Human Metapnueumovirus(HMPV)

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Abstract- *Human metapneumovirus (HMPV) is a relative newly described virus. It was first isolated in 2001 and currently appears to be one of the most significant and common human viral infections. Retrospective serologic studies demonstrated the presence of HMPV antibodies in humans more than 50 years earlier. Although the virus was primarily known as causative agent of respiratory tract infections in children, HMPV is an important cause of respiratory infections in adults as well. Almost all children are infected by HMPV below the age of five; the repeated infections throughout life indicate transient immunity. HMPV infections usually are mild and self-limiting, but in the frail elderly and the immunocompromised patients, the clinical course can be complicated. Since culturing the virus is relatively difficult, diagnosis is mostly based on a nucleic acid amplification test, such as reverse transcriptase polymerase chain reaction. To date, no vaccine is available and treatment is supportive. However, ongoing research shows encouraging results. The aim of this paper is to review the current literature concerning HMPV infections in adults, and discuss recent development in treatment and vaccination.*

I. INTRODUCTION

Human metapneumovirus (HMPV) and severe acute respiratory syndrome coronavirus are two of the novel or emerging respiratory infections that have been discovered to cause sickness in humans since the beginning of the twenty-first century. The enclosed, non-segmented, negative-sense, single-stranded RNA viruses are known as metapneumoviruses.They are made up of two species: HMPV and avian metapneumovirus. The virus known as respiratory syncytial virus (RSV) and other metapneumoviruses are members of the family Pneumoviridae and order Mononegavirales. The Human Metapneumovirus (HMPV) is an enclosed, negative-stranded virus that belongs to the Pneumovirinae subfamily (genus Metapneumovirus) .genome of HMPV, a single-stranded RNA virus, is around 13 kilobases in size and eight genes located within the HMPV genome code for nine distinct proteins including matrix protein (M), fusion protein (F), small hydrophobic (SH) protein, glycoprotein (G), large (L) polymerase protein, matrix protein (M), phosphoprotein (P), nucleoprotein (N), and matrix-2 proteins (M2-1 and M2-2)(1–3).

Avian metapneumovirus

In 1978, avian metapneumovirus—formerly known as turkey rhinotracheitis virus—was identified in South African turkeys(4). Since then, it has been known that the virus may infect ducks, chickens, and turkeys all over the world, which has a big financial impact. The virus causes severe upper respiratory infections and reproductive problems that reduce egg production. Its fatality rate is modest and erratic, but its morbidity rate can reach 100%. According to the genetic variety of the attachment (G) protein, there are now four subgroups of avian metapneumovirus. Subtype B was found in a number of European nations after subtype A was initially isolated in South Africa. Subtype D was found in France in 2000, whereas subtype C was found in the United States in 1996.(5–8).

Human metapneumovirus discovery

Researchers in the Netherlands used electron microscopy and random reverse transcription-polymerase chain reaction (RT-PCR) methods to identify HMPV for the first time in 2001 from archived nasopharyngeal samples from 28 children who had respiratory illnesses. This new virus showed a cytotoxic effect on tertiary monkey kidney epithelial cells, but no hemadsorption. The closest relative of the genome was the avian metapneumovirus serotype C (homology up to 88%). Nevertheless, the recently identified virus was able to replicate effectively in monkeys but not in birds. There were neutralizing antibodies against HMPV in serum from the 1950s. AUS research foundHMPV in specimens taken from patients with respiratory illnesses between 1976 and 2001, while two retrospective Canadian investigations found HMPV in specimens taken from patients with respiratory illnesses between 1993 and 2000. These investigations collectively demonstrate that HMPV has been in circulation for many decades without being discovered(9,10).

Epidemiology

In the Northern Hemisphere, acute respiratory infections, such as human metapneumovirus (MPV) illness, are also more common during the winter months. Healthcare institutions experience a seasonal load from infections with numerous respiratory viruses, such as HMPV, RSV, and seasonal influenza. According to surveillance data pertaining to China, the number of Acute Respiratory Infections is expected to rise until December 29, 2024. Regardless of age, influenza is the most commonly reported infectionThe majority of the world has seen reports of HMPV since the Dutch researchers first reported it in 2001. North America (the United States and Canada), Europe (the United Kingdom, France, Germany, Italy, Spain, and Finland), Asia (Hong Kong and Japan), and Australia have all reported cases. The virus has also been found in South African youngsters who are HIV-positive and those who are not immunocompromised. Furthermore, research has demonstrated that HMPV is not a novel pathogen, with viral isolation occurring in Europe and Canada throughout the last 10 to 20 years and serological evidence of human infection dating back to 1958 in the Netherlands.Even though HMPV infection is ubiquitous in childhood, cases of severe infection in adults and reinfection in immunocompromised patients indicate that new infections might arise throughout life as a result of immune responses that are not fully protective and/or the acquisition of novel genotypes. According to surveys, the majority of HMPV cases are reported in the winter and early spring, and its temporal distribution overlaps that of HSRV circulation.(11–15)

Pathophysiology

Once the virus is implanted into the nasopharyngeal mucosa, it can swiftly travel into the respiratory system. Nine different proteins that cause host cell infection are encoded by roughly eight genes in HMPV. With the help of the addon glycoprotein (G), the fusion glycoprotein (F) initiates transmembrane fusion and enables entry into the host cell by attaching to integrins on the outside of the cell. The viral nucleocapsid then enters the host's cytoplasm and begins to reproduce(16).

Pathogenesis

A weak and delayed immune response, as well as delayed cytotoxic T-lymphocyte activity and poor virus clearance during the initial infection, may be the cause of persistent HMPV infection. 70 HMPV infects dendritic cells, preventing superantigen-induced T cell activation. Thus, long-term immunity generation is hindered and antigen-specific CD4+ T cell proliferation is limited. It is known that respiratory viruses alter cytokine responses.The cytokines interleukin (IL)-12, tumor necrosis factor alpha (TNF-α), IL-6, IL-1β, IL-8, and IL-10 are less effectively induced by HMPV than by RSV and influenza.71 In BALB/c mice and cotton rats, HMPV infection causes pulmonary inflammatory changes and raises the levels of interleukins (IL-2, IL-8, IL-4), interferon (IFN-α), macrophage inflammatory protein 1α, and monocyte chemotactic proteins in the lungs and bronchoalveolar lavage fluid. These alterations also result in inflammation and perivascular and peribronchiolar infiltration(17–21).

Causes and diagnosis

The clinical signs of HMPV infection in infants, the elderly, and those with weakened immune systems primarily include fever, coughing, and difficulty breathing, among other symptoms. Prompt identification of HMPV infection can facilitate the implementation of effective strategies to combat the disease, such as controlling outbreaks and ensuring timely patient care. Given the highly conserved amino acid sequences of the F protein in HMPV and RSV, various molecular diagnostic techniques aimed at detecting viral nucleic acids have been developed for HMPV. These techniques primarily consist of reverse transcription polymerase chain reaction (RT-PCR), real-time quantitative reverse transcription polymerase chain reaction (RT-qPCR), and reverse transcription loop-mediated isothermal amplification (RT-LAMP), among others. A wide range of established and cutting-edge methods are available for identifying HMPV.Detection of pathogens has been accomplished through immunoassays and conventional diagnostic methods, like virus culture. Recent developments in assays that use nucleic acid amplification and melting curve analysis have allowed clinical laboratories to rapidly and accurately detect HMPV(22–26).

Symptoms

Over a 17-month period, we retrospectively evaluated the signs and symptoms and incidence of human metapneumovirus (HMPV) infection in patients at a Dutch university hospital. All available nasal aspirate, throat swab, vomit, and bronchoalveolar lavage samples (N=1515) were analysed for HMPV RNA using a reverse-transcriptase polymerase chain reaction. HMPV RNA was detected in 7% of samples from patients who had respiratory tract infections (RTIs) during the previous two winter seasons, making it the second most prevalent viral pathogen identified in these patients.The majority of HMPV cases were found in immunocompromised people and extremely young children. When it came to young children, the clinical signs of HMPV infection were comparable to those of HSRV infection; however, children infected with HSRV were more likely to experience dyspnoea, feeding issues, and hypoxaemia. Among children infected with HMPV, treatment with corticosteroids and antibiotics was reported more frequently. We deduce from these data that HMPV is a significant pathogen linked to RTI(27).

Clinical features

Human metapneumovirus (HMPV), identified recently in the Netherlands, leads to lower respiratory infections, especially in young children and the elderly. This study aimed to outline the features of HMPV infections in infants under 2 years old who were hospitalized and to compare these characteristics with those of infections resulting from respiratory syncytial virus (RSV). A prospective study was carried out to examine the clinical features of infants admitted for respiratory infections over a span of 5 years. The detection of influenza A, B, and C viruses, RSV, and adenoviruses in clinical samples was carried out using a multiple reverse transcription nested-PCR assay. The presence of HMPV was evaluated in all samples through two different RT-PCR tests. Respiratory viruses were identified in 70.5% of the 1,322 children who participated in the study.HMPV was detected in 101 of the positive nasopharyngeal aspirates (10.8%), and was the most prevalent virus after RSV and rhinovirus. March was the month with the highest incidence. More than 80 percent were younger than 12 months. Bronchiolitis (49.5%) and recurrent wheeze (45.5%) were the most frequently diagnosed conditions. One percent needed assisted ventilation, and 54 percent needed oxygen therapy. Co-infections accounted for 30% of cases, and their clinical features were identical to those of single infections. A comparison was made between 71 HMPV single infections and 88 RSV single infections. For babies older than six months, HMPV infections were substantially more common than RSV infections ($P = 0.04$).Patients with HMPV had a higher diagnosis rate of recurrent wheeze ($P = 0.001$). Every other test variable was comparable between the two groups. In infants under two years old hospitalised for respiratory infections, HMPV was the third most common virus after rhinovirus and RSV. It was linked to recurrent wheezing and bronchiolitis(27–30).

Treatment

Since no particular antiviral treatments have been approved for HMPV, supportive care is the mainstay of treatment. The goal of management is to enhance patient outcomes by addressing complications and symptom relief.

Supportive Care

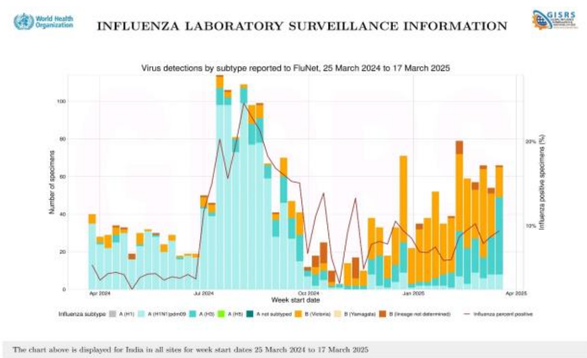
1. **Oxygen Therapy**:
   - Administered to patients with hypoxemia to maintain adequate oxygen saturation levels.
   - High-flow nasal cannula or mechanical ventilation may be required in severe cases.
2. **Hydration**:
   - Ensuring adequate fluid intake to prevent dehydration, particularly in young children and the elderly.
   - Intravenous fluids may be necessary in cases of severe dehydration.
3. **Antipyretics and Analgesics**:
   - Used to manage fever and relieve discomfort associated with HMPV infections.
   - Common medications include acetaminophen and ibuprofen.
4. **Bronchodilators**:
   - Administered to relieve wheezing and improve airflow in patients with bronchospasm.
   - Their effectiveness in HMPV remains variable and patient-specific.

Experimental Therapies

1. **Monoclonal Antibodies**:
   - Targeting the fusion (F) protein, these antibodies are designed to neutralize the virus and prevent its entry into host cells.
   - Several monoclonal antibodies are in preclinical and clinical development.
2. **Antiviral Agents**:
   - Ribavirin has been evaluated for HMPV treatment but is not widely recommended due to limited evidence and potential toxicity.
   - Novel small-molecule inhibitors targeting viral proteins are under investigation.
3. **Corticosteroids**:
   - Occasionally used to reduce airway inflammation in severe cases, although their routine use is not recommended due to potential adverse effects(31)

Current trends

This time of year sees a rise in acute respiratory infection patterns in several Northern Hemisphere nations. Seasonal epidemics of respiratory pathogens, including respiratory syncytial virus (RSV), seasonal influenza, human metapneumovirus (HMPV), and mycoplasma pneumoniae, are usually the cause of these increases. Numerous nations regularly monitor for common respiratory bacteria and acute respiratory illnesses.In many Northern Hemisphere nations, seasonal influenza activity is high. RSV detection trends, where surveillance data is available, currently differ by region, with most regions reporting declines, with the exception of North America. Interest in HMPV cases in China has recently grown, with some speculating that hospitals are overburdened. Although not all nations regularly test for and report on trends in HMPV, the common respiratory virus is known to circulate in many countries from winter to spring(32)



(33)

In order to minimize the spread of respiratory infections and lower the dangers they represent, particularly to the most vulnerable, WHO advises people living in winter-prone areas to take the usual precautions. Mildly ill people should rest and stay at home to prevent spreading the illness. People should get medical help right away if they are at high risk or if their symptoms are severe or complex. As advised by doctors and local public health officials, people should also think about donning a mask in crowded or poorly ventilated areas, cover coughs and sneezes with a tissue or bent elbow, wash their hands frequently, and receive the appropriate vaccinations(34).

II. CONCLUSION

The human metapneumovirus (HMPV) has become a serious respiratory disease that Primarily affects immunocompromised people, the elderly, and young children. Retrospective studies reveal its presence for decades before 2001, when it was first Identified. Worldwide, HMPV is common, with seasonal outbreaks mostly in the winter And early spring. Its symptoms, which include bronchiolitis, wheezing, and in extreme Situations, respiratory distress, frequently resemble those of respiratory syncytial virus (RSV). Even though HMPV usually resolves on its own, it can seriously harm susceptible Groups. Because of the difficulties in growing the virus, diagnosis depends on molecular Methods like RT-PCR. As there is currently no licensed vaccination or specialized Antiviral treatment, supportive care is provided with an emphasis on symptom alleviation And averting consequences. Nonetheless, encouraging studies on antiviral drugs and Monoclonal antibodies are still being conducted, providing promise for future tailored Treatments. Increased surveillance, early detection, and ongoing research into viable Therapies and vaccines are essential to lowering the global burden of HMPV infections Due to its clinical relevance and potential for severe disease

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