COMMENTARY

The new China virus - Human Metapneumovirus, its infectivity and rapid spread- is it a threat?

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Abstract

Human Metapneumovirus (HMPV) causes a highly infectious respiratory disease for all ages and is part of the Pneumoviridae family, but causes diseases for respiratory, milder to most severe; from pneumonia, to bronchiolitis, up to COPD. The virus is pleomorphic in shape and size, varying between 150 nm to 600 nm but very contagious and easily spread by droplets via coughing or sneezing. Children are more at risk giving it a name of kid's virus. People with a weak immune system as those with heart or lung diseases are also easy victims. The symptoms of HMPV include runny nose, nasal congestion, cough, and fever. HMPV is also known to cause pneumonia. The incubation period is estimated to be 3-6 days with most cases lasting two to five days and then resolving on their own. At times, more severe respiratory symptoms appear as pneumonia requiring hospitalization. The treatment is symptomatic and includes antihistamines, fever reducers, and broncodilators.

Keywords: HMPV, Human, Metapneumovirus, Pneumonia, Paramyxoviridae, Pneumovirinae, Pneumoviridae.

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Introduction

This virus is classified under the order Mononegavirales and the family Paramyxoviridae. It is not a new virus; the disease was found in 2001 caused by an RNA virus. Bernadette G. van den Hoogen[1] and her team in Netherlands first identified HMPV as the first human member of the Metapneumovirus genus, which is part of the Pneumovirinae subfamily. The new strain of this virus once again emerged recently in northern China and has been named HMPV. 'Human Meta Pneumonia Virus.[2,3]

Nature and Taxonomy of the Virus: Human metapneumovirus (hMPV) is an enveloped, negative-sense, single-stranded RNA virus with 8 genes encoding nine proteins (N, P, M, F, M2-1, M2-2, SH, G, and L). The viral genome is enveloped with the N, P, L, M2-1, and M2-2 proteins, surrounded by a matrix protein, and enveloped with F, SH, and G glycoproteins. HMPV uses the G and F proteins to attach to and fuse with host cells. Upon entry, it replicates and new virions bud off of the cell membrane. The "P" protein is required for polymerase (L protein) function, and the "M" protein is important for assembly and budding. The "N" protein shields the viral genome, while "M2-2" contributes to virulence by downregulating the host's innate immune response. HMPV disrupts the host's immune system by acting on pattern recognition receptors and influencing dendritic cell activity and 'T' cell activation, resulting in inefficient virus removal and increased risk of re-infection.[2]

Replication of HMPV in Host Cell: Step 1: The replication cycle of human metapneumovirus (hMPV) initiates with the virus attaching to host cells, primarily utilizing the variable G protein. This protein contains one section acting as a membrane-anchoring signal and many places where sugars are attached, hence is suspected to share similarities with other membrane proteins. Though this G protein was initially seen being attached in some sort of signalling mechanism, virus still replicate successfully without the use of the G protein.

Step 2: The "F" protein facilitates the fusion of the virus and host cell membranes. This is produced as an inactive precursor, which needs to be activated through cleavage by proteases. The hMPV is different from other paramyxoviruses in that its cleavage depends on external proteases, but some variants have the ability to cleave by themselves. F protein is useful for fusion besides attaching to the host cells via a specific site that recognizes integrins. HMPV has another protein called SH, whose role is not well defined. The deletion of the SH protein does not affect the replication ability of the virus significantly. Transcription

Step 3: The viral RNA, after fusion with the host cell cytoplasm, can be transcribed for making more mRNA and additional copies of the vRNA. It has the end sequences which regulate this transcriptional process although it is less complementary to other similar viruses.

Translation step 4: The virus has two RNA-related

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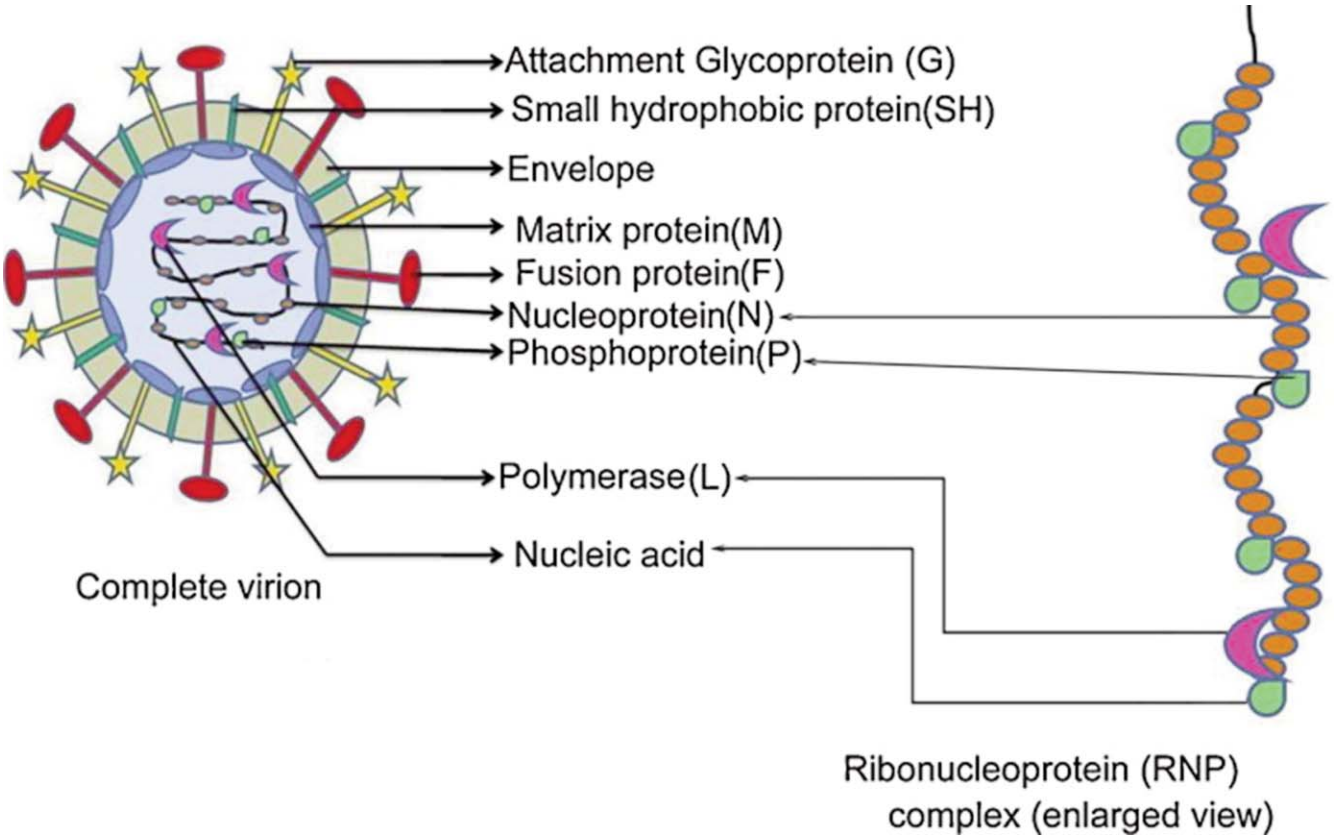

Figure-1: Genetic structure of Human Metapneumovirus adopted thorough by Panda S etal 2014.[2]

Figure-2: Preventive measure for the HMPV and all other respiratory viruses including the COVID-19 [4]

proteins called M2-1 and M2-2. M2-2 is involved in regulation of the amount of RNA to be produced for new viruses vs mRNA. HMPV has noncoding regions between its genes that help regulate how and when genes are expressed. These regions are useful for use in research to help express other genes, like green fluorescent protein for study purposes. The final stages of how the virus assembles and leaves the host cell are similar to those of other paramyxoviruses but are poorly described.[2-3]

Pathogenesis of HMPV: The pathogenesis of human metapneumovirus (hMPV) is characterized by a weak and delayed immune response, particularly limited cytotoxic T-lymphocyte activity, which hinders effective virus clearance during initial infection. hMPV disrupts T cell activation by infecting dendritic cells, restricting the proliferation of antigen-specific CD4+ T cells and impairing long-term immunity. Compared to other respiratory viruses such as RSV and influenza, hMPV elicits a reduced cytokine response and inflammatory markers, with marked pulmonary inflammation in infected animals. Histopathological changes include infiltration of inflammatory cells, alveolar damage, and the presence of specific macrophage types. Although hMPV activates toll-like receptor signaling, its role in host defense against infection is not well defined. There are indications that hMPV may not be limited to the respiratory tract, as it has been found in other tissues like middle ear fluid and brain tissue, though further research is warranted to explore its potential for systemic infection.[2]

Diagnosis of HMPV: Diagnosis of human metapneumovirus (hMPV) infection generally requires the growth and isolation of the virus using different cell lines, with human Chang conjunctiva and feline kidney CRFK cells being the best. hMPV grows slowly in cell cultures, which leads to late cytopathic effects, hence detection through antigen assays using anti-hMPV antibodies is very common. Yet in most cases diagnosis using cell cultures is not possible since molecular tools, such as real-time RT-PCR with much higher sensitivities and specificity, are normally applied. Since multiplex RT-PCR that is rapid as well as very sensitive for hMPV detection may allow the differential identification of dual infections, numerous clinical laboratories also fail to consider routinely performing an RT-PCR for hMPV. Therefore, initially, a combination of immunofluorescence assays and direct fluorescent antibody methods are used, while RT-PCR is carried out on negative samples. Further advances like shell vial centrifugation culture and hMPV monoclonal antibodies would further strengthen rapid diagnosis in the clinical arena.[2-3]

Has the World Health Organization declared it a global pandemic? So far, unlike COVID-19, the World Health Organization (WHO) remains silent but is closely monitoring the situation. This does not mean that the virus has become more lethal or deadly than before. In such a case when this disease has the potential of spreading among the children, old people, and populations of every country, WHO is preparing its response to address the outbreak on a global basis and is presently involved in responding measures.WHO will continue cooperating with governments and partners worldwide for avert the HMPV transmissibility so that children and elderly are shielded from HMPV.

Is there any information available regarding HMPV by NIH Islamabad? - There is much information on the internet about HMPV, but also many myths and false claims circulating. For example, there are reports of how this disease spreads, what measures can be taken to prevent it, and what you should do if you think you have caught the HMPV infection. Be very careful where you are getting this information and advice from social media. This explanatory material has been prepared to provide you with necessary information and precautions. Through it, you will understand how to reduce the risks of the HMPV infection, whether you should keep your child from going to school, whether breastfeeding is safe for mothers, and what precautions to take if you are travelling. The Pakistan health department, in a statement along with the senior officials of NIH Islamabad said that "there is no cause for concern but precautionary measures are recommended. The National Institute of Health is closely monitoring the current situation and no guidance has been issued by the World Health Organization."

How does HMPV spread?:The virus spreads through small droplets released from the cough or sneeze of an infected person and by touching surfaces contaminated with the virus. HMPV can survive on surfaces for 3-8 hours but can be eliminated with common disinfectant solutions.

What are the symptoms of HMPV? : Symptoms of HMPV include nasal congestion, cough, fever, and difficulty breathing. In severe cases, pneumonia and significant difficulty in breathing may occur. The disease is rarely fatal. The fatality rate among individuals with COPD or other chronic illnesses can reach as high as 1.2%.

Common symptoms: The common symptoms of this disease are almost identical to flu or common cold, which are far more common diseases than HMPV. So, proper diagnosis usually is very much needed with examination (PCR test) for establishing whether the patient is actually

infected with HMPV or not.

What are Preventive measures of HMPV: It is to be remembered that the preventive measures for colds and HMPV are alike. For example, frequent hand washing and care of respiratory health (covering your mouth with your elbow or a tissue when coughing or sneezing, and disposal of used tissues or tissues in bins with lids) is important.

How can one prevent contracting HMPV? With these preventive measures, you and your family can safeguard yourselves from HMPV. No vaccine is available for HMPV. However, a vaccine does exist for influenza, so it is vital to protect yourself and your family by immunizing with this vaccine "because co-infection of HMPV with other respiratory viruses significantly worsens the severity of the illness".

Adopting the respiratory etiquettes of sneezing or coughing hygiene is very important because this infection spreads through droplets. Avoid touching your nose and eyes and shaking hands with any other person if you are infected. By donning a mask, washing hands frequently, coughing or sneezing into your tissue or towel or into your elbow. Avoid individuals suffering from a cold or cough. Consult your doctors in case you fall sick.You should also look after your immunological health.

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