



Perspective

Human metapneumovirus (hMPV): A chronological review of a growing respiratory threat

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Abstract

Human metapneumovirus (hMPV) has been recognized as a significant contributor to acute respiratory tract infections (ARTIs), particularly in young children, elderly individuals, and immune-compromised patients since its discovery in 2001. With clinical manifestations similar to respiratory syncytial virus (RSV), hMPV has been associated with bronchiolitis, pneumonia, and asthma exacerbations, often leading to hospitalizations. Over the years, genetic studies, epidemiological surveillance, and diagnostic advancements have enhanced our understanding of hMPV's impact. This article provides a chronological review of key research developments on hMPV, emphasizing its prevalence, clinical implications, genetic diversity, and potential therapeutic approaches.

Keywords: Hman metapneumovirus, Acute respiratory infections, Respiratory infections, Pneumonia

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1. Background and Future

1.1. Genetic evolution and seasonal trends (2015–2024)

Recent research has deepened our understanding of hMPV's seasonal patterns, genetic diversity, and emerging lineages. Surveillance studies conducted between 2021 and 2024 confirmed hMPV's widespread circulation and its role in acute respiratory infections in both children and adults.

1.2. Epidemiological studies from different regions

1. India (2021–2024)

- A study in Puducherry found that hMPV was detected in 9.6% of respiratory infections during an outbreak from November 2022 to March 2023.
- The virus was most prevalent in infants under one year old, with common symptoms including wheezing (67%) and seizures (6.9%).
- Genetic sequencing identified the A2.2.1 and A2.2.2 lineages, highlighting ongoing viral evolution (Devanathan N, Philomenadin FS et al).¹

2. Nepal (2023)

- A study conducted at Kanti Children's Hospital found that hMPV was the most common respiratory virus (13.3%) detected among children with ARIs. The virus was most prevalent in children under three years old, causing pneumonia (42.9%) and bronchiolitis (28.5%).
- The highest infection rates were recorded in late winter and early spring (Lamichhane J, Upreti M et al).²

3. Thailand (2016–2017)

- Surveillance in Bangkok examined 8,842 nasopharyngeal samples and identified hMPV in 3.6% of cases, often co-circulating with RSV and influenza virus. The rainy season (June to September) was associated with peak hMPV infections. Predominant hMPV genotypes included A2, B1, and B2, aligning with global strain patterns (Thongpan I, Suntronwong N et al).³

4. Eastern Uttar Pradesh, India (2022)

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- a. In a study conducted at ICMR-RMRC, Gorakhpur, hMPV was detected in 4% of pediatric ARI cases, with one in four positive cases resulting in death. Phylogenetic analysis showed similarities with Singapore and USA hMPV isolates, indicating international strain circulation. (Deval H, Kumar N et al).⁴

1.3. Early identification and virological characterization (2001–2006)

The human metapneumovirus was first described in 2001, when it was identified as a new member of the Pneumovirinae subfamily, closely related to avian metapneumovirus type C. This discovery marked the beginning of an era of intensive research on the virus's structure, transmission, and pathogenicity.

Early studies revealed that hMPV shares several similarities with RSV, but differs in gene order and lacks nonstructural genes. Researchers also identified two genetic subgroups (A and B) and four subtypes, which contributed to seasonal winter outbreaks that overlapped with RSV epidemics.

Epidemiological studies in hospitalized children showed that hMPV was detected in 9.7% of cases, making it one of the leading causes of ARTIs after RSV (37%), rhinovirus (18%), influenza virus (14.5%), adenovirus (9%), and parainfluenza virus (5%). Despite its prevalence, hMPV was difficult to isolate in cell culture, limiting diagnostic options to TS-CRP assays, until the introduction of direct antigenic tests improved rapid diagnosis. (Freymuth F, Vabret A et al).⁵

1.4. Expanding epidemiological understanding and clinical relevance (2007–2014)

By the late 2000s, research confirmed that hMPV was a globally circulating respiratory virus, responsible for 5–10% of hospitalizations due to ARTIs in children. The virus was shown to cause infections early in childhood, but reinfections were common throughout life, particularly in older individuals. Molecular diagnostic methods, such as reverse transcriptase polymerase chain reaction (RT-PCR), became the preferred detection tool, replacing unreliable cell culture techniques. This period also saw the development of experimental models to study hMPV pathogenesis and evaluate potential treatments, such as ribavirin, which showed antiviral activity in vitro and in animal models (Deffrasnes C, Hamelin ME et al).⁶ Research also revealed that hMPV infections were often indistinguishable from RSV infections, contributing to bronchiolitis, pneumonia, and asthma exacerbations in children (Panda S, Mohakud NK et al).⁷ Although a few vaccine candidates showed promise in preclinical studies, none were commercially available. Furthermore, retrospective serological studies indicated that hMPV had likely been circulating in human populations for over 50 years, further solidifying its global impact. The virus

was now recognized as an important cause of respiratory infections in both children and adults, with severe disease outcomes in elderly and immunocompromised patients (Haas LE, Thijsen SF et al).⁸

1.5. On-going challenges and future directions

Despite over two decades of research, no vaccine or targeted antiviral treatment for hMPV has been approved for clinical use (Kumar P, Srivastava M).⁹ The development of immunogens and therapeutic strategies is ongoing, with promising results in laboratory studies. One of the most pressing challenges in hMPV research is understanding the pathogenesis and immune response, which will be critical for vaccine development (Kahn JS study).¹⁰ Additionally, the virus's genetic evolution and global spread highlight the need for continuous surveillance and updated diagnostic methods.

2. Conclusion

Since its discovery in 2001, human metapneumovirus has emerged as a leading cause of respiratory infections worldwide, particularly affecting young children, the elderly, and immunocompromised individuals. The virus exhibits seasonal outbreaks, genetic diversity, and a clinical spectrum ranging from mild upper respiratory infections to severe pneumonia. Key advancements in molecular diagnostics (RT-PCR), genetic characterization, and epidemiological studies have enhanced our understanding of hMPV. However, the lack of an approved vaccine or antiviral therapy remains a significant challenge. Moving forward, expanded surveillance, improved diagnostic capabilities, and accelerated vaccine research will be critical to mitigating the impact of hMPV on global public health. As new viral strains emerge, continued efforts in monitoring genetic variations, assessing clinical outcomes, and exploring effective therapeutic strategies will be essential in managing hMPV-related respiratory diseases.

3. Conflict of Interest

None.

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