

Perspective

Human Metapneumovirus (HMPV): A Brief Overview

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ABSTRACT

Background: Human metapneumovirus (HMPV), discovered in 2001, is a significant respiratory pathogen in the *Paramyxoviridae* family that is responsible for substantial global morbidity and mortality. Despite its clinical impact, HMPV remains underdiagnosed and lacks specific treatments and vaccines. **Objective:** This perspective aims to provide a comprehensive analysis of HMPV as an emerging respiratory pathogen, examining its virological characteristics, epidemiology, clinical manifestations, pathogenesis, diagnostic methods, and management approaches. **Methods:** This review synthesizes the current literature on HMPV, examining its virological characteristics, epidemiology, clinical manifestations, pathogenesis, and management approaches through an analysis of peer-reviewed publications from 2001-2025. **Results:** HMPV accounts for 5–10% of pediatric respiratory hospitalizations globally, with an estimated 14.2 million lower respiratory tract infections in children under five annually, resulting in 643,000 hospital admissions and 16,100 in-hospital deaths annually. The virus predominantly affects children, elderly individuals, and immunocompromised patients, who present with symptoms ranging from mild upper respiratory infections to severe pneumonia. Diagnostic advances, particularly in molecular techniques, have improved detection capabilities. Current management relies primarily on supportive care, whereas therapeutic research focuses on antiviral agents, monoclonal antibodies, and vaccine candidates utilizing novel platforms, including nanoparticle and mRNA technologies. **Conclusion:** Increased global surveillance, accelerated vaccine development, and novel therapeutic approaches are needed to address HMPV. Research priorities include understanding long-term immunity, immune evasion mechanisms, and the environmental influences on transmission. Collaborative efforts among academia, industry, public health institutions, and regulatory bodies are essential to translate scientific discoveries into effective interventions that reduce the public health burden of HMPV.

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INTRODUCTION

Human metapneumovirus (HMPV) is a respiratory pathogen that has garnered significant attention since its discovery in 2001. This genus belongs to the *Paramyxoviridae* family and is closely related to respiratory syncytial virus (RSV), which shares many clinical and virological characteristics. Despite being recognized relatively recently, serological evidence suggests that HMPV has been circulating in human populations for decades, causing widespread respiratory illnesses. Its ubiquitous nature and capacity to affect individuals of all age groups make it a critical subject of study in respiratory virology [1,2].

HMPV is a leading cause of acute respiratory infections (ARIs), especially in young children, elderly individuals, and immunocompromised individuals. Its clinical manifestations range from mild upper respiratory tract infections to severe lower respiratory diseases such as bronchiolitis and pneumonia. Infections are often indistinguishable from those caused by other respiratory viruses, complicating diagnostic efforts and contributing to the underrecognition of their true public health impact. Furthermore, HMPV has been implicated in nosocomial outbreaks and coinfections, exacerbating the burden on healthcare settings [3,4].

Globally, HMPV is estimated to be responsible for 5%–10% of all pediatric hospitalizations due to acute respiratory infections. Wang et al. (2021) estimated that in 2018, HMPV caused approximately 14.2 million lower respiratory tract infections in children under five years of age, leading to approximately 643,000 hospital admissions and 16,100 in-hospital deaths. Mortality is especially high in low- and middle-income countries where access to intensive supportive care is limited. In adults, particularly those over 65 years of age and individuals with comorbidities or immunosuppression, HMPV contributes significantly to wintertime hospitalizations and may cause fatal respiratory failure. Mortality rates in hospitalized adults with HMPV infection range from 4% to 10%, depending on the population and healthcare context [5,6].

The seasonal and geographical variability of HMPV infections underscores the importance of understanding their epidemiology. Although it primarily peaks in late winter and early spring, regional variations in prevalence and strain distribution have been observed. Advances in molecular diagnostics have significantly improved our ability to detect HMPV, shedding light on its contribution to global respiratory morbidity and mortality rates. However, challenges in treatment and prevention persist, highlighting the need for continued research and innovation [4,5,6]. This review provides a comprehensive overview of HMPV, focusing on its virological aspects, epidemiology, clinical features, pathogenesis, diagnostic approaches, treatment options, and preventive strategies. Additionally, emerging research and future directions in HMPV science are discussed, offering insights into ongoing efforts to mitigate its impact.

PERSPECTIVE

Virological aspects of HMPV

HMPV belongs to the Pneumovirinae subfamily and shares genetic and structural similarities with respiratory syncytial virus (RSV). The HMPV genome comprises single-stranded, negative-sense RNA that encodes nine proteins essential for replication, immune evasion, and virulence. These include fusion (F), attachment (G), and matrix (M) proteins, which facilitate host cell entry and viral assembly (Figure 1). Genetic analyses classify HMPV into two major genotypes, A and B, which are further subdivided into sublineages (A1, A2, B1, and B2), with periodic shifts in dominance contributing to global epidemiological patterns [7,8].

The viral life cycle begins with the G protein mediating attachment to host epithelial cells, followed by F protein-mediated fusion. Subsequent replication occurs in the cytoplasm, with progeny viruses budding from the cell membrane. Despite its genetic stability, mutations in key proteins occasionally result in antigenic drift, complicating vaccine and therapeutic development [7]. HMPV has considerable environmental stability and survives on surfaces for extended periods. This resilience contributes to its transmission via respiratory droplets, fomites and direct contact. Understanding these virological properties is crucial for designing effective control strategies [7].

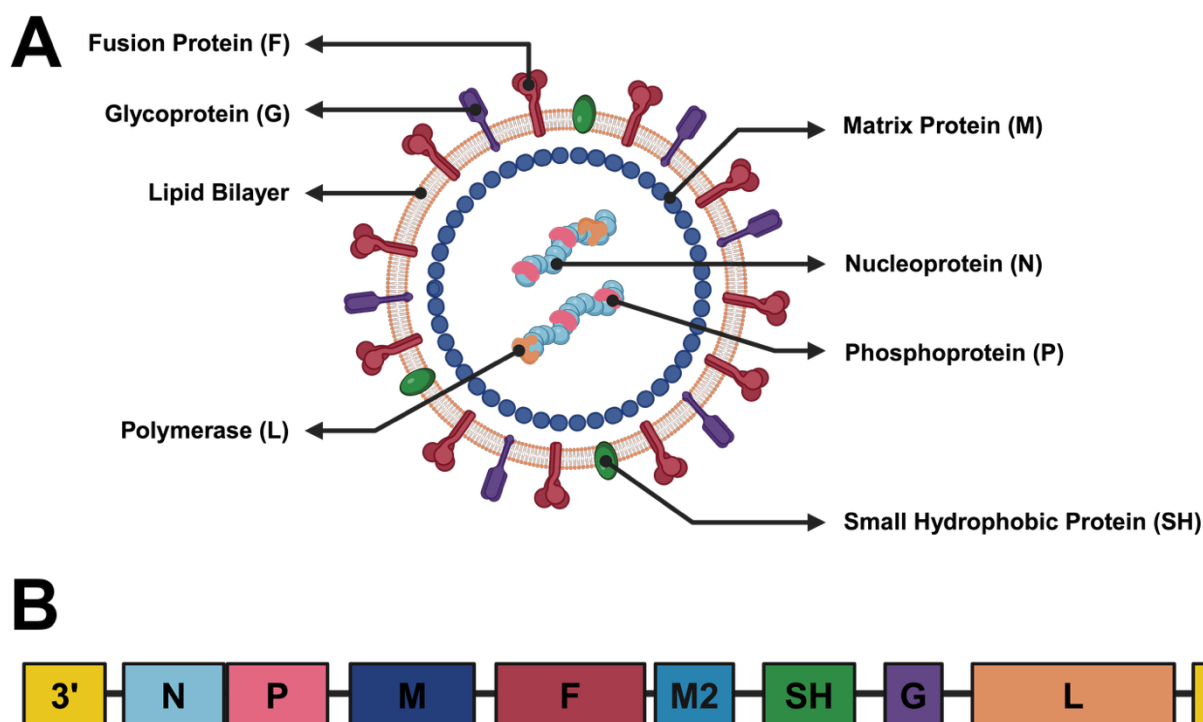


Figure 1. HMPV protein and model structures. The structure of the HMPV model (a) shows the viral proteins encoded by (b) the genome. This figure was created via BioRender.com and was used with permission under a license.

Epidemiology

Since its discovery, HMPV has been detected in populations worldwide, with seasonal peaks occurring during late winter and early spring. Prevalence rates vary geographically, with studies reporting that 5–15% of respiratory infections are attributed to HMPV. Serological data indicate near-universal exposure by the age of five, underscoring its ubiquitous nature [9,10]. In children, HMPV is a leading cause of bronchiolitis and pneumonia, rivaling the clinical significance of RSV. The impacts of outbreaks in long-term care facilities and hospitals on elderly and immunocompromised individuals are highlighted. Risk factors for severe disease include prematurity, chronic lung disease, congenital heart defects, and immunosuppression [10].

HMPV coinfection with other respiratory viruses, such as influenza, RSV, or rhinovirus, exacerbates disease severity and complicates diagnostic efforts. Global surveillance initiatives aim to elucidate the epidemiological trends of viruses and inform public health interventions [10]. Emerging research suggests that environmental conditions play a significant role in HMPV transmission and seasonality. Like many respiratory viruses, HMPV shows increased activity during colder months in temperate regions. Factors such as low ambient temperatures and reduced humidity can increase virus stability and transmission while impairing host mucosal defenses, thus increasing susceptibility to infection. Indoor crowding during the winter months further facilitates person-to-person spread [11].

Climate change may influence HMPV dynamics by altering seasonal patterns, shifting geographic distributions, and increasing the frequency of extreme weather events that impact air quality and respiratory health. For example, increased urban air pollution, particularly fine particulate matter (PM_{2.5}), may exacerbate respiratory conditions and increase susceptibility to viral infections, including HMPV. Warmer winters in certain regions may modify the traditional epidemiological calendar of HMPV, potentially extending the transmission seasons or changing the peak periods [11].

Clinical manifestations

Children, HMPV predominantly affects young children, causing a spectrum of illnesses ranging from mild upper respiratory tract infections to severe lower respiratory tract diseases, such as

bronchiolitis and pneumonia. The common symptoms include fever, cough, rhinorrhea, and wheezing. In severe cases, respiratory distress necessitates hospitalization and supplemental oxygen therapy [12,13].

Adults, while infections in healthy adults are typically mild or subclinical, older adults often experience significant morbidity. Symptoms mirror those in children but may progress to exacerbations of chronic obstructive pulmonary disease (COPD) or heart failure in adults. Community-acquired pneumonia attributed to HMPV underscores its clinical relevance in this demographic group [14,15].

Immunocompromised individuals, in immunosuppressed patients, including organ transplant recipients and individuals receiving chemotherapy, HMPV infections are often severe and prolonged. Complications include secondary bacterial infections, respiratory failure, and increased mortality. Early detection and intervention are critical in these high-risk groups [16,17].

Pathogenesis

HMPV primarily targets the respiratory epithelium and initiates infection through interactions with glycosaminoglycans and cellular receptors. Viral replication induces epithelial cell death, leading to barrier disruption and inflammation. The innate immune response, characterized by cytokine and chemokine release, contributes to tissue damage and disease symptomatology. [18]. Adaptive immunity plays a dual role in the pathogenesis of HMPV. While T cells and neutralizing antibodies are essential for viral clearance, an exaggerated immune response can exacerbate lung injuries. Studies in animal models have highlighted the role of type I interferons and regulatory T cells in modulating disease severity [19]. HMPV employs immune evasion strategies, such as inhibiting interferon signaling and altering antigen presentation, to establish infection. These mechanisms complicate host defense and present challenges in vaccine development [20].

Diagnostics

An accurate diagnosis of HMPV requires a combination of clinical suspicion and laboratory confirmation [21,22]. Common diagnostic modalities include (a) Molecular techniques, reverse transcription-polymerase chain reaction (RT-PCR) is the gold standard for HMPV detection and offers high sensitivity and specificity. Multiplex PCR assays enable the simultaneous detection of coinfecting respiratory viruses, facilitating comprehensive diagnostic evaluation. (b) Antigen detection, rapid antigen detection tests (RADTs) provide point-of-care results but exhibit lower sensitivity than do molecular methods. Recent advancements in immunoassay design have aimed to improve diagnostic accuracy. (c) Serology, while serological assays detect past exposure and immune responses, their utility in acute diagnosis is limited. Paired acute and convalescent serum samples are needed to demonstrate a significant increase in antibody titers. Emerging diagnostic technologies, including next-generation sequencing and biosensors, hold promise for enhancing HMPV detection and monitoring capabilities.

Treatment and prevention

Currently, no specific antiviral therapy is available for HMPV. Management primarily involves supportive care, including oxygen supplementation, hydration, and mechanical ventilation, in severe cases. Inhaled bronchodilators and corticosteroids are used selectively, with mixed evidence regarding their efficacy [22,23]. Ribavirin, a broad-spectrum antiviral, has demonstrated in vitro activity against HMPV but is limited by its high cost and adverse effects. Monoclonal antibodies targeting the F protein are under investigation as potential therapeutic agents and have shown promise in preclinical studies [22,23].

Preventive strategies focus on a combination of personal and institutional infection control measures. These include rigorous hand hygiene, respiratory etiquette (e.g., covering the mouth and nose during coughing or sneezing), and environmental sanitation. Specifically, environmental cleaning refers to the routine disinfection of high-touch surfaces (e.g., bed rails, doorknobs, medical equipment, countertops, and shared electronic devices) via EPA-approved disinfectants that are effective against enveloped viruses. In healthcare settings, protocols often

involve terminal cleaning of patient rooms, frequent air exchange in enclosed areas, and surface cleaning schedules tailored to infection risk [24].

In addition to behavioral and technical measures, regulatory frameworks play a crucial role in preventing the spread of infectious diseases such as HMPV. Public health regulations can mandate surveillance reporting; standardize infection prevention protocols in hospitals, schools, and childcare facilities; and require training healthcare personnel in respiratory hygiene. Furthermore, during outbreaks, regulations may facilitate coordinated responses such as temporary isolation policies, visitor restrictions in healthcare facilities, and enhanced cleaning mandates [23,24].

On a broader scale, national immunization policies and international cooperation, coordinated by organizations such as the WHO, are essential to accelerate vaccine development, allocate funding, and support equitable access once a vaccine becomes available. Regulatory preparedness also includes the ability to swiftly authorize the emergency use of promising antiviral agents or monoclonal antibodies during outbreaks [22,23]. Vaccine development efforts are currently underway, with candidates utilizing live-attenuated, subunit, and vector-based platforms for vaccine development. However, challenges remain, including achieving robust and long-lasting immunity across diverse age groups, particularly infants and older adults, and addressing safety and manufacturing concerns [22].

Emerging research and future directions

Advances in molecular biology, immunology, and computational science are driving a new wave of discoveries aimed at understanding the pathogenesis, immune response, and evolution of HMPV. These developments have opened new avenues for the design of vaccines and targeted therapies, as well as for deepening insights into host-pathogen interactions [24,25,26].

Vaccine development remains a top priority because no licensed vaccine currently exists for HMPV. Encouraging progress has been made with novel platforms, such as nanoparticle-based vaccines, which mimic the structure of native viral proteins and enhance immune responses. These vaccines often incorporate the prefusion form of the F protein, a key target of neutralizing antibodies. In parallel, messenger RNA (mRNA) vaccines, validated during the coronavirus disease 2019 (COVID-19) pandemic, are now being tailored for HMPV, resulting in strong T-cell and neutralizing antibody responses in early preclinical trials. Live-attenuated and vector-based vaccines are also under development, particularly for pediatric use, as they have the potential to induce mucosal immunity; however, safety and efficacy across age groups remain critical concerns [27].

Efforts to develop antiviral therapies have focused on targeted strategies that disrupt viral replication. Small-molecule inhibitors that interfere with viral polymerase activity, fusion processes, or proteolytic cleavage have shown promise in early laboratory studies. RNA-based approaches, such as RNA interference (RNAi) and antisense oligonucleotides, aim to degrade viral RNA within host cells, thereby reducing viral loads and inflammatory responses. In addition to direct-acting antivirals, host-directed therapies are being explored. These factors modulate the host immune response, particularly in severe cases where immune dysregulation contributes to pathology [28].

The integration of systems biology approaches has played an increasingly important role in HMPV research. High-throughput technologies, including transcriptomics, proteomics, and metabolomics, provide detailed maps of host responses to infection. These data reveal biomarkers that predict disease severity and reveal the mechanisms of immune evasion. Precision medicine approaches on the basis of these findings could eventually enable risk-based clinical decision-making. Furthermore, single-cell RNA sequencing and spatial transcriptomics have been used to analyze respiratory tissues, offering unprecedented resolution of cellular dynamics during infection [29].

Another critical area of focus is the evolution of HMPV and its implications for vaccine and drug development. Genetic variability, particularly in F and G glycoproteins, can influence antigenicity and immune recognition. The simultaneous circulation of multiple genotypes and subtypes within the same season adds complexity to control efforts. Therefore, continuous

genomic surveillance is essential to monitor the emergence of new strains and ensure that immunological interventions remain effective [28,30].

The role of coinfection in HMPV pathogenesis is also gaining attention. HMPV frequently co-occurs with other respiratory viruses, such as RSV and influenza, or with bacterial pathogens, such as *Streptococcus pneumoniae*. These coinfections are associated with increased severity of illness and complicated clinical management. Additionally, the respiratory microbiome is being studied for its influence on susceptibility to HMPV and recovery outcomes, offering potential new targets for therapy [31].

Key research priorities include understanding the duration and quality of long-term immunity following HMPV infection or vaccination, elucidating the mechanisms of immune evasion in high-risk populations, and identifying how environmental and climate-related factors influence transmission dynamics. There is also a growing need to develop scalable and affordable diagnostic tools, especially in low-resource settings where HMPV remains underdiagnosed [32]. To accelerate progress, strong collaboration among academia, industry, public health institutions, and regulatory bodies is essential. These partnerships are crucial for translating laboratory discoveries into clinical tools and public health strategies that can reduce the global burden of HMPV.

CONCLUSIONS

Human metapneumovirus is a critical cause of respiratory illness worldwide, particularly in young children, elderly individuals, and immunocompromised individuals. Despite its clinical importance, no specific antiviral treatment or licensed vaccine is currently available, underscoring the urgent need for further research. Advances in molecular diagnostics, immunology, and vaccine development have improved our understanding of the virus. However, significant gaps remain in disease management and prevention. Strengthening global surveillance, investing in vaccines and therapeutic innovations, and enhancing healthcare preparedness are essential steps to mitigate the impact of HMPV on global health.

CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

AUTHOR CONTRIBUTIONS

Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Data Curation, Writing - Original Draft, Writing - Review & Editing, Visualization, Supervision: ANMA.

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