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Human metapneumovirus

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ABSTRACT

Human metapneumovirus (HMPV) is a pre-existing negative sense RNA virus of the family Paramyxoviridae, manifesting lower respiratory tract infections in children and adults above the age of 65 years. It replicates in a gradient manner similar to other paramyxovirus and spreads through droplets (released during cough or sneeze) or direct contact with contaminated surfaces. This virus and its history of infections show a characteristic curve with time increasing periodically during the winter, like other respiratory infections such as influenza.

Key words: Human metapneumovirus; RNA virus; Respiratory infection; Pneumovirus; Inflammation; Cytokines

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INTRODUCTION

The current increasing cases of respiratory infections in China and also in India are caused by a strain of the human metapneumovirus (HMPV) which is not at all new. This virus was discovered in 2001, in the Netherlands. Its genome analysis by sequencing the randomly primed polymerase chain reaction (PCR) revealed a genome sequence and organization similar to a paramyxovirus of the subfamily Pneumovirinae, which is related to avian pneumovirus of the genus metapneumovirus. The oldest case of this disease can be traced back to 1956.

Although the strain that is currently spreading is not known, the mechanism of replication of the genome and mode of infection was found to be somewhat similar to its close relative, the human respiratory syncytial virus (HRSV).

HMPV particles are enveloped pleomorphic, spherical, or filamentous particles, having a diameter of around 209 nm. Like other paramyxoviruses, it also contains a negative sense of single-stranded RNA genome, and viral replication occurs in a gradient manner.[1]

HOW DOES IT SPREAD?

HMPV, from the droplets of an infected person after entering into the respiratory tract of a healthy individual, attaches to the respiratory epithelial cells through the glycoprotein (G) cells with certain glycosaminoglycans, mostly heparan sulfate. Another adhesion protein, the fusion (F) protein, encodes an RGD (Arg-Gly-Asp) motif (a cell adhesion sequence) that helps in the fusion of the viral envelope and cell membrane in a pH-independent

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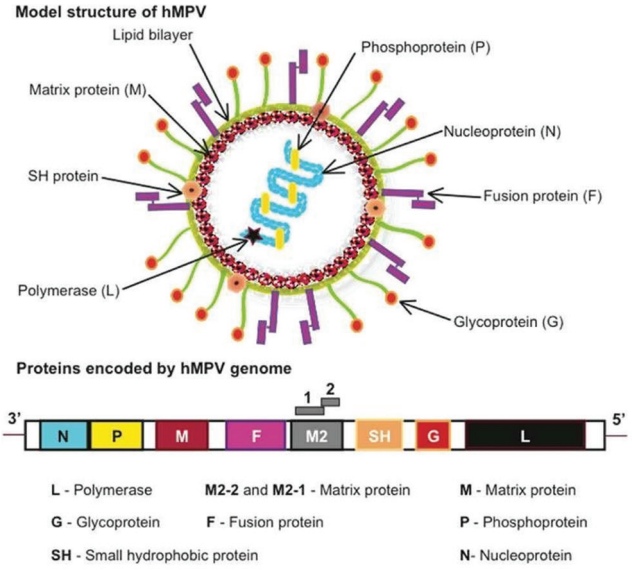

Figure 1: Model structure and Genome of HMPV.
Source: Wikipedia (https://en.wikipedia.org/wiki/Human_metapneumovirus#/media/File:Pathogens-04-00682-g001.png/2)[2]

fashion. It then induces the response of chemokines and cytokines such as interleukin (IL)-6, interferon-alpha, tumor necrosis factor-alpha, IL-2, and macrophage inflammatory proteins, leading to peribronchiolar and perivascular infiltration and inflammation.[2]

Similar to HRSV replication, HPMV also, on entering the cytoplasm, transcription of its negative strand viral RNA is facilitated by the coordinated action of the proteins L, N, P, and M2-1; producing a set of mRNAs, which further direct the vital proteins to be synthesized. The number of transcripts produced from the DNA decreases from its 3' end to 5' in a gradient manner. The polymerase complex can switch from mRNA transcription to viral-RNA replication, generating an RNA of opposite polarity to that of the genome (antigenome) that in terms, serves as a template for the polymerase complex that generates negative-sense RNA genomes of the progeny. The preference for replication over transcription is mainly determined by the viral protein M2-2.[1]

The replicated viruses, after assembling (Figure 2), infect other individuals using droplets through cough, sneezing or direct contact with contaminated surfaces.[1]

Though the G and SH proteins are required for the cell-virus interaction, they are not required for replication. Complete genome sequencing revealed that the positioning of the genes between M and L is different for HPMV in comparison with other pneumoviruses, and also, the former lacks NS1 and NS2 genes.[1]

The figure 2 shows the virus replication process in that gradient manner.

EPIDEMIOLOGY

The past cases of spreading this virus show that it is most common in temperate countries, mostly during winter and spring. The most affected age group is infants <12 months of age and males, which leads to lower respiratory tract problems, followed by old individuals with impaired immunity (>65 years).[1]

The current increasing cases of HMPV in China and other countries, including India, are actually not very drastic and can be correlated with the overall increase in common respiratory infectious diseases, such as influenza, during this time of the year.[3]

Recent data from the HYPERLINK "https://www.chinacdc.cn/jksj/jksj04_14275/202501/t20250102_303654.html"China Center for Disease Control and Prevention (CDC) , shows a predictable increase in Acute Respiratory Infections (including HMPV) during this time of the year in the northern areas (Figures 3 a,b).[4]

In the USA, cases of HPMV also show a periodic seasonal increase during winter, according to data from the HYPERLINK "https://www.cdc.gov/nrevss/php/dashboard/index.html" CDC website (Figure 3A).

Figure 3A shows, In USA, according to the data of https://ukhsa-dashboard.data.gov.uk/respiratory-viruses/other-respiratory-viruses, there is a sharp rise in cases of HMPV from the third week of December 2024:[6]

The same increasing trend is also seen in UK (Figure 3B and Table 1).

In South Korea, the cases of HPMV infections and hospitalized patients increased over the last weeks of December 2024 (Figure 4). The acute respiratory infection patient monitoring conducted by the Agency recorded 83 hospitalizations in week 49, 82 in week 50, 144 in week 51, and 180 in week 52. Out of the 489 hospitalized patients in the last four weeks, nearly half, 48.5% (237 patients), were aged 0-6 years. This was followed by those aged 65

Table 1: HMPV cases in UK in 2024-2025

Date	Amount
13 Jan 2025	4.92
6 Jan 2025	4
30 Dec 2024	4.29
23 Dec 2024	4.2
16 Dec 2024	3.81
9 Dec 2024	2.3

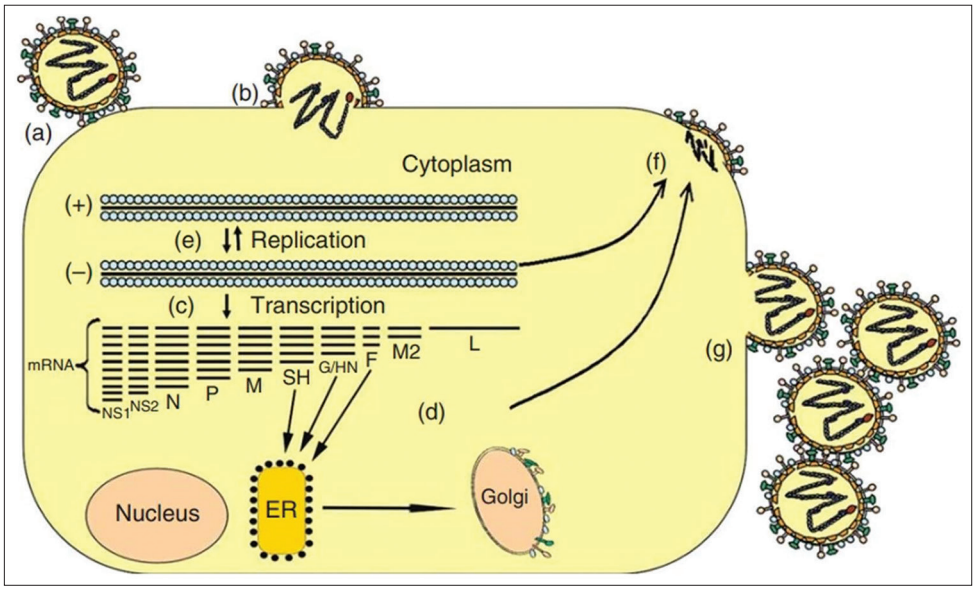

Figure 2: Diagram describing different stages of viral RNA replication
(ref: Encyclopedia of Microbiology, Third Edition, 2009)[1]
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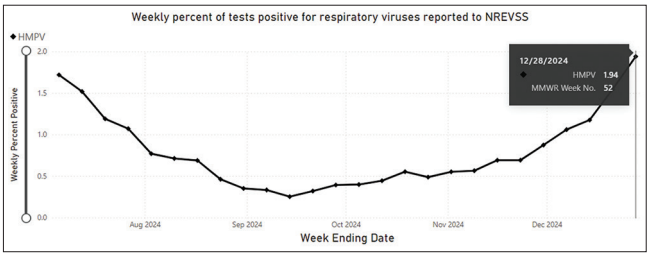

Figure 3A: Cases of HMPV infections in USA in 2024-2025

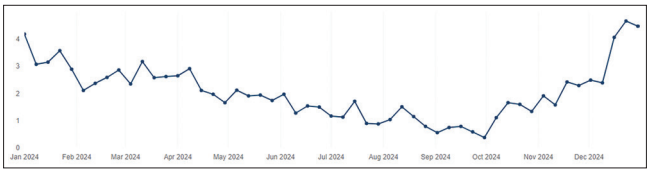

Figure 3B: Rise in cases in UK as also evident from Table 1

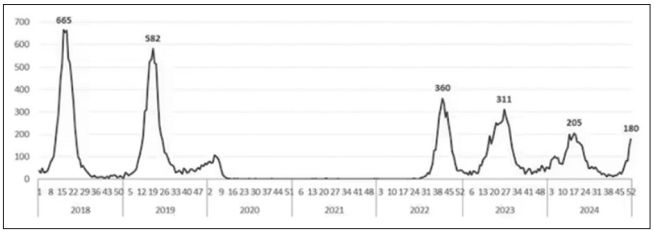

Figure 4: Cases of HMPV (hospitalized)

and older at 20.4% (100 patients), ages 7-12 at 18.2% (89 patients), and ages 50-64 at 5.7% (28 patients).[7]

Figure 4 shows the cases of HPMV infections and hospitalized patients increased over the last weeks of December 2024 in S Korea.

In a Tropical Country, Malaysia: The current data from HYPERLINK "https://economictimes.indiatimes.com/news/international/global-trends/hmpv-cases-now-rising-in-malaysia-after-china-govt-issues-advisory/articleshow/116968693.cms?from=mdr" Economic Times tells that there is an increase of 45% in cases of HMPV in 2024 than 2023 but the numbers (225 cases in 2023 and 327 cases in 2024) are not that much.[7]

In India, till 12th January, 2025, there are 17 cases of HMPV reported this year. Though it has been present for many years (Table 2) .

The date presented in Table 2 clearly shows that HMPV infections are limited to children and adults over age of 65 and having very less complications. According to ICMR- Regional Medical Research Centre, NE, Lahowal (Dibrugarh) Senior Scientist Dr Biswajit Borkakoty, Since 2014, 110 HMPV cases have been detected in Dibrugarh district.[12]

SYMPTOMS

Pathological studies of human individuals with HMPV showed acute and organizing lung injury, diffuse alveolar damage, sloughed epithelial cells with eosinophilic cytoplasmic inclusions, multinucleated giant cells, histiocytes, and hyaline membrane formation. Fever, tachypnea, dyspnea, cough, hypoxia, wheezing, stridor, rhinitis, and sore throat are the major symptoms. HPMV infections, along with HRSV infections, worsen the conditions up to tenfold. Apart from lower tract difficulties, it can also affect the upper respiratory tract like other

Table 2: Few cases and their distribution[9-13]

State	Individuals affected	Age	History
Karnataka (Bengaluru)	2	• 3-month-old female • 8-month-old male	• Bronchopneumonia • No international travel history
Gujarat	4	• 9 months old • 8-year-old boy (in ventilation) • 80-year-old male • 2 month old (from Rajasthan)	• No history of foreign travel
Puducherry	1	• 3-year-old boy (discharged)	
Tamil Nadu	2		
Maharashtra	2	• 7 years old • 13 years old (Stable and recovering from home)	
Assam	1	• 10 months old	

respiratory diseases. It is found to be a frequent cause of wheezing in children; case studies showed wheezing was present in 47% of HMPV-infected children in Brazil (31% having chest indrawing) but conversely only 8% in Finland. The symptoms worsen in the case of patients with comorbid and immunosuppressive conditions.[1]

DIAGNOSIS

Reverse transcription PCR is currently the most widely adopted method for HMPV detection. Primer sets targeting the N and L genes are reported to be the most sensitive to detecting HMPV of both genetic groups. Real-time PCR assay for HMPV has now become the gold standard.[1]

POSSIBLE TREATMENTS

Other than supportive measures, oxygen therapy, corticosteroids, and mechanical ventilation, there is no specific antiviral treatment for HMPV. As this disease is very closely linked with HRSV, for the treatment of HMPV infections also, passive immunization with humanized monoclonal antibodies can be used. Bronchodilators, such as alpha- and beta-adrenergic, anticholinergics, and nebulized epinephrine, can also be used, though it is not proven that these have a positive impact on disease outcomes.[1]

CONCLUSION

The HMPV is not a new virus. Its infection is most common in temperate countries and shows a periodic increase in winter, mainly affecting children below the age of 5 years and adults aged more than 65. The emerging cases of this infection in China this year (2025) are not different from its trend of regular spread cycle over the years. The complications of this infection are very low and can be treated with oxygen therapy, corticosteroids, and bronchodilators, but it has a tendency to affect individuals already suffering from HRSV and manifest drastic effects. The cases in India show specific age groups being affected and no severe complications following similar trends in other countries.

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