UNRAVELING THE IMPACT OF HUMAN METAPNEUMOVIRUS (HMPV) ON PEDIATRIC RESPIRATORY HEALTH IN INDIA

ABSTRACT

Human metapneumovirus (hMPV) is an emerging respiratory pathogen first identified in 2001, belonging to the *Paramyxoviridae* family. It predominantly affects pediatric populations, leading to a spectrum of respiratory illnesses ranging from mild upper respiratory infections to severe lower respiratory conditions such as bronchiolitis and pneumonia. While hMPV can infect individuals of all ages, young children and immunocompromised individuals are particularly vulnerable, often requiring hospitalization. The virus is classified into two primary subtypes, A and B, with genetic variations influencing disease severity and epidemiological trends.In India, recent surveillance has identified confirmed cases of hMPV, emphasizing the need for enhanced public health monitoring. The Indian Council of Medical Research (ICMR) has reported cases in Karnataka, underscoring the virus's circulation in the country. Despite its clinical significance, no specific antiviral treatment or vaccine is currently available, and management remains supportive, focusing on symptom relief and respiratory support in severe cases. This study explores the epidemiology, clinical manifestations, diagnostic methods, and treatment strategies for hMPV, with a particular focus on its impact on pediatric respiratory health in India. Understanding the virus's prevalence and disease burden is essential for guiding public health policies and developing targeted preventive measures.

Keywords: Human metapneumovirus, hMPV, India, Pediatric respiratory disease

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1. INTRODUCTION

Human metapneumovirus (hMPV) was first identified and isolated in 2001 by van den Hoogen et al. from children with respiratory infections.[1] Since then, it has been found worldwide, primarily circulating in winter in temperate regions. The symptoms of hMPV are similar to those of respiratory syncytial virus, ranging from mild upper respiratory issues to severe lower respiratory tract diseases that may require hospitalization.[2]

While hMPV can affect all age groups, it especially impacts children, accounting for many hospitalizations due to lower respiratory infections. Common diagnoses in hospitalized children include bronchiolitis and pneumonia, with some cases needing intensive care. Most children with hMPV are treated on an outpatient basis, but no population-based studies have been done on the incidence and effects of hMPV in unselected children. [2,3]

2. HUMAN METAPNEUMOVIRUS hMPV

2.1 Discovery and classification of hMPV

Human metapneumovirus (hMPV) is an RNA virus from the Paramyxoviridae family, first described in the Netherlands. It has been found in samples as old as 50 years, indicating it may have been affecting humans for more than five decades. The virus is challenging to isolate in cell cultures, which has delayed its recognition as a common cause of respiratory infections in children. Over the past few years, hMPV has been identified in several countries, including Canada, Finland, and the United States. It is genetically similar to avian pneumovirus and respiratory syncytial virus (RSV), sharing traits like infectivity and illness types. The purpose of recent studies is to assess hMPV's role in respiratory infections among infants in Spain and compare its epidemiological characteristics to RSV over three years. [4,5,6]

hMPV was first discovered in 28 nasopharyngeal aspirates (NPAs) taken from children under 5 years of age with respiratory tract infections over a 20-year period in the Netherlands.7 The virus produced cytopathic effects similar to respiratory syncytial virus and replicated very slowly in monkey tertiary kidney cells. The supernatant of infected cells, detected by electron microscopy, contained paramyxovirus-like pleomorphic particles with a diameter of 150–600 nm and short protrusions with a length of 13–17 nm (Figure 1[36]). Unlike other paramyxoviruses such as RSV and parainfluenza, the nucleocapsid was not evident. It does not agglutinate red blood cells and is inactivated by chloroform. Various respiratory virus-specific primers used in the reverse transcription reactions did not yield promising results. Based on morphological characteristics and genome structure, it was classified into the Paramyxoviridae, Pneumoviridae, and Metapneumovirus genus. [8]

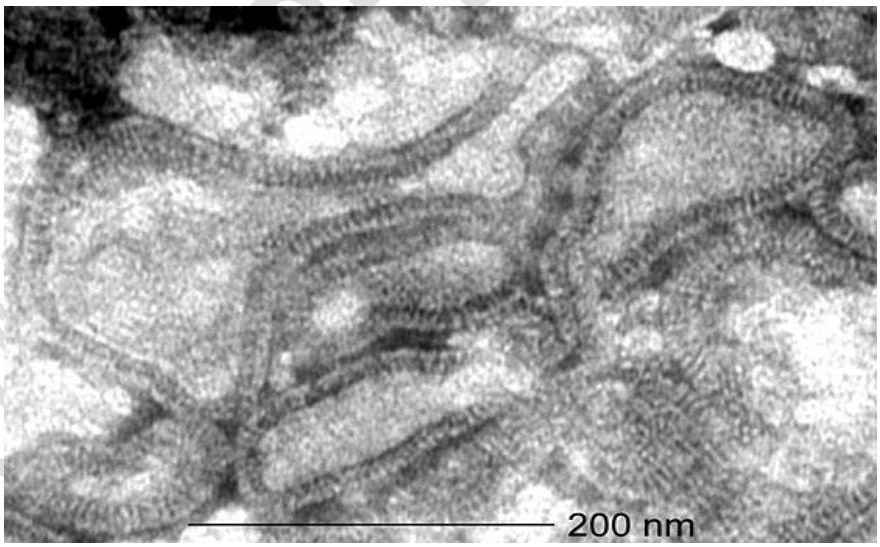

Figure 1 Electron micrograph of hMPV particles

2.2 Evolution of hMPV

The evolution the hMPV based on the age group, Number of cases and complications according to the region affected was given in table 1. [33,34,35]

Table 1 Evolution of hMPV

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Year Range	Age Group	Number of Cases (Estimated)	Complications	Countries/Regions Affected
2001	All Ages	Initial identification	Respiratory infections in children	Netherlands
2002 - 2010	Young Children (<5 years)	Sporadic reports	Mild to moderate respiratory illness	Global
2011 - 2019	Children (<5 years), Older Adults	Increasing numbers	Bronchitis, pneumonia	Global
2020	Primarily Children	Decreased due to COVID focus	Mild symptoms	Global
2021	Infants and Young Children	Emerging cases	Increased hospitalizations	Global
2022	Children (<5 years)	~5-10% of pediatric hospitalizations	Severe respiratory illness	USA, UK, India
2023	Infants and Young Children	Notable increase	Severe respiratory infections requiring hospitalization	Northern China, India
2024	Predominantly Infants	~17 confirmed cases by January	Bronchiolitis and pneumonia	India
January 2025	Various age groups	Total of ~17 confirmed cases	Cough, fever, wheezing	India

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2.3 Genotypes of hMPV

"HMPV and RSV genomic tissue are similar, but HMPV has no NS1 and NS 2, and the HMPV Antissen RNA genome is RSV (3'-N-P-M-F-M2-S H-G-L-5')" (given in figure 2).[9] Especially the bird meteemovirus A, B, and C are genetically related to human mete virus (HMPV). The two major genetic lineages of hMPV, designated subtypes A and B, with their respective subgroups A1/A2 and B1/B2, were identified by phylogenetic analysis. Compared with hMPV-A, subtype B of the virus was associated with more lasting cough and general respiratory complaints, according to genotyping based on F and G gene sequences.[10] hMPV infects cells lining the airways in the nose and lungs. The glycoprotein

(G) of hMPV interacts with heparan sulfate and other glycosaminoglycans as well as enables it to attach to target cells. To ensure fusion of the viral envelope with the cell membrane in a pH-independent manner, presumably within endosomes, the hMPV fusion protein (F) encodes an RGD (Arg-Gly-Asp) motif that binds RGD-binding integrins as cellular receptors. [11]

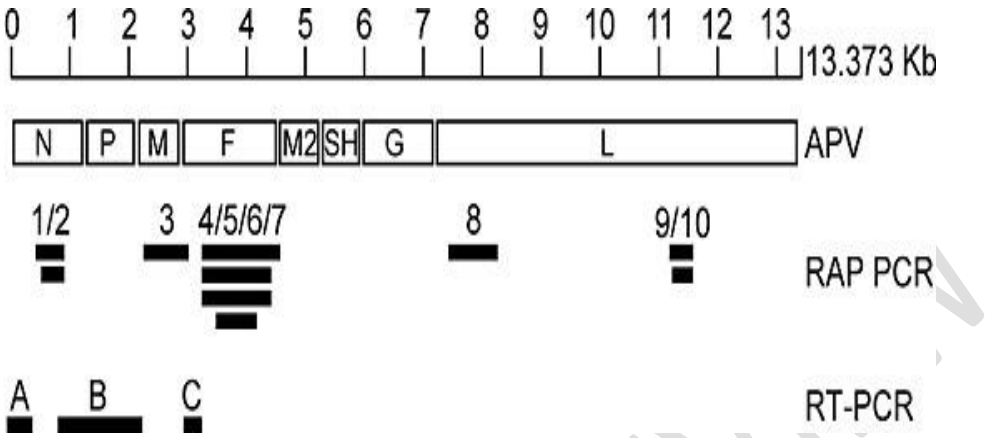

Figure 2 Schematic representation of genomic fragments obtained from hMPV[37]

2.4 Prevalence of hMPV

hMPV is most commonly detected in children, mainly under two years of age, with a median age of 22 months. According to seroprevalence studies, between 5 and 10 years of age, 90 to 100% of children are infected with hMPV. Acute lower respiratory tract infections due to hMPV account for 5–10% of pediatric hospitalizations. Overall, infants infected with hMPV are three times more likely to be hospitalized compared with infants aged 6 months to 5 years.[12] Different genotypes of the virus or insufficient immunity to the initial infection can cause reinfection. Although adults usually have only mild flu symptoms, complications can occur in older adults, people with weakened immune systems, and people with chronic lung disease. [13]

2.5 Clinical Manifestations of hMPV

When the hMPV enters the body, it infects the cells of the respiratory tract, including the mouth, nose, and throat. The immune system responds whenever these cells become infected, producing symptoms like pain, low-grade fever, cough, runny nose, headache, and sore throat. The disease which can affect the bronchial tubes and large airways in some people. The spread of the virus can cause coughing and wheezing. Children under one year of age may experience fever and weight loss. In certain patient populations, hMPV can cause severe illness requiring hospitalization. This includes patients with weakened immune systems, cardiac disease, or respiratory conditions. These patients are more likely to develop acute respiratory failure requiring high-flow supplemental oxygen. In some cases, their condition may worsen and may need to be placed on a ventilator. Patients should be continuously observed in the intensive care unit.[14]

2.6 Diagnosis of hMPV

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The different Diagnostic technique for hMPV were described in the table 2 with the details of diagnosis method. [15,16,17]

Table 2 Diagnostic technique for hMPV

Diagnostic Technique	Details
Cell Culture	- hMPV reproduces ineffectively in conventional cell cultures. - Mild cytopathic effects observed after 10-11 days of incubation. - Cell lines used: monkey tertiary kidney cells, Vero cells, LLC-MK2 cells, BEAS-2B cells, A549 cells, HepG2 cells.
Shell Bottle Method	- Quick method involving centrifugal separation and fluorescent color for rapid identification.
Direct Immunofluorescent Analysis	- Uses labeled antibodies to detect hMPV antigens in respiratory samples.
Nucleic Acid Amplification Tests (NAAT)	- Most common and accurate method is reverse transcription PCR (RT-PCR) to amplify viral RNA. - Targets include F, N, G, L, and M genes; F and N genes are specific and conserved for hMPV identification.
Antigen Detection	- Tests identify hMPV antigens in respiratory secretions for quicker diagnosis.
Serological Methods	- Blood tests measure antibodies to determine recent or past hMPV infection.

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2.7 Treatment of hMPV

The treatment provided for hMPV are briefly represented in table 3, in this various medication list and their approval for use in hMPV. [18, 19]

Table 3 Treatment of hMPV

Antiviral Treatment	No FDA-approved specific antiviral treatment for hMPV.
Symptomatic	Essential part of management; focuses on alleviating symptoms.

Treatment	
Supportive Care	Cornerstone of treatment; includes rest and hydration.
Fever Management	Antipyretics such as paracetamol or ibuprofen are used to reduce fever.
Hydration	Intravenous hydration recommended if the patient is dehydrated and cannot tolerate oral hydration.
Respiratory Support	Supplemental oxygen may be required in severe cases, using high-flow nasal cannula or mechanical ventilation, especially for high-risk patients.
High-Risk Groups	Patients with pre-existing respiratory or cardiac diseases, or those with weakened immune systems are at higher risk and may need closer monitoring.
Recovery Rate	Most patients recover fully with appropriate care.
Prevention Measures	Isolation of hMPV patients to prevent the spread of the disease.
Vaccine Availability	No vaccines currently available; several candidates tested in rodents and non-human primates show promise but not yet in humans.
Secondary Complications	If secondary bacterial infection (e.g., pneumonia), antibiotics may be prescribed.

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2.8 HPV prevention

People should continue to focus on preventive measures for treating other respiratory illnesses, such as covering their mouth and nose with a tissue when coughing or sneezing into their sleeve instead of their hands, discarding used tissues immediately, and washing their hands properly with soap and water for at least 20 seconds. Do not touch your mouth, nose, or eyes with unwashed hands. Avoid being close to sick people. [20]

2.9 Genome organization

The genome organization of hMPV were described as the flow map in the below figure 3.

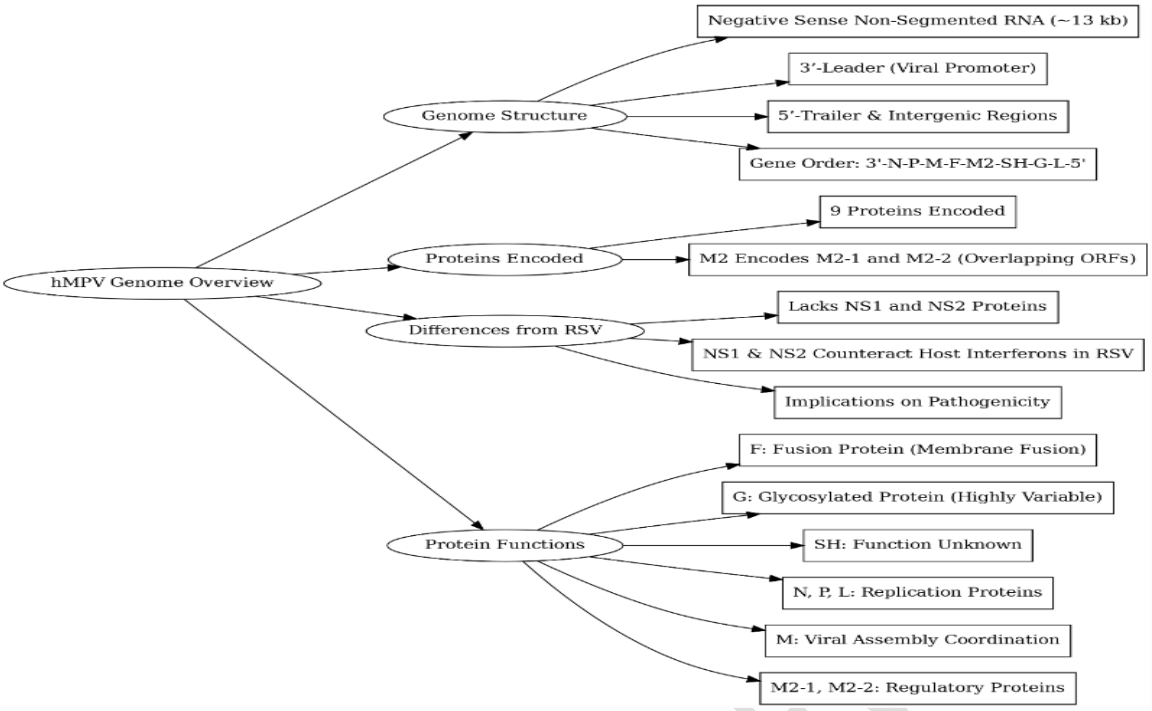

Figure 3 Genome organization of hMPV[20,21]

2.10 Genetic and antigenic diversity

The genetic and antigenic diversity of hMPV given as follow

Genotypes [22]	Two major genotypes: **A** and **B**
Subgenotypes [23]	Each genotype is further divided into two sub-genotypes: **A1, A2** and **B1, B2**
Sublineages [24]	Sub-genotype A2 has been subdivided into **A2a** and **A2b**
Genetic Diversity [25]	- SH protein: 59% identity between subgroups A and B - G protein: 37% identity between subgroups A and B
Nucleotide Identity [26]	Whole genome nucleotide sequence identity: **80%** Whole proteome amino acid sequence identity: **90%**
Antigenic Relation [27]	Two strains found to be 48% antigenically related based on cross-neutralization assays
Cross-Protection [27]	High level of resistance to reinfection with either the same or different strains

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Major Antigenic Determinant [27]	The F protein mediates broad cross-neutralization and protection

2.11 Pathogenesis

To visualize the pathogenesis of human metapneumovirus (hMPV) in a flowchart format, the following steps can be outlined sequentially: [26,27,28,29,30]

1. **Viral Attachment**
    - The G protein of hMPV interacts with host cell surface molecules (glycosaminoglycans or heparin-like molecules) for attachment.
2. **Fusion Process**
    - Following attachment, the F glycoprotein facilitates pH-independent fusion between the virus envelope and the host cell membrane.
3. **Entry into Host Cell**
    - The fusion process allows the internal components of the virus to enter the cytoplasm of the host cell.
4. **Viral Replication**
    - Inside the cytoplasm, viral replication occurs, leading to the production of new virions.
5. **Clinical Symptoms**
    - Infection can lead to clinical symptoms, notably observed in certain primate models and BALB/c mice.
6. **Immune Response**
    - The immune reaction involves a rise in different cytokines and chemokines (e.g., IL-2, IL-8, IL-4), which may play a role in lung inflammation.
7. **Persistence of Viral RNA**
    - hMPV RNA can persist in the lungs for extended periods (over 180 days), indicating an aberrant immune response that impairs virus clearance.
8. **Inflammatory Changes**
    - Significant pulmonary inflammatory changes are noted in infected animal models, with prolonged inflammation observed even after viral clearance.

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2.12 Epidemiology

The basic epidemiology of hMPV was given detailly in the given table 4.[30]

Table 4 Epidemiology of hMPV

Initial Description	First isolated in 2001 in the Netherlands.
Global Distribution	Detected on every continent, including:
	- **Europe**: UK, Finland, Italy, France, Germany, Spain, Norway
	- **America**: Canada, USA, Brazil
	- **Asia**: Hong Kong, Japan, Korea, Thailand
	- **Africa**: Yemen, South Africa
	- **India**: Detected in Pune and Delhi (12% of ARI cases)
Prevalence in Children	Detected in 5-10% of acute respiratory infections (ARI) among young hospitalized children (Peret et al 2002; Bastein et al 2003; Bovin et al 2003; Esper et al 2003).
Hospitalization Rates	Vary from 7-43% in Italy due to hMPV infection (Maggi et al 2003).
Detection Rates in Adults	Generally lower than in children, around 3% in the general community (Stockton et al 2002).
Study Observations	Higher detection rates in retrospective studies compared to prospective studies; indicates a need for large prospective studies to clarify hMPV's role in clinical conditions (Hamelin et al 2004).
Age Group Affected	Most infections occur in children under 5 years of age.

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Outbreak Patterns	Localized outbreaks; strains differ from community to community. For example, genetically similar strains found in the Netherlands and Australia.
Circulation of Lineages	In Delhi, two lineages circulated during the same season: A2b (predominant) and B1 (Broor S, unpublished data).
Transmission Route	Likely through large particle respiratory secretions and fomites; nosocomial transmission reported (Pieris et al 2003).

2.13 Detection Methods of hMPV on Different age groups

The detection methods used for the identification of hMPV was given in the table 5 as follow. [2]

Table 5 Detection Methods of hMPV

Age Group	Complications	Detection Methods
Infants (< 1 year)	- Severe respiratory complications (e.g., bronchiolitis, pneumonia)	- Reverse transcription PCR (RT-PCR) to amplify viral RNA.
	- Higher hospitalization rates compared to older children	- Direct immunofluorescent assays for rapid detection of hMPV antigens.
	- Symptoms include cough, fever, wheezing	
Young Children (1-5 years)	- Commonly experience bronchiolitis and pneumonia	- Nucleic acid amplification tests (NAAT) for accurate diagnosis.
	- Acute otitis media (AOM) is frequently diagnosed (61% in children <3 years)	
	- Symptoms similar to infants, including cough and fever	
Older Adults (≥ 65 years)	- Increased risk of prolonged illness and complications	- Serological methods to detect antibodies against hMPV.

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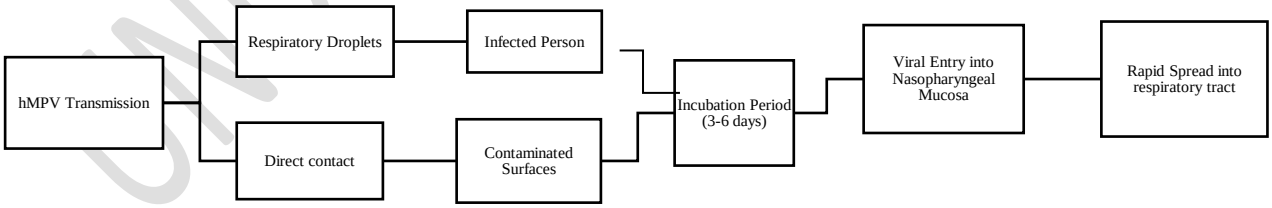
Age Group	Complications	Detection Methods
	- Higher likelihood of pneumonia and respiratory failure	
	- More severe symptoms such as dyspnea and wheezing	
Immunocompromised Individuals	- Severe infections due to weakened immune response	- Viral culture from respiratory samples, although this method is less common due to time constraints.
	- Higher risk of respiratory failure and prolonged hospitalization	-
Individuals with Chronic Conditions	- Flare-ups of chronic respiratory diseases (e.g., asthma, COPD)	-
	- Increased risk of pneumonia and bronchitis	-

3. MODE OF TRANSMISSION

The mode of transmission of the hMPV given as the flow chart. [21]



4. hMPV IN INDIA

4.1 Description of hMPV in India

In the Northern Hemisphere, many countries are experiencing an increase in acute respiratory infections (ARIs) this season, typically linked to seasonal epidemics of respiratory viruses like influenza, RSV, and mycoplasma pneumoniae. The co-circulation of these viruses can put extra pressure on healthcare systems during winter.

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Influenza-like illness (ILI) and ARI rates have risen recently in several temperate Northern Hemisphere countries, according to usual seasonal patterns. Influenza activity is higher in various regions, including Europe, Central America, Western Africa, and parts of Asia. The main types of influenza vary by location, as seen in previous years, though activity was low during most of the COVID-19 pandemic. Currently, SARS-CoV-2 activity is low after a high level in the summer. RSV trends differ by region; most of the Americas show a decrease in RSV, while North America has seen increases in recent weeks.[31]

There is growing concern about respiratory virus transmission in China, especially regarding hMPV. China has a solid surveillance system for ILI and other acute respiratory infections and posts detailed reports regularly. Recent data indicates a rise in common respiratory infections in line with seasonal expectations, with influenza being the leading cause across all age groups, except for children aged 5-14 years where mycoplasma pneumoniae predominates. SARS-CoV-2 levels stay low even as serious COVID-19 cases have raised. Overall, China's levels of respiratory infections are within expected ranges for winter, and the healthcare system is not overwhelmed. Public health messages are being shared to minimize the spread of these infections. [31]

4.2 Current Cases in India

Media reports indicate that certain cases of Human Metapneumovirus (HMPV) have been identified in Karnataka. The Indian Council of Medical Research (ICMR) has identified two instances of Human Metapneumovirus (HMPV) in Karnataka. Both instances were detected via standard surveillance for various respiratory viral pathogens, as part of ICMR's continuous efforts to track respiratory diseases nationwide.[31]

It is emphasized that HMPV is already in circulation globally, including in India, and cases of respiratory illnesses associated with HMPV have been reported in various countries. Moreover, according to the latest information from ICMR and the Integrated Disease Surveillance Programme (IDSP) network, there has been no abnormal increase in Influenza-Like Illness (ILI) or Severe Acute Respiratory Illness (SARI) cases across the Nation. [32]

The details of the detected HMPV cases are as under:

1. A 3-month-old female infant, who was diagnosed with HMPV after being admitted to Baptist Hospital, Bengaluru with a history of bronchopneumonia. She has been since discharged.
2. An 8-month-old male infant, who tested positive for HMPV on January 3, 2025, after being admitted to Baptist Hospital, Bengaluru, with a history of bronchopneumonia. The infant is now recovering.

It is important to note that neither of the affected patients have any history of international travel. [32]

4.3 Advice on hMPV in India

Union Health Ministry is monitoring the situation through all available surveillance channels. ICMR will continue to track trends in HMPV circulation throughout the year. The

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World Health Organization (WHO) is already providing timely updates regarding the situation in China to further inform ongoing measures.

The recent preparedness drill conducted across the country has shown that India is well-equipped to handle any potential increase in respiratory illnesses and public health interventions can be deployed promptly if needed.

Union Health Secretary emphasised that there is no cause of concern for the public from HMPV which has been present globally since 2001. They advised states to strengthen and review the ILI/SARI surveillance. She reiterated that an increase in respiratory illnesses is usually seen during the winter months. She also stated that the country is well prepared for any potential surge in respiratory illness cases.[33]

Human metapneumovirus (HMPV) is among the various respiratory viruses capable of causing infections in individuals of all ages, especially during the winter and early spring seasons. The viral infection is typically a mild and self-resolving condition, with most instances resolving independently. It was reported that sufficient diagnostic resources are present at the ICMR-VRDL laboratories.

The states were advised to enhance IEC and awareness among the population regarding prevention of transmission of the virus with simple measures such as washing hands often with soap and water; avoid touching their eyes, nose, or mouth with unwashed hands; avoid close contact with people who are exhibiting symptoms of the disease; cover mouth and nose when coughing and sneezing etc. [33]

5. CLINICAL EFFECTS OF HMPV IN CHILDREN

Typical Symptoms: hMPV usually leads to respiratory issues that may vary from mild to serious. Typical signs consist of:

- Coughing
- Fever
- Nasal blockage
- Difficulty breathing
- Wheezing

Seriousness in Young Kids: Kids younger than two, especially those below six months, face an increased risk of severe sickness. Research shows that 5-10% of childhood cases can result in hospitalization because of acute lower respiratory tract infections. Infants within this age range are three times more likely to require hospitalization than older children ranging from 6 months to 5 years.

Hospital Admission Rates: The recent increase in cases has sparked worries regarding hospitalizations. Reports indicate that children with hMPV may experience complications like bronchiolitis or pneumonia, requiring medical attention.

Complications: Acute otitis media (AOM) frequently arises as a complication linked to hMPV infections, impacting a notable portion of affected children. [33]

5.1 Present Condition in India

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Geographic Distribution: Verified cases have been documented in several states such as Karnataka, Gujarat, Maharashtra, and Tamil Nadu. The initial instances involved babies who were admitted to the hospital but have now healed. [34]

Government Reaction: The Indian government has highlighted that although hMPV is present, it is not a novel virus and presents a controllable risk. Health authorities have recommended heightened monitoring and public education regarding preventive practices like hand hygiene and respiratory etiquette. [34,35]

Public Health Advice: Parents should keep an eye on their children for symptoms and obtain medical help if serious respiratory issues arise. Preventive actions consist of using masks in crowded areas and upholding proper hygiene practices. [36]

6. PREVENTION METHODS

Preventing hMPV infection is similar to preventing other respiratory illnesses with actions such as:

- Wearing a mask in crowded or poorly ventilated spaces
- Improving ventilation where possible (such as by opening a window for air flow)
- Cleaning hands regularly and thoroughly, with either soap and water or an alcohol-based hand rub
- Avoiding touching eyes, nose or mouth without cleaning hands first.

Having a strong immune system can also help fend off the infections. Eating a balanced diet, exercising regularly, and sleeping properly help with that.

When someone is sick, they can avoid making others sick by

- Staying at home if they feel ill
- Covering nose and mouth with a tissue or bent elbow when coughing or sneezing
- Wearing a mask when around other people
- Improving ventilation, especially in shared spaces
- Regularly cleaning hands and disinfecting frequently touched surfaces.

There is currently no vaccine licensed for use against hMPV, but research is ongoing for future development of vaccine against hMPV. [35]

7. CONCLUSION

In India, recent cases of hMPV have been reported, though health authorities emphasize that there is no cause for public concern. The Indian Council of Medical Research (ICMR) continues to monitor the situation closely, ensuring that surveillance systems are in place to track respiratory illnesses. Public health recommendations focus on preventive measures similar to those for other respiratory viruses, emphasizing proper hygiene practices and avoiding contact with sick individuals to minimize transmission risk.

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