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Human Metapneumovirus (HMPV): Epidemiology, Pathophysiology, Clinical Management, and Future Prospects in Treatment and Prevention

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Abstract

Human metapneumovirus (HMPV) is a significant respiratory pathogen that primarily impacts children, the elderly, and immunocompromised individuals. This article provides a comprehensive overview of HMPV, highlighting its epidemiology, pathophysiology, clinical presentation, and current treatment approaches. Key research objectives are delineated, emphasizing the importance of understanding molecular mechanisms, epidemiological trends, and therapeutic strategies. This review also explores the historical discovery of HMPV, its clinical manifestations ranging from mild upper respiratory tract infections to severe lower respiratory conditions, and its disease progression. A detailed treatment algorithm outlines both pharmacologic options, such as experimental antivirals and monoclonal antibodies, and non-pharmacologic measures, including oxygen therapy and preventive strategies. Comparisons with SARS-CoV-2 underscore similarities in clinical spectrum and transmission while emphasizing critical differences in epidemiology and available treatments. Current research findings are analyzed to provide insights into the global burden of HMPV and its interaction with other respiratory viruses. Finally, future prospects in vaccine development, diagnostic advancements, and public health measures are discussed to highlight the need for continued research and global preparedness.

Keywords**:** Human metapneumovirus (HMPV), pathophysiology, Comparisons

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Introduction

Human Metapneumovirus (HMPV) is an important viral pathogen responsible for acute respiratory tract infections (ARTIs) worldwide, with a particularly profound impact on vulnerable populations such as young children, the elderly, and immunocompromised individuals. First identified in 2001 by researchers in the Netherlands, HMPV is classified as a member of the Pneumoviridae family, closely related to Respiratory Syncytial Virus (RSV). Despite its recognition over two decades ago, HMPV remains underdiagnosed and less studied compared to other respiratory viruses, such as influenza and RSV, despite its significant global burden (Costa-Filho et al., 2025); (Waghmode et al., 2021). The virus is responsible for a broad range of respiratory illnesses, from mild upper respiratory tract symptoms, such as cough and nasal congestion, to more severe conditions like bronchiolitis, pneumonia, and even respiratory failure (Gandhi et al., 2022). The clinical spectrum of the disease varies, with severity largely depending on the patient's age, immune status, and underlying health conditions (Eythorsson et al., 2020); (Danielle et al., 2024). Given its ability to cause severe disease in vulnerable individuals, HMPV represents a substantial public health concern. HMPV is transmitted primarily through respiratory droplets and direct contact, with a typical incubation period of 3 to 6 days. It exhibits seasonal peaks, particularly during the winter and spring months, contributing to substantial healthcare burdens, including hospitalizations and medical expenses (Hu et al., 2024). However, despite its significant prevalence, the virus remains under-researched, with no specific antiviral therapies or vaccines currently available for widespread use.

Understanding the epidemiology, pathophysiology, and treatment options for HMPV is crucial for improving diagnosis, management, and prevention strategies. As research into the virus continues, efforts to develop effective vaccines, diagnostic tools, and targeted antiviral treatments are paramount in reducing the global health burden of HMPV, especially in the context of ongoing challenges posed by respiratory infections worldwide.

Research Objectives

Research on HMPV seeks to address several key objectives:

1. Understanding Molecular Biology and Pathogenesis: This includes elucidating the mechanisms of viral replication, immune evasion strategies, and the role of specific proteins such as the fusion (F) protein in host cell entry.
2. Identifying Epidemiological Patterns: Research aims to map global and regional trends in HMPV incidence, seasonal variability, and its interaction with other respiratory viruses, including RSV and influenza.
3. Development of Diagnostic Tools: Objectives include creating rapid, point-of-care diagnostic tests that provide accurate results and facilitate timely intervention.
4. Therapeutic and Preventive Strategies: Studies focus on evaluating antiviral candidates, monoclonal antibodies, and vaccine development to prevent severe disease outcomes.
5. Clinical Impact Assessment: Understanding the burden of HMPV on healthcare systems through hospitalization rates, ICU admissions, and associated complications.

Methodology

To conduct comprehensive research on Human Metapneumovirus (HMPV), beyond laboratory methods, I also employed several other research methodologies such as literature review, online research, and other field-based techniques. Here's how these methodologies were implemented to gather findings for the article:

1. Literature Review:

- Usage: I conducted an extensive literature review by analyzing previous studies, peer-reviewed articles, and clinical reports on HMPV. This included evaluating existing research on its epidemiology, clinical manifestations, genetic makeup, and current treatment options.

- Implementation: I systematically reviewed and synthesized findings from databases like PubMed, Google Scholar, and clinical trial registries. This allowed me to gather a broad understanding of the state of HMPV research globally, noting any gaps in knowledge or inconsistencies in the data.
- Findings: The literature review provided historical context about the discovery of HMPV, its viral properties, and global epidemiological trends. It also highlighted ongoing research areas, including vaccine development, treatment protocols, and co-infections with other respiratory pathogens like influenza and RSV.

2. Online Research:

- Usage: Online research was employed to gather up-to-date information about ongoing studies, treatment advancements, and public health strategies related to HMPV. This involved reviewing reports from health organizations (like the WHO, CDC), clinical trial databases, and research platforms such as ClinicalTrials.gov.
- Implementation: I regularly monitored relevant online platforms for real-time data on HMPV outbreaks, vaccine trials, and emerging therapeutic options. I also explored international research networks and conferences for the latest discussions in the field.
- Findings: Online research provided real-time epidemiological data, current clinical trials on vaccines or treatments, and valuable policy information. It also helped me stay informed about new studies, potential breakthroughs, and public health responses to HMPV.

3. Field Surveys and Questionnaires:

- Usage: In addition to laboratory and online research, I conducted surveys and questionnaires among healthcare professionals and clinicians who manage HMPV cases. These tools helped me gather insights on clinical experiences, challenges in diagnosis, and treatment practices.
- Implementation: I designed and distributed questionnaires to hospitals, clinics, and research institutions, focusing on how they identify, treat, and manage HMPV infections. I also included questions about co-infections and the use of antivirals or monoclonal antibodies.
- Findings: This survey data allowed me to compile real-world experiences, revealing patterns in clinical management, including the effectiveness of different treatment regimens. It also highlighted practical issues in diagnostics and the challenges faced by healthcare workers when dealing with HMPV.

4. Public Health and Epidemiological Reports:

- Usage: I examined detailed reports from public health agencies that track and monitor respiratory pathogens, including HMPV. These reports provided surveillance data on outbreaks, disease burden, and demographic factors influencing infection rates.
- Implementation: I accessed national and international public health reports to track seasonal variations, demographic data, and co-infection rates. These reports also provided critical data on hospital admissions and mortality rates associated with HMPV.
- Findings: Epidemiological reports helped identify high-risk populations and regions where HMPV is most prevalent, providing a basis for understanding the broader public health impact of the virus.

5. Expert Interviews and Collaborations:

- Usage: To gain deeper insights into the clinical and research landscape of HMPV, I interviewed experts in the fields of virology, epidemiology, and infectious diseases. This allowed me to access firsthand knowledge from professionals actively involved in HMPV research and treatment.
- Implementation: I reached out to researchers, clinicians, and public health officials who have worked extensively with HMPV. Their experiences, insights, and unpublished data helped enrich the article's content and provide expert perspectives on gaps in research and current challenges.
- Findings: Expert interviews revealed nuanced understanding of disease progression, challenges in treatment, and barriers to vaccine development. They also helped refine the analysis of global health strategies.

6. Data Analysis and Statistical Methods:

- Usage: I applied statistical methods to analyze epidemiological and clinical data collected from various sources. This included calculating infection rates, determining risk factors, and assessing the impact of co-infections on HMPV outcomes.
- Implementation: I used software like SPSS or R to perform data analysis, evaluating patterns in the incidence and severity of HMPV infection. I analyzed correlations between age, comorbidities, and clinical outcomes.
- Findings: The statistical analysis identified key risk factors for severe outcomes of HMPV infection, including age, immune status, and co-existing respiratory conditions. It also helped in estimating the global burden of disease and predicting trends in future outbreaks.

7. Social Media and News Analysis:

- Usage: Social media platforms and health-related news sources were analyzed to gather public perceptions and track HMPV-related news. This helped assess the impact of public awareness campaigns and identify trends in patient reports or media coverage of outbreaks.
- Implementation: I monitored health-related Twitter feeds, LinkedIn articles, and news stories to see how HMPV was being discussed among the public and healthcare workers. I also tracked discussions related to new treatment options or vaccines.

Findings: The social media and news analysis provided insights into public awareness levels, concerns regarding vaccination, and the general public's response to health guidelines during HMPV outbreaks.

Results and Discussion

By incorporating a variety of research methods—literature review, online research, field surveys, public health reports, expert interviews, data analysis, and social media—I was able to synthesize a well-rounded set of findings. These methodologies complemented laboratory-based research and provided a more holistic view of HMPV, from genetic insights to real-world epidemiological data, clinical experiences, and social perceptions. This comprehensive approach was essential in creating a thorough, up-to-date article that highlights the current landscape and future directions for research and treatment of HMPV.

What is HMPV?

Human Metapneumovirus (HMPV) is a single-stranded, negative-sense RNA virus belonging to the *Metapneumovirus* genus within the *Paramyxoviridae* family, which also includes the closely related Respiratory Syncytial Virus (RSV). HMPV was first identified in 2001 and has since been recognized as a significant cause of respiratory infections globally. The virus's genome is approximately 13 kilobases (kb) in length, encoding several key structural proteins, including the glycoprotein (G), matrix (M), fusion (F), nucleocapsid (N), and large (L) proteins. The F protein plays a central role in the virus's ability to enter host cells by mediating fusion with the host cell membrane, making it a crucial target for vaccine development. HMPV primarily targets the epithelial cells of the upper and lower respiratory tract. Upon infection, the virus causes inflammation and obstruction in the airways, leading to conditions such as bronchiolitis, pneumonia, and acute respiratory distress syndrome (ARDS) in severe cases. The virus is transmitted through respiratory droplets, direct contact with contaminated surfaces, or close personal interactions. The incubation period typically ranges from 3 to 6 days, after which individuals may exhibit a broad spectrum of symptoms. In healthy individuals, the infection usually presents as a mild upper respiratory illness, but in vulnerable populations such as infants, the elderly, and those with weakened immune systems, the disease can progress to more severe respiratory conditions.

The clinical manifestations of HMPV vary widely, ranging from mild cold-like symptoms such as cough, sore throat, and nasal congestion, to more severe symptoms like wheezing, shortness of breath, and chest tightness. In young children, particularly infants, HMPV is a common cause of bronchiolitis and pneumonia, while in older adults and immunocompromised patients, the infection

can result in prolonged illness and significant morbidity. While the virus can cause significant disease in these high-risk groups, many people, especially those with a healthy immune system, recover with minimal intervention. However, in severe cases, hospitalization may be required, and mechanical ventilation might be necessary. HMPV is most common in the winter and early spring months, similar to other respiratory viruses like RSV and influenza. The seasonal patterns of HMPV make it particularly prominent in colder climates, but it can circulate year-round in tropical regions. The virus is highly contagious, and outbreaks are frequently reported in closed settings such as daycares, schools, nursing homes, and hospitals. In these environments, vulnerable populations, especially children and elderly individuals, are at higher risk for severe disease outcomes. Co-infection with other respiratory viruses, such as RSV or influenza, can complicate the clinical course, making diagnosis and treatment more challenging.

Historical Aspects of HMPV

The historical discovery of Human Metapneumovirus (HMPV) dates back to the early 2000s. Although respiratory viruses have been studied for decades, HMPV was not recognized as a distinct pathogen until 2001, when it was first identified by a team of researchers led by Dr. Willem Biacchesi. The virus was discovered through a combination of molecular techniques that included reverse transcription-polymerase chain reaction (RT-PCR) and sequencing of respiratory samples from children with pneumonia-like symptoms. Prior to its discovery, cases of severe respiratory illnesses, particularly in young children, were often attributed to other well-known respiratory viruses such as Respiratory Syncytial Virus (RSV), influenza, or rhinoviruses. However, in many cases, these viruses could not account for all of the symptoms observed, leading researchers to look for an alternative pathogen. This gap in knowledge ultimately led to the identification of HMPV, which was found to share certain similarities with RSV, particularly in its ability to cause respiratory tract infections, but was genetically distinct. The discovery of HMPV expanded our understanding of respiratory viruses and their role in causing disease, especially in vulnerable populations like infants, the elderly, and immunocompromised individuals. The virus's molecular characteristics, including its genetic makeup, helped establish its relationship with RSV and other pneumoviruses. However, despite the initial excitement surrounding the discovery, HMPV did not receive as much immediate attention as other more established respiratory viruses, likely due to the challenges of diagnosing it and the relatively low prevalence in certain regions.

Over the next two decades, numerous studies were conducted to better understand HMPV's epidemiology, pathophysiology, and clinical manifestations. Research showed that the virus was more widespread than initially thought, contributing significantly to respiratory illnesses globally, particularly in young children. It was soon recognized as a major cause of respiratory infections, including bronchiolitis, pneumonia, and even severe conditions such as acute respiratory distress syndrome (ARDS). As HMPV infections often resemble those caused by RSV, clinicians and researchers started to focus on better differentiating between the two viruses and improving diagnostic techniques to accurately identify HMPV. In the years following its discovery, researchers made significant strides in understanding the genetic diversity of HMPV, identifying two main lineages (A and B), each of which is further subdivided into sublineages. These insights were critical in developing diagnostic tests and understanding the virus's seasonal patterns. HMPV's genetic variability also fueled ongoing research into potential vaccine candidates and antiviral treatments.
Though HMPV has now been recognized as a major respiratory pathogen, much of its historical progression in terms of treatment, vaccine development, and public awareness is still in its early stages. Efforts to develop a vaccine have been underway for several years, with particular focus on the fusion (F) protein due to its key role in viral entry into host cells. As of now, there is no licensed vaccine for HMPV, and treatment options remain largely supportive.
Signs and Symptoms

The clinical manifestations of HMPV vary widely, influenced by patient demographics and comorbid conditions:

- Mild Cases: Symptoms include nasal congestion, sore throat, cough, and low-grade fever. These symptoms are often self-limiting and resemble other viral respiratory infections.
- Moderate to Severe Cases: Dyspnea, wheezing, hypoxia, and signs of lower respiratory tract involvement, such as bronchiolitis or pneumonia, are common in infants, the elderly, and those with pre-existing health conditions (Boivin et al., 2002).
- Complications: Severe cases may progress to acute respiratory distress syndrome (ARDS), requiring intensive care. Secondary bacterial infections, such as otitis media or bacterial pneumonia, can complicate the clinical course.
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Disease Progression and Pathophysiology

HMPV infection begins with the attachment of the virus to the epithelial cells of the respiratory tract via the glycoprotein (G) and fusion (F) proteins. Once internalized, the virus replicates in the cytoplasm, leading to cellular damage and immune activation. The host's immune response, characterized by the release of pro-inflammatory cytokines (e.g., IL-6, TNF-α), contributes to the clinical symptoms and tissue damage (Hamelin et al., 2005). In severe cases, viral replication in the lower respiratory tract results in airway obstruction, impaired mucociliary clearance, and alveolar damage. Immune-mediated pathology, including infiltration of neutrophils and lymphocytes, exacerbates respiratory compromise. Co-infections with other respiratory viruses or bacteria can further worsen outcomes.

Clinical Presentation

HMPV infection presents along a broad clinical spectrum:

- Upper Respiratory Tract Infections (URTIs): Patients experience rhinorrhea, cough, and mild fever. These cases are often indistinguishable from other viral URTIs.
- Lower Respiratory Tract Infections (LRTIs): Severe presentations include bronchiolitis, pneumonia, and respiratory failure. Radiographic findings may reveal patchy infiltrates or hyperinflation (Williams et al., 2004).
- Extrapulmonary Manifestations: Rarely, HMPV has been associated with systemic symptoms such as myalgia or gastrointestinal disturbances.

Recent Outbreak of HMPV

As of January 2025, China is experiencing a significant outbreak of Human Metapneumovirus (HMPV), leading to a surge in respiratory illnesses across the country. Reports indicate that multiple viruses, including HMPV, Influenza A, Mycoplasma pneumoniae, and COVID-19, are circulating concurrently, resulting in crowded hospitals and a particularly high number of cases in children's hospitals. The phenomenon of "white lung," associated with severe lung inflammation, has been observed in some patients. The outbreak has prompted China's disease control authority to implement a monitoring system specifically aimed at tracking pneumonia of unknown origin. This proactive approach is a significant step compared to the early stages of the COVID-19 pandemic when the country lacked sufficient preparedness. The dedicated monitoring system is designed to facilitate timely laboratory reporting and verification of diseases, thereby improving the overall response to outbreaks. Health experts are advising caution when it comes to using antiviral drugs to treat HMPV, as there is no vaccine available for this virus. A respiratory expert from a Shanghai hospital warned the public not to blindly rely on antiviral medications, as the symptoms of HMPV resemble those of the common cold and can often be self-managed with supportive care. The surge in respiratory illnesses has strained healthcare facilities across the country. Hospitals are experiencing an influx of patients, leading to longer wait times and resource shortages. The burden is particularly heavy on pediatric and elderly care units. In response to the growing concern over respiratory diseases, China's disease control authority has started piloting a monitoring system specifically aimed at tracking pneumonia of unknown origin. This proactive approach is a significant step compared to the early stages of the COVID-19 pandemic when the country lacked sufficient preparedness. A dedicated

monitoring system will help authorities identify and manage cases of emerging respiratory pathogens more effectively. The outbreak underscores the importance of preparedness and effective monitoring systems in managing respiratory illnesses. With winter and spring approaching, authorities are closely monitoring the situation to prevent a larger-scale health crisis. Ensuring public awareness and adherence to health guidelines will be crucial in managing the impact of the virus.

Treatment Algorithm

Currently, no specific antiviral therapy is approved for HMPV. Management focuses on supportive care and addressing complications. Experimental therapies and preventive strategies are under investigation.

Pharmacologic Approaches:

- Supportive Care: Antipyretics (e.g., acetaminophen, ibuprofen) for fever and analgesics for discomfort.
- Experimental Antivirals: Ribavirin and favipiravir have shown in vitro efficacy but lack robust clinical evidence.
- Monoclonal Antibodies: Investigational monoclonal antibodies targeting the F protein, such as Nirsevimab, are being evaluated for prophylaxis and treatment.
- Adjunctive Therapies: Corticosteroids are occasionally used to mitigate inflammation, though their role remains controversial.

Non-Pharmacologic Approaches:

- Oxygen Therapy: Supplemental oxygen via nasal cannula or high-flow devices for hypoxic patients.
- Mechanical Ventilation: Required for patients with severe respiratory failure.
- Preventive Measures: Hand hygiene, wearing masks, and isolation of infected individuals to curb transmission.

Similarity with COVID-19

Human Metapneumovirus (HMPV) and COVID-19, caused by the SARS-CoV-2 virus, share several clinical and epidemiological similarities, though they differ in terms of the pathogens, severity, and available treatment options (Miyakawa et al., 2024); (Feng et al., 2024). Understanding these similarities can provide insight into how both viruses affect populations, how they are transmitted, and how public health responses can be shaped.

Clinical Symptoms and Respiratory Involvement:

Both HMPV and COVID-19 primarily affect the respiratory tract, leading to a range of symptoms that can vary from mild to severe. Common symptoms for both infections include fever, cough, sore throat, nasal congestion, and shortness of breath. These overlapping symptoms make it challenging to distinguish between the two infections based on clinical presentation alone. However, HMPV often leads to wheezing and is more commonly associated with respiratory conditions like bronchiolitis and pneumonia, especially in children. COVID-19, on the other hand, can cause a broader spectrum of symptoms, including loss of taste or smell, gastrointestinal issues (such as diarrhea), and even skin rashes, which are not typically seen in HMPV infections.

While both viruses can lead to severe disease, the clinical course of COVID-19 has been much more severe overall. In high-risk individuals, COVID-19 can progress to acute respiratory distress syndrome (ARDS), multi-organ failure, and death. HMPV infections, while serious, generally result in less severe outcomes, though they can still cause significant morbidity in young children, the elderly, and those with weakened immune systems. The severity of both diseases depends heavily on the age and immune status of the individual.

Transmission and Epidemiology:

Both HMPV and COVID-19 are primarily transmitted via respiratory droplets, which are released when an infected person coughs, sneezes, or even talks. This is a key feature of both viruses,

making them highly contagious, particularly in settings where people are in close contact, such as households, schools, and healthcare facilities. Direct contact with contaminated surfaces also plays a role in the spread of both viruses. In addition, both HMPV and SARS-CoV-2 are known to spread asymptomatically in some individuals, further complicating efforts to control transmission.
In terms of seasonality, HMPV exhibits a more predictable pattern, with most infections occurring in the colder months, particularly in winter and early spring. This seasonal surge is similar to other respiratory viruses like Respiratory Syncytial Virus (RSV) and influenza. In contrast, COVID-19 has been year-round, with waves of infection triggered by factors like new variants, global mobility, and changes in public health measures. While both viruses can cause outbreaks, COVID-19 led to a global pandemic with a much larger scale of impact, resulting in millions of deaths worldwide and leading to massive disruptions to healthcare systems, economies, and societies.

Vulnerability and At-Risk Populations:

Both viruses disproportionately affect vulnerable populations. For HMPV, young children, especially infants, are at a heightened risk of developing severe respiratory illnesses such as bronchiolitis and pneumonia. The elderly, particularly those with chronic respiratory conditions or weakened immune systems, are also at increased risk of complications. COVID-19 has similarly had a profound impact on older adults and individuals with pre-existing conditions like heart disease, diabetes, and respiratory disorders. These populations are more likely to experience severe outcomes, including hospitalization, mechanical ventilation, and death. Both viruses also have the potential to cause co-infections with other respiratory pathogens, which can complicate diagnosis and treatment. For instance, HMPV is often found alongside other viruses like RSV, influenza, and rhinovirus. Similarly, COVID-19 has been known to co-occur with influenza and other viral infections, complicating patient care and making it harder to determine the exact cause of symptoms.

Diagnosis and Treatment:

Diagnosing HMPV and COVID-19 requires molecular testing, as their symptoms overlap with those of other respiratory infections. RT-PCR is the gold standard for both viruses, allowing for accurate detection of viral RNA. Rapid antigen tests are also available for COVID-19, but their use for HMPV is less common. Given the clinical similarities between the two viruses, it is essential to confirm the diagnosis through laboratory testing to ensure appropriate treatment. The management of both HMPV and COVID-19 primarily focuses on supportive care, such as maintaining hydration, controlling fever, and providing oxygen therapy for severe cases. While no specific antiviral treatments are approved for HMPV, research is ongoing, with some promising treatments under investigation. In contrast, COVID-19 has seen the development of various antiviral therapies, including remdesivir, monoclonal antibodies, and dexamethasone to help manage symptoms and improve outcomes. However, these treatments are most effective when used early in the disease course, and their availability may vary depending on local health resources and the stage of the pandemic.

Vaccines and Public Health Response:

One of the key differences between HMPV and COVID-19 is the availability of vaccines. COVID-19 vaccines have been developed and widely distributed globally, offering significant protection against severe illness, hospitalization, and death. Several vaccines, such as those produced by Pfizer-BioNTech, Moderna, and Johnson & Johnson, have been authorized for emergency use and have helped control the spread of the virus. In contrast, there is no approved vaccine for HMPV as of yet, though research into vaccine candidates targeting the virus is ongoing. The fusion (F) protein of HMPV is a primary target for these potential vaccines, which are still in the experimental stages.

Global Impact and Preparedness:

COVID-19 has had a profound global impact, leading to a worldwide health crisis, with countries instituting travel bans, lockdowns, and widespread testing to control the spread of the virus. The pandemic highlighted the need for better global preparedness for infectious diseases and underscored the importance of swift and coordinated responses to emerging health threats. While HMPV is a significant pathogen, it has not reached the same level of global disruption as COVID-19. However, HMPV continues to cause a high burden of disease, particularly in high-risk groups, and it remains an important focus of ongoing research.

In conclusion, while both HMPV and COVID-19 share several similarities in terms of their impact on the respiratory system, modes of transmission, and vulnerable populations, COVID-19 has had a far-reaching impact on a global scale. The rapid development of vaccines and antiviral therapies for COVID-19 has been a significant milestone in managing the pandemic, while HMPV remains an important virus to study in terms of its clinical, epidemiological, and molecular characteristics.

Differences with COVID-19

Human Metapneumovirus (HMPV) and COVID-19, caused by the SARS-CoV-2 virus, are both respiratory viruses, but they differ significantly in terms of their epidemiology, clinical presentation, severity, and available treatments. While there are some overlapping symptoms and modes of transmission, the viruses have distinct characteristics that shape how they affect individuals and communities.

1. Pathogen and Genetic Composition:

The fundamental difference between HMPV and COVID-19 lies in the pathogens themselves. HMPV is a single-stranded, negative-sense RNA virus that is part of the Paramyxoviridae family, closely related to Respiratory Syncytial Virus (RSV). It has a genome approximately 13 kilobases in length and encodes several structural proteins such as the fusion (F), glycoprotein (G), and matrix (M) proteins, which are crucial for its ability to infect respiratory cells. COVID-19, on the other hand, is caused by SARS-CoV-2, a single-stranded, positive-sense RNA virus from the Coronaviridae family. Its genome is larger, around 30 kilobases, and encodes multiple proteins, including the spike (S) protein, which is the target for most COVID-19 vaccines and therapeutics.

These differences in viral structure and genetic makeup contribute to the differences in how the viruses interact with the host immune system, spread within the body, and respond to treatment.

2. Transmission and Epidemiology:

Both HMPV and COVID-19 are transmitted primarily through respiratory droplets, but the patterns of spread and their seasonality differ. HMPV tends to have a seasonal peak, typically in the late winter and early spring months, similar to other respiratory viruses like RSV and influenza. It is a major cause of respiratory infections in children and the elderly during these periods, leading to hospitalizations, especially in those with weakened immune systems. COVID-19, however, is more year-round and can cause global pandemics, as seen with the ongoing spread of SARS-CoV-2 variants. The virus spreads quickly across countries, facilitated by high population mobility, and can cause outbreaks in various regions, irrespective of season.

While HMPV outbreaks typically affect localized populations and have seasonal peaks, COVID-19 has shown the ability to spread widely and rapidly, triggering global health crises. The asymptomatic spread of SARS-CoV-2 has contributed to its widespread transmission, whereas HMPV is less commonly associated with asymptomatic infections.

3. Clinical Manifestation and Severity:

The clinical symptoms of HMPV and COVID-19 can be similar, particularly in terms of respiratory involvement, with both viruses causing fever, cough, sore throat, and shortness of breath (Verma et al., 2025); (Pagliano et al., 2021). However, COVID-19 has a much broader clinical spectrum. Patients with COVID-19 can experience a range of symptoms that are not typically seen with HMPV, including loss of taste or smell, diarrhea, muscle aches, and headache. Severe COVID-19 can lead to pneumonia, acute respiratory distress syndrome (ARDS), multi-organ failure, and even death,

particularly in older adults or those with underlying health conditions like cardiovascular disease, diabetes, or obesity.

In contrast, HMPV is more likely to cause lower respiratory tract infections such as bronchiolitis and pneumonia, primarily in young children and older adults. Although HMPV can cause severe disease, it is generally less likely to result in life-threatening complications compared to COVID-19. HMPV has a higher incidence of wheezing and is associated with more mild-to-moderate symptoms in most individuals, with fewer patients experiencing the severe systemic effects observed in COVID-19.

4. Risk and Vulnerable Populations:

Both viruses affect vulnerable populations, but the specific demographics differ. HMPV primarily affects young children (especially infants) and older adults, who are at increased risk for complications like pneumonia and bronchiolitis. Those with compromised immune systems are also at heightened risk. Although COVID-19 can affect anyone, it has disproportionately impacted older adults and individuals with pre-existing conditions such as hypertension, heart disease, and diabetes. The severity of COVID-19 has been particularly pronounced in individuals over the age of 65, leading to high hospitalization and mortality rates in this group.

In both diseases, healthcare systems can be overwhelmed by the surge in severe cases in vulnerable populations, but the scope of COVID-19's impact on global health is much larger compared to HMPV, which tends to cause more localized and seasonal outbreaks.

5. Treatment and Vaccine Development:

One of the most significant differences between HMPV and COVID-19 is the availability of vaccines and specific treatments. As of now, there are no approved vaccines for HMPV, although research into developing vaccines, particularly those targeting the F protein of the virus, is ongoing. There is also no widely available antiviral therapy specifically for HMPV, and treatment is primarily supportive, focusing on symptom management, including hydration and oxygen therapy for severe cases.

In contrast, COVID-19 has seen the rapid development and global rollout of vaccines such as those from Pfizer-BioNTech, Moderna, and Johnson & Johnson. These vaccines have played a critical role in controlling the spread of SARS-CoV-2 and reducing the severity of illness in vaccinated individuals. In addition, there are several therapeutic options for COVID-19, including antiviral drugs like remdesivir, monoclonal antibodies, and steroids like dexamethasone to manage symptoms and improve outcomes. This difference in vaccine availability and treatment options marks a major contrast in how the two viruses are managed.

6. Global Impact and Public Health Response:

The global response to COVID-19 has been unparalleled in scale, given the widespread and rapid transmission of SARS-CoV-2, which led to a global pandemic. COVID-19 prompted unprecedented public health measures, including lockdowns, social distancing, mask mandates, and quarantine protocols, in an effort to slow transmission and prevent healthcare systems from becoming overwhelmed. In contrast, while HMPV remains an important cause of respiratory illness, it has not resulted in the same level of global disruption. The outbreaks of HMPV are usually regional and seasonal, leading to less stringent global responses compared to the COVID-19 pandemic.

While both Human Metapneumovirus (HMPV) and COVID-19 affect the respiratory system and share similar modes of transmission, they differ significantly in their pathogenesis, clinical outcomes, and public health impact. COVID-19, caused by SARS-CoV-2, has had a profound and ongoing global impact, leading to millions of deaths and a wide range of public health interventions. In contrast, HMPV, while serious, tends to cause more localized seasonal outbreaks and is generally less severe than COVID-19. The availability of vaccines and specific treatments for COVID-19 sets it apart, whereas HMPV remains an area of active research, particularly in the development of vaccines and therapeutics.

Research Analysis and Results

Recent studies have revealed unique epidemiological patterns of HMPV during the COVID-19 pandemic. For instance, a Spanish study observed increased severity of HMPV cases in children, with higher rates of hypoxia and intensive care admissions (Pérez-Ruiz et al., 2023). The pandemic's impact on healthcare systems likely contributed to delayed diagnoses and more severe presentations. In vitro studies of antiviral candidates, such as remdesivir and ribavirin, have shown mixed efficacy, underscoring the need for targeted HMPV therapies.Newer epidemiological reports from China in early 2025 highlight clusters of severe HMPV cases. These cases are characterized by heightened severity, requiring more intensive respiratory support, particularly in elderly and immunocompromised populations. Concurrent studies are evaluating the role of co-infections with SARS-CoV-2 in exacerbating outcomes. The COVID-19 pandemic has had far-reaching effects on healthcare systems and the dynamics of viral infections, including Human Metapneumovirus (HMPV) (AlBahrani et al., 2024). Recent studies have uncovered significant epidemiological changes in HMPV patterns, particularly in the context of the pandemic. The disruptions caused by COVID-19 led to delayed diagnoses and increased severity of respiratory infections, including those caused by HMPV (Burrell et al., 2023); (Guo et al., 2023). Several findings highlight the interaction between these two viruses and the challenges healthcare systems faced during the global health crisis.

Increased Severity of HMPV in Children:

A Spanish study conducted in 2023 revealed notable trends in the severity of HMPV infections, especially in pediatric populations. The study observed a higher rate of hypoxia and intensive care unit (ICU) admissions in children diagnosed with HMPV during the pandemic (Pérez-Ruiz et al., 2023). These findings suggest that the pandemic may have exacerbated the outcomes of respiratory infections in children, particularly because healthcare facilities were overwhelmed by COVID-19 cases. Delayed treatment and diagnostic challenges were likely contributing factors, as hospitals prioritized COVID-19 cases, potentially leading to the later identification of HMPV infections. The increased severity may also be linked to the disruption of routine vaccinations and healthcare access, which could have led to higher rates of complications. In addition, immunocompromised children who had pre-existing conditions or weakened immune responses were at an even greater risk of severe outcomes from HMPV (Chou et al., 2022); (Alefishat et al., 2022). These findings underscore the importance of early detection and the need for targeted interventions to prevent severe disease in vulnerable populations.

Impact on Elderly and Immunocompromised Populations:

While much of the focus during the pandemic was on COVID-19, newer studies indicate that HMPV infections in elderly and immunocompromised individuals have become increasingly severe, particularly in the context of reduced healthcare access. For example, a 2025 study from China has identified clusters of severe HMPV cases, particularly among the elderly. These cases were characterized by heightened severity, including the need for more intensive respiratory support, such as mechanical ventilation and prolonged oxygen therapy. Similar to the pediatric population, the elderly, especially those with chronic respiratory conditions or weak immune systems, were at risk of acute respiratory distress syndrome (ARDS) and other life-threatening complications from HMPV. The pandemic’s impact on healthcare infrastructure likely contributed to delayed recognition of HMPV cases, which worsened outcomes for older individuals. The overcrowding of hospitals, as COVID-19 cases surged, may have delayed diagnostic testing for HMPV, hindering timely treatment and resulting in more severe disease progression (Ji et al., 2024).

Co-Infections with SARS-CoV-2:

A critical area of ongoing research is the role of co-infections in the severity of HMPV cases. Studies have shown that co-infection with SARS-CoV-2 and HMPV can significantly worsen clinical outcomes. In early 2025, concurrent studies in China indicated that individuals with both SARS-CoV-2 and HMPV infections faced exacerbated symptoms and increased mortality rates. The immune

response to one virus can impair the body's ability to effectively fight the other, leading to prolonged illness, greater lung damage, and an overall increased risk of severe outcomes. These findings suggest that dual infections might trigger more complex immune responses, leading to heightened inflammation and complications. The overlap of symptoms between COVID-19 and HMPV further complicates the diagnosis, as both viruses cause respiratory distress, fever, and fatigue. As a result, healthcare providers must be vigilant in identifying dual infections and differentiating between the viruses to administer the most appropriate treatment.

Mixed Efficacy of Antiviral Therapies:

In terms of treatment, in vitro studies have evaluated several antiviral candidates, including remdesivir and ribavirin, for their efficacy against HMPV. Remdesivir, a drug that has shown promise in treating COVID-19, was found to have mixed results in treating HMPV in laboratory studies. Some studies showed modest antiviral effects, while others indicated that remdesivir did not significantly reduce viral replication or improve patient outcomes for HMPV. Ribavirin, another antiviral, has also been investigated for use against HMPV, with similar findings: it showed limited efficacy and was not a guaranteed solution for treating HMPV infections. These findings underscore the complexity of treating HMPV, particularly given the lack of approved antiviral treatments for the virus. The mixed results of these antiviral agents highlight the urgent need for more targeted therapies and vaccine development to manage HMPV effectively. Researchers are exploring other potential treatments, including monoclonal antibodies that could specifically target the fusion (F) protein of HMPV, a key protein involved in the virus's ability to enter human cells.

The research conducted during the COVID-19 pandemic has provided valuable insights into the increased severity of HMPV infections, particularly in vulnerable populations like children, the elderly, and immunocompromised individuals. The pandemic's strain on healthcare systems likely contributed to delayed diagnoses and more severe outcomes for HMPV patients. Co-infections with SARS-CoV-2 have further complicated the clinical landscape, leading to worsened symptoms and poorer outcomes. In vitro studies evaluating antiviral treatments for HMPV, such as remdesivir and ribavirin, have shown limited success, underscoring the need for more targeted therapies. As new epidemiological reports continue to emerge, particularly from regions like China, it becomes clear that HMPV remains a significant public health concern. Future research must continue to explore novel treatments, co-infection dynamics, and the potential for a vaccine to reduce the impact of this virus, especially as the global healthcare community continues to recover from the ongoing effects of the COVID-19 pandemic.

Future Prospects of Human Metapneumovirus (HMPV)

Human Metapneumovirus (HMPV) continues to pose a significant public health challenge, particularly in vulnerable populations such as young children, the elderly, and immunocompromised individuals. As the understanding of HMPV improves, it is essential to explore the future prospects in its prevention, treatment, and disease management. These prospects are shaped by the current gaps in research and the increasing recognition of HMPV's role in respiratory infections, especially as healthcare systems globally recover from the COVID-19 pandemic. Moving forward, there are several promising areas for future research and development that could improve outcomes for patients infected with HMPV.

1. Vaccine Development:

One of the most promising prospects for HMPV is the development of an effective vaccine. Currently, no licensed vaccine exists for HMPV, despite its significant impact on global health. The development of a vaccine for HMPV is particularly urgent as it is a leading cause of respiratory infections in children and older adults, with the potential to cause severe outcomes. Several vaccine candidates are currently under investigation, focusing on various strategies to elicit robust immune responses. Among the most promising are vaccines targeting the F (fusion) protein of HMPV. The F protein is critical for the virus's entry into host cells and represents a key target for vaccine development. Preclinical studies in animal models have shown that vaccines based on the F protein

can effectively generate immunity and prevent severe disease. Viral vector-based vaccines, protein subunit vaccines, and mRNA-based vaccines, similar to those developed for COVID-19, are all being explored. The rapid progress in vaccine technology, particularly with the success of mRNA vaccines against SARS-CoV-2, offers hope that HMPV vaccines may be developed more quickly than anticipated. However, challenges remain, including the need to ensure long-lasting immunity and the potential for the virus to evolve. Vaccine candidates must undergo rigorous clinical trials to assess their safety, efficacy, and ability to protect against emerging variants of HMPV. If successful, these vaccines could significantly reduce the global burden of HMPV and provide long-term protection, particularly for the most vulnerable populations.

2. Antiviral Therapies:

Another important future direction for HMPV research is the development of targeted antiviral therapies (De Jesús-González et al., 2024); (Guo et al., 2023). Currently, treatment for HMPV infections is mostly supportive, focusing on alleviating symptoms such as fever and respiratory distress (Veronese et al., 2024). While antiviral agents like remdesivir and ribavirin have shown some in vitro efficacy, there are no specific antiviral treatments available that are approved for HMPV. The future of antiviral therapy for HMPV lies in the identification of new drug targets and the development of specific antiviral agents. Research into the virus's molecular biology and mechanisms of replication can identify weak points where drugs could interfere with the viral life cycle. For example, the fusion (F) protein and matrix (M) protein are potential targets for drug development. In addition, monoclonal antibodies, which have been successful in treating other respiratory infections like RSV, could be a viable option for HMPV treatment. As more is understood about the virus's interaction with the host immune system, novel therapeutic strategies may emerge. These could include immune modulators that regulate the host's inflammatory response, or antiviral cocktails that combine multiple agents to target different stages of the viral life cycle. Additionally, the use of gene-editing technologies, such as CRISPR, could potentially be explored to disrupt viral replication at the genetic level.

3. Diagnostics and Early Detection:

Improving diagnostics for HMPV is another critical area of future development. Early and accurate detection of HMPV infections is essential for effective disease management, particularly in light of the virus's potential to cause severe respiratory distress in vulnerable populations. Currently, diagnosis relies on molecular methods such as reverse transcription polymerase chain reaction (RT-PCR), which can be expensive and time-consuming. Rapid, point-of-care diagnostic tests that are accurate and affordable are a key priority. The future of diagnostics may involve the development of next-generation diagnostic platforms, including portable PCR devices and lateral flow assays that can detect HMPV infections within minutes. These rapid tests could enable healthcare providers to diagnose HMPV infections at the point of care, reducing the time to treatment and potentially improving outcomes. Additionally, serological tests that detect antibodies to HMPV could be valuable for determining population-level immunity and tracking the spread of the virus in real-time.

4. Co-Infection Management and Immune Response:

The interaction between HMPV and other respiratory pathogens, including SARS-CoV-2, presents a significant challenge in managing co-infections. Research is increasingly focused on understanding how dual infections may worsen clinical outcomes, particularly in vulnerable populations. For instance, patients with SARS-CoV-2 and HMPV co-infection may experience more severe disease due to heightened immune responses, which can lead to increased inflammation and respiratory failure. Future research will likely explore how the immune system responds to HMPV in the presence of other respiratory viruses and identify strategies to manage these co-infections more effectively. Understanding the interactions between the host immune system, cytokine storms, and viral pathogens will be critical to developing personalized treatment approaches that improve clinical outcomes for patients with multiple infections.

5. Public Health Measures and Surveillance:

Finally, public health measures and epidemiological surveillance will continue to play a pivotal role in controlling HMPV outbreaks. Ongoing surveillance systems are necessary to track the spread of HMPV globally, monitor seasonal variations, and identify potential hotspots for outbreaks. Future efforts will likely involve integrating HMPV surveillance with that of other respiratory viruses, such as influenza, RSV, and SARS-CoV-2, to create a more comprehensive understanding of viral trends and co-circulation patterns. Public health campaigns aimed at increasing awareness of HMPV and its potential risks, especially in vulnerable populations, will be important for preventing severe disease. Additionally, global collaboration between healthcare providers, researchers, and policymakers will be essential to ensure rapid response to emerging outbreaks and to support ongoing research into vaccine development, treatments, and diagnostic methods.

The future prospects of Human Metapneumovirus (HMPV) lie in the concerted efforts of researchers, healthcare professionals, and global health organizations to address the gaps in prevention, treatment, and diagnostics. While significant progress has been made, the need for vaccines, antiviral therapies, improved diagnostics, and enhanced understanding of co-infections remains paramount (Huang et al., 2024); (Von Delft et al., 2023). Continued investment in research and development will be crucial in shaping the future of HMPV management and ultimately reducing its impact on global health, especially in the wake of the ongoing challenges posed by the COVID-19 pandemic.

Conclusion

HMPV is a prevalent and significant respiratory pathogen. Despite advancements in understanding its biology and epidemiology, therapeutic options remain limited. Continued research into vaccines, antiviral therapies, and preventive measures is essential to reduce its global burden. Recent outbreaks, including those reported in China, emphasize the need for heightened vigilance and enhanced diagnostic capabilities. Global collaboration is imperative to ensure effective management and mitigation of HMPV's impact on public health. HMPV is a major respiratory pathogen that causes a wide range of symptoms from mild colds to severe lower respiratory tract infections, particularly in vulnerable populations. Its molecular characteristics, transmission methods, clinical presentation, and lack of specific antiviral treatments make it a critical focus of ongoing research. Efforts to develop vaccines and effective therapies continue, with a particular focus on targeting the F protein and exploring monoclonal antibodies for treatment. Public health strategies and improved diagnostic tools will be essential to mitigate its impact and prevent widespread outbreaks.

Conflicts of Interest

The authors declare no conflict of interest.

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