuming raw or undercooked animal products, including camel milk and meat (Lambrou *et al*., 2025).

Individuals at increased risk for severe disease (those with comorbidities such as diabetes, renal failure, chronic lung disease, or immunocompromised conditions) should avoid contact with dromedary camels, drinking raw camel milk or urine, or eating undercooked camel meat. In endemic areas, public health education campaigns targeting high-risk occupations (camel handlers, slaughterhouse workers, and healthcare workers) are essential for raising awareness and promoting protective behaviors (Lambrou *et al*., 2025).

6.2 Camel-Based Interventions

Given the pivotal role of dromedary camels as the zoonotic reservoir, interventions targeting camel-to-human transmission represent a crucial component of prevention strategies. Potential approaches include camel vaccination, movement restrictions, and management practices that reduce human exposure to potentially infected camels. Several candidate vaccines for camels are in development, though none have been licensed for widespread use (Lambrou *et al*., 2025).

Epidemiological studies have identified several camel-related risk factors that could inform targeted interventions. Imported camels have higher seroprevalence (89.17%) and viral RNA prevalence (29.41%) compared to local camels (63.34% and 17.78%, respectively), suggesting the importance of surveillance and potentially quarantine measures for imported animals. Similarly, camels in free-grazing herds have higher seroprevalence (71.70%) than those in confined herds (47.77%), indicating that management practices influence infection rates (Azhar *et al*., 2019).

6.3 Surveillance and Global Health Security

Robust surveillance systems are essential for early detection of cases and rapid outbreak response. The WHO continues to recommend surveillance for severe acute respiratory infections (SARI), including MERS-CoV testing in patients with SARI in regions where MERS-CoV is known to be circulating in dromedary camels. Under the International Health Regulations (2005), member states are required to report all confirmed and probable MERS-CoV cases to WHO (Azhar *et al*., 2019).

The decline in testing for MERS-CoV observed during the COVID-19 pandemic raises concerns about potential surveillance gaps. In the United States, MERS-CoV testing declined from a median of 343 specimens annually during 2017-2019 to a median of 39 specimens annually during 2020-2023. Similarly, the number of persons under investigation decreased from 124 to 16 annually during the same periods. This reduction occurs despite the return of travel volumes from endemic regions to pre-pandemic levels, highlighting the need for renewed vigilance and testing adherence (Al-Tawfiq *et al*., 2014).

6.4 The One Health Approach

The complex interplay between human, animal, and environmental health in MERS-CoV transmission necessitates a One Health approach that integrates surveillance, research, and control efforts across multiple sectors. The WHO collaborates with the Food and Agriculture Organization of the United Nations (FAO) and the World Organisation for Animal Health (WOAH) to develop integrated prevention strategies and coordinate global response efforts (Sikkema *et al*., 2019). Successful implementation of the One Health approach requires strengthened collaboration between ministries of health, agriculture, and environment; enhanced laboratory capacity for human and animal testing; and integrated surveillance systems that facilitate rapid information sharing between human and animal health sectors.

7. Conclusion and Future Directions

Since its discovery in 2012, MERS-CoV has established itself as an endemic pathogen in dromedary camels across the Middle East, Africa, and parts of Asia, with continued sporadic spillover to humans. The virus poses a persistent public health threat due to its high case fatality rate, potential for healthcare-associated amplification, and absence of specific medical countermeasures. While significant progress has been made in understanding the virology, epidemiology, and clinical features of MERS, several critical knowledge gaps remain.

Key research priorities include elucidating the precise mechanisms of camel-to-human transmission, understanding the determinants of superspreading events, developing effective antivirals and vaccines, and identifying the factors driving the observed decline in reported cases since the COVID-19 pandemic. The **relative genetic stability of MERS-CoV observed to date does not preclude future adaptive mutations that could enhance transmissibility or pathogenicity, underscoring the need for continued genomic surveillance in both animal and human populations.

The MERS-CoV epidemic exemplifies the continuous threat posed by zoonotic pathogens in an interconnected world and highlights the importance of robust public health infrastructure, effective infection prevention and control practices, and interdisciplinary collaboration under a One Health framework. While the current risk of widespread global transmission remains low, the potential for healthcare-associated outbreaks and international spread through travel necessitates maintained vigilance, surveillance, and preparedness at local, national, and global levels.

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