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A research article on effect on pediatrics and general populations of hmpv

Mr. Jeevan Anil Kharde[1], Dr. Sunil S. Jaybhaye[2], Mr. Yogiraj P. Muley[3]

[1]. Student,institute of pharmacy pathrikar campus ,badnapur
[2].Faculty,institute of pharmacy ,badnapur
[3].Faculty,institute of pharmacy ,badnapur

1.ABSTRACT :

Among young people in developing countries, acute respiratory tract infections (ARTIs) are a leading cause of disease and death. These illnesses are extremely dangerous because of their high level of contagion, extensive occurrence, and person-to-person transmissibility, especially for susceptible populations including small children, the elderly, and people with weakened immune systems. The World Health Organization (WHO) estimates that 2.6 million juvenile deaths worldwide are caused by ARTIs annually.

Additionally, it has been determined that some viral agents, such the human metapneumovirus (hMPV), are responsible for the higher prevalence of ARTIs in pediatric patients. Notably, in terms of the prevalence of upper and lower respiratory tract infections, hMPV has been identified as the second leading etiological agent responsible for baby bronchiolitis, ranking only behind the respiratory syncytial virus (RSV). This emphasizes the need for continued study and public health initiatives to lower the prevalence and consequences of ARTIs in communities that are already at risk.

KEYWORDS : Human Metapneumovirus (HMPV); epidemiology; respiratory viruses ; Pediatric Infections; Respiratory Tract Infections; Epidemiology; Antiviral Therapy; Vaccination; Public Health

INTRODUCTION:

Acute respiratory tract infections (ARI) continue to be the primary cause of morbidity and mortality globally.. In 2000, ARIs were responsible with around 20% of all mortality in children under five, with southern Asia and Sub-Saharan Africa accounting for almost 70% of these deaths. Children are affected by these diseases regardless of their financial situation, leading to similar prevalence rates in developed and developing countries, although the death rates in developing countries are still much higher.[1]

Children in underdeveloped countries are particularly vulnerable to pneumonia, with incidence rates estimated to be between 10% and 20%, which is significantly higher than the 3% to 4% seen in industrialized countries. These differences in morbidity underscore the urgent need for focused public health initiatives in high-risk regions. [2, 3]

Children's respiratory issues can be caused by a wide range of etiological factors, including bacterial and viral infections. Although upper respiratory tract infections are typically seen as less serious, they nevertheless have a significant negative impact on society because of missed productivity, lower attendance at school, and higher medical costs. Thus, it is of great importance to identify the causative agents of these illnesses. In [4] The significance of a number of recognized viral infections, such as the coronavirus, rhinovirus, influenza virus, parainfluenza virus, and human respiratory syncytial virus (hRSV), has been highlighted by extensive research and epidemiological studies. Yet, no known pathogen has been shown to account for a significant percentage of respiratory tract illnesses. [5]
Our knowledge of respiratory diseases advanced significantly in 2001 with the identification of the human metapneumovirus (hMPV) in the Netherlands.. Since its isolation from a juvenile patient displaying symptoms similar to a hRSV infection, hMPV has been found in 4% to 16% of ARI patients. Notably, the incidence of hMPV might change from year to year within the same geographic location. Despite its primary association with pediatric illness, hMPV can also infect adults and immunocompromised individuals. From minor upper respiratory tract infections to serious illnesses like potentially fatal bronchiolitis and pneumonia, the clinical signs of hMPV infection can vary greatly. [6,7]

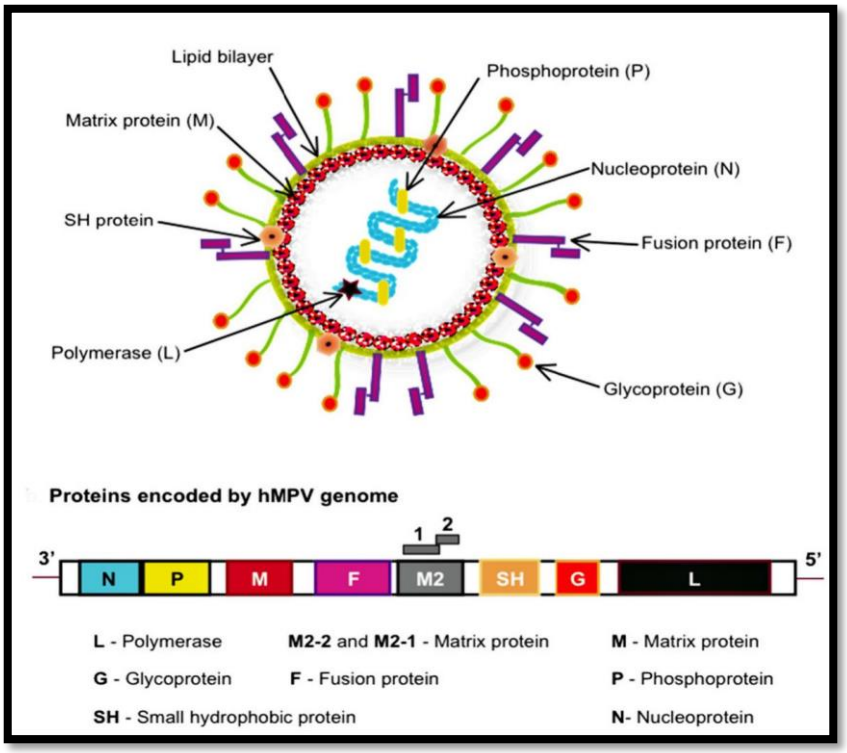

Fig 1: STRUCTURE OF HUMAN METAPNEUMOVIRUS (HMPV)

The human metapneumovirus (hMPV), which was discovered in 2001, is mostly to blame for upper and lower respiratory tract infections, with young children being especially vulnerable. However, consideration must also be given to its effects on older people and those with weakened immune systems. According to epidemiological data, between 5% and 10% of pediatric hospitalizations for acute respiratory infections are caused by hMPV. The symptoms of a hMPV infection are similar to those of infections brought on by the human respiratory syncytial virus, and they can cause serious illnesses including pneumonia and bronchiolitis in children. [8]

Early childhood is usually when hMPV is first encountered, however it is important to understand that re-infections are often seen throughout a person's life. Due to the virus's low viability in cell culture, molecular diagnostic methods—like reverse transcriptase PCR (RT-PCR)—have become the go-to approaches for hMPV detection. No vaccinations have yet to become commercially available, despite the fact that a number of vaccine candidates have shown promise in delaying the onset of clinical disease.

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The current body of knowledge about the molecular biology and epidemiology of hMPV has been greatly increased by recent discoveries. In addition to analyzing current treatment methods and tactics used to control hMPV infections, this paper attempts to give a comprehensive summary of these advancements. Additionally, a focus will be on investigating novel strategies that may eventually aid in the creation of a successful hMPV vaccine.

3. Discovery and Classification of hMPV

Analysis of nasopharyngeal aspirates taken from 28 pediatric kids, all under five, who presented with respiratory tract infections in the Netherlands more than 20 years ago led to the discovery of human metapneumovirus (hMPV). Upon analysis, the virus showed slow replication rates in tertiary monkey kidney cells and a cytopathic effect similar to that of respiratory syncytial virus (RSV).

Later studies using electron microscopy showed that the superannuate of the infected cellular cultures included pleomorphic particles that resembled paramyxoviruses. These particles had a diameter ranging from 150 to 600 nm and were accompanied by brief 13–17 nm surface protrusion. Unlike RSV and parainfluenza viruses, which are part of the Paramyxoviridae family, hMPV did not exhibit the distinctive nucleocapsid. Additional investigation revealed that this virus was amenable to chloroform inactivation and did not cause erythrocyte agglutination. [9, 10]

Furthermore, inconclusive results were obtained from attempts to amplify the viral genome using several respiratory virus-specific primers in reverse transcriptase experiments. hMPV was assigned to the genus Metapneumovirus and the subfamily Pneumovirinae of the Paramyxoviridae family based on its genomic features and morphological traits.

HIGH-RISK POPULATION FOR HUMAN METAPNEUMOVIRUS (HMPV)

- **Young Children:** The health outcomes of infants and toddlers can be greatly impacted by their increased vulnerability to serious respiratory conditions including pneumonia and bronchiolitis.

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- **Increased Risk in Older Adults:** People 65 years of age or older are more likely to experience consequences from HMPV infections, especially if they have long-term health issues such asthma or chronic obstructive pulmonary disease (COPD). [11]

- **Pregnant Women:** When HMPV occurs during pregnancy, there is a chance that respiratory issues will arise, endangering the mother's and the growing fetus's health and requiring close observation and care.

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- **Impact on Immunocompromised Individuals:** Individuals with weakened immune systems, whether as a result of underlying illnesses or as a side effect of therapies such as chemotherapy, are more likely to experience severe HMPV symptoms and should get special consideration in therapeutic settings. [12]

5.SYMPTOMS :

Human metapneumovirus (HMPV) symptoms usually include cough, fever, constricted nasal passages, and dyspnea. Over the course of an HMPV infection, the clinical symptoms may progress to more serious respiratory diseases including pneumonia or bronchitis. Other viral infections that cause illnesses of the upper and lower respiratory tract share similarities with the symptoms of HMPV infection. [12, 13]

- **Symptoms In Adults**
  Adult HMPV symptoms frequently mimic those of the flu or common cold. These consist of:
  - Constant coughing,
  - Frequently with mucous production.
  - Congestion or runniness of the nose.
  - Usually mild to moderate fever.
  - General body aches and fatigue.
  - A sore throat.
  - Breathlessness in extreme situations.

- **Symptoms In Children**

Children are more prone to have severe symptoms, such as

:

- Breathlessness
- Wheezing and persistent cough
- High fever and Poor feeding and dehydration, especially in infants.

▪ HMPV usually produces symptoms that resemble those of other respiratory diseases, including:

- Fever
- Cough
- Nasal congestion
- Wheezing
- Shortness of breath
- Runny or stuffy nose
- Sore throat

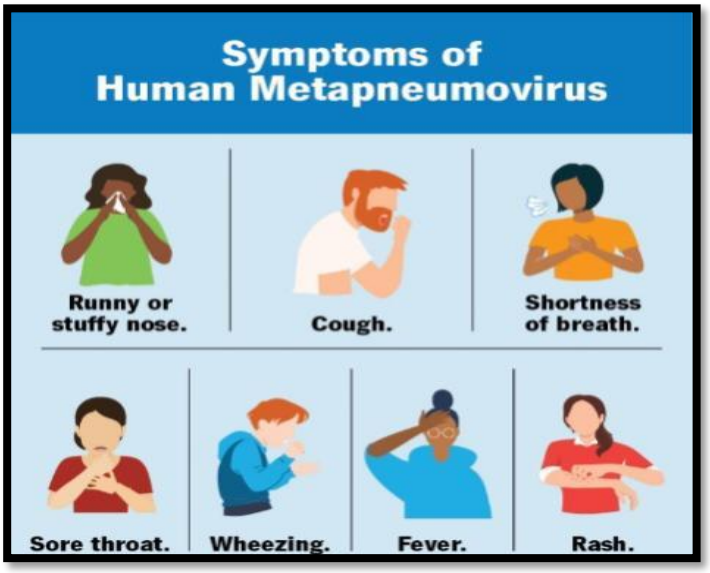


Fig. 2

Human metapneumovirus (hMPV) attacks the cells of the respiratory system, which includes the throat, nasal passages, and oral cavity, when it enters the human body. The immune system reacts to the infection of these cells by producing a range of symptoms, such as pain, low-grade fever, coughing, rhinorrhea, cephalalgia, and pharyngodynia. In some people, the disease's pathophysiology may also spread to the bronchi or main airways, which could make coughing and wheezing worse. [13]

Additional symptoms include a lower fever and weight loss may appear in pediatric populations, especially those under a year old. Additionally, in some patient groups, hMPV has been linked to severe illness manifestations that need hospitalization. This include people with weakened immune systems, as well as those with underlying respiratory or cardiac conditions. These patients are far more likely to suffer from acute respiratory failure that necessitates high-flow oxygen assistance; in extreme situations, symptoms may worsen to the point where mechanical ventilation is required. As a result, these high-risk patients require close observation and care in an intensive care unit. [13-14]

6.HOW DOES HMPV SPREAD:

HMPV is extremely contagious and can spread in a number of ways:

- **Respiratory Droplets:** When an infected person coughs, sneezes, or speaks, respiratory droplets are released into the air, which is how the virus spreads.
- **Transmission through Direct Contact:** Interaction with an infected person can spread the virus through physical contact. When the face, eyes, or lips are touched, this risk is more noticeable.
- **Surface Contamination:** A significant danger of infection arises from the virus's ability to survive on different surfaces. Transmission is far more likely when contaminated things, such as doorknobs and mobile devices, come into contact with one another.
- **Airborne Particles**: Small respiratory particles have been found to be able to stay suspended in the atmosphere, particularly in settings with a high population density or insufficient ventilation.

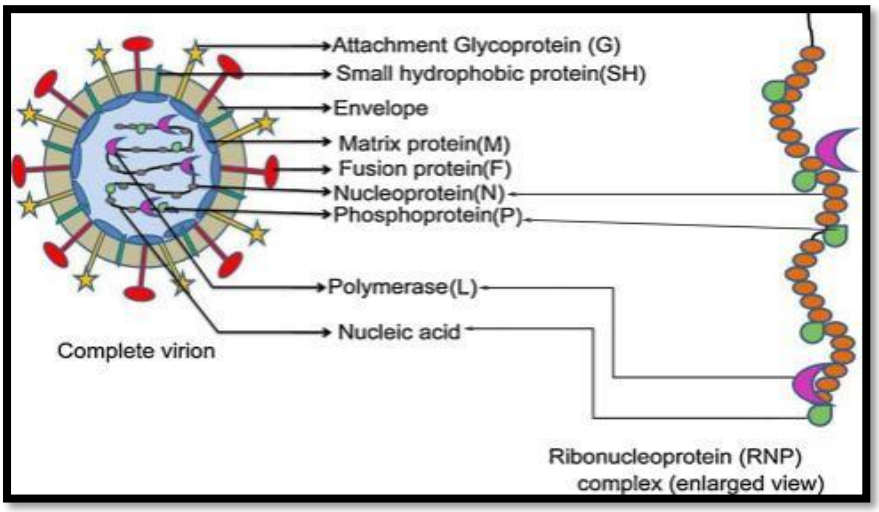
Human metapneumovirus (hMPV) has a mean age of 22 months at diagnosis, making it more likely to be detected in pediatric populations, especially in children less than two. Seroprevalence studies show evidence that a significant majority (90–100%) of children have been infected with hMPV by the time they are five to ten years old. Approximately 5 to 10% of pediatric hospital admissions have been found to be related to acute lower respiratory tract infections caused by hMPV. In addition, a comparison investigation shows that infants with hMPV have a threefold higher likelihood of needing hospitalization than their counterparts who are six months to five years old. [15, 16]

7. EPIDEMIOLOGY :

The human metapneumovirus (hMPV) is a respiratory infection-causing pathogen that is present worldwide in people of all ages. Serological investigations have verified the historical prevalence of hMPV by finding antibodies in samples as early as 1958, proving the virus has been around for more than 50 years.

When it comes to seasonal variation, hMPV infections occur all year long; however, in temperate regions, the number of cases increases noticeably from December to February. Human respiratory syncytial virus (hRSV), another respiratory virus, frequently appears around this peak time. Notably, several strains of hMPV can coexist in a single geographic location, and different genotypes of the virus may circulate within different populations. [17]

The virus is primarily disseminated by aerosolized droplets that patients release when they cough or sneeze. Following exposure, there is typically a contagious phase of two to fourteen days, followed by an incubation period of four to six days.



Schematic diagram of the human metapneumovirus particle and the ribonucleoprotein (RNP) complex.

According to epidemiological data, between 7% and 19% of pediatric populations' acute respiratory tract infections (ARTIs), including both hospitalized and outpatient presentations, are linked to hMPV. About 1 in 1,000 children are hospitalized each year as a result of hMPV infections; this is lower than the rate for hRSV but comparable to influenza. Out of 1,000 children, 13 may need emergency medical treatment due to hMPV, and 55 typically seek outpatient care. The projected hMPV detection rate in adult populations is much lower, at about 3%.

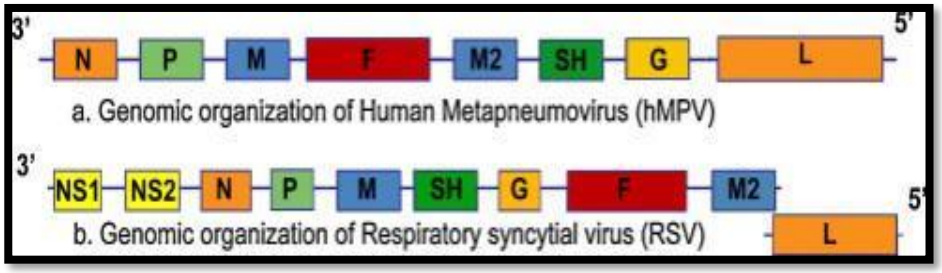


Fig . 4

A. Genomic organization of Human Metapneumovirus (HMPV) .
B. Genomic organization of Respiratory syncytial virus (RSV)

Early childhood is when most hMPV infections are seen, especially in kids under the age of two. Although maternal antibodies can offer some protection during infancy, the initial infection usually happens around the age of six months. According to estimates, more than 90% of kids will have contracted hMPV by the time they are five years old. Children with prior medical issues are more likely to develop severe clinical symptoms, even though the majority of them only get minor illness. [18.19]

Due to the presence of antibodies developed from prior exposure, hMPV infections are rare in the adult population, especially among healthy young adults. On the other hand, people 65 years of age and older, those with long-term illnesses including cancer, asthma, chronic obstructive pulmonary disease (COPD), or those who have had lung transplants are more vulnerable to reinfection by hMPV.

8. DIAGNOSIS:

The Human Metapneumovirus (HMPV) might be difficult to diagnose since its symptoms can be confused with those of other respiratory viruses. These are the primary methods for diagnosing it.

8.1.Molecular Methods

- The most effective technique for detecting HMPV RNA is reverse transcription-polymerase chain reaction, or RT-PCR.
- Multiplex PCR Panels: These assays are capable of simultaneously detecting HMPV and other viruses. [19.20]

8.2. Serological Testing :

- This checks for HMPV-specific antibodies (IgM and IgG) in the blood.

8.3. Antigen Detection :

- Although rapid assays that target the HMPV F protein are being developed, they are not as accurate as PCR.

Rapid tests are faster but less sensitive than RT-PCR, which is, in summary, the most dependable technique. (20)

Human metapneumovirus (hMPV) has been isolated and grown using a range of cell lines, including Vero cells, Hep-2 cells, Hep G2 cells, 293 cells, and LLC-MK2 cells. A recent study that cultivated hMPV in 19 distinct cell lines found that the human Chang conjunctiva cell line (clone 1-5C4) and the feline kidney CRFK cell line were the most effective cell lines for hMPV growth. Cytopathic effects appear late in the culture phase, and hMPV's growth dynamics in cell culture are characterized by a slow growth rate. Small syncytia development and cellular rounding and eventual detachment from the culture matrix are examples of these effects. [18,20]

The detection of hMPV antigens has become more dependent on the employment of anti-hMPV antibodies in direct fluorescence or enzyme-linked immunosorbent assay (ELISA) techniques due to the difficulties posed by cell culture methods. When compared to real-time reverse transcription polymerase chain reaction (RT-PCR) techniques, the efficacy of cell culture-based detection techniques has been measured, yielding sensitivity and specificity rates of 68% and 99%, respectively. Despite this, cell culture is still rarely employed as a diagnostic technique for hMPV infection, and molecular techniques like RT-PCR and real-time RT-PCR are currently recommended. [21]

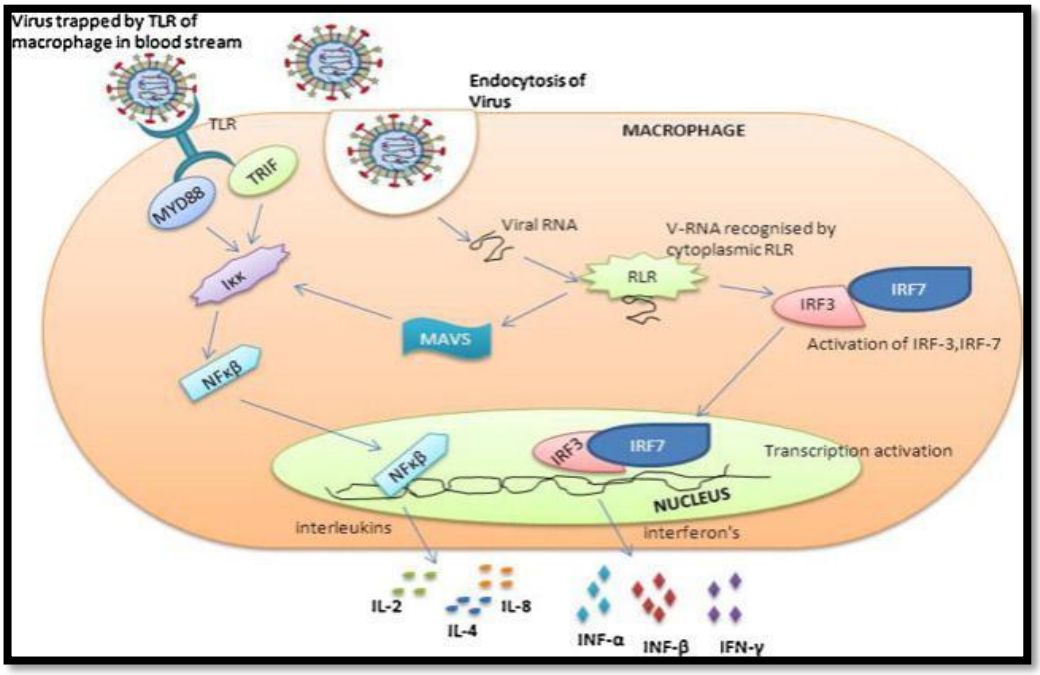


Fig . 5

Molecular events in the pathogenesis of hMPV infection

Molecular processes involved in the etiology of hMPV infection. Nuclear factor kappa beta (NFkB) is activated when a virus attaches to the toll-like receptors (TLR) of macrophages and/or dendritic cells, activating multiple immune system adaptor molecules (TRIF and MYD88). The cytoplasmic RIG1-like receptor (RLR) detects the RNA of the internalized virus and then triggers NFkB by activating transcription activators interferon regulatory factors and mitochondrial antiviral signaling protein (MAVS). 3.
(IRF-3 and IRF-7) and 7. Lastly, a number of interleukins and interferons are produced in response to NFkB and IRFs. [20, 21]

A wider variety of respiratory viruses may now be detected because to the development of multiplex PCR tests. Specifically, multiplex RT-PCR (mRT-PCR) has been created to improve the speed and sensitivity of hMPV identification, exhibiting both specificity and sensitivity.

96% and 100% of the time, respectively. On the other hand, 54.6% and 100% are the similar rates ki for conventional rRT-PCR. The capacity of mRT-PCR to identify co-infections, particularly those with low virus loads that could go undetected using traditional cell culture or immunostaining methods, is one of its key benefits. [21, 22]

However, many clinical labs are not yet equipped to perform diagnostic RT-PCR for hMPV detection on a regular basis. Combining immunofluorescence tests and direct fluorescent antibody approaches has been suggested as a feasible first-line diagnostic strategy for hMPV infections. If samples show negative results, RT-PCR is then carried out. Rapid diagnostic procedures for hMPV in clinical laboratory settings may be considerably improved by the potential combination of shell vial centrifugation culture with hMPV-specific monoclonal antibodies. [22]

9. TREATMENT :

For hMPV infection, there isn't yet an FDA-approved antiviral medication. The primary method of treating hMPV is supportive care, which aids with symptom management. Acetaminophen or ibuprofen are prescribed to people who have a fever. Fluids may be administered by intravenous (IV) if the patient becomes dehydrated and is unable to consume fluids. In extreme situations where breathing becomes challenging, patients could require oxygen support via a ventilator or a high-flow nasal cannula. This is particularly crucial for persons with compromised immune systems or those who already have heart or lung issues. Most patients get better completely. [23,24]
Patients are put under droplet precautions to stop hMPV from spreading. A few vaccines have shown promise in animal studies, but there is currently no vaccination for hMPV. No human trials have been conducted on these vaccinations yet. [24]

For human metapneumovirus (hMPV) infection, supportive care is now the main therapeutic option. However, data from multiple studies points to the possible therapeutic use of immunoglobulin, fusion inhibitors, ribavirin, and small

using ribonucleic acids to interfere with the treatment of hMPV infections. The various therapy approaches used for hMPV are summarized. [25]
A number of vaccine candidates that target hMPV have been evaluated in rodent and non-human primate models in the field of immunization. Even though these studies showed encouraging results, none of the vaccine candidates have advanced to clinical trials involving humans. Safety concerns have been raised; for example, it was shown that a heat-inactivated virus vaccination exacerbated lung illness in mice.

Studies on T cell epitope vaccines have shown that immuno-modulation decreases after hMPV exposures. To be more precise, after being exposed to hMPV, mice that were given a hMPV cytotoxic T cell epitope vaccination produced fewer Th1 and Th2 cytokines than their counterparts who were not. Additionally, research on chimeric vaccines against hMPV has shown encouraging outcomes. Chimeric vaccinations produced neutralizing antibodies and provided protection in subsequent challenges with wild-type hMPV, according to tests on hamsters and African green monkeys. [26, 27]

Additionally, it has been shown that subunit vaccines that use the hMPV fusion protein generate cross-protective immunity against hMPV challenges in hamster models. Studies on rats, hamsters, and non-human primates have demonstrated significant protection from a number of hMPV F subunit vaccines. Virus-like particles (VLPs) that resemble the viral surface features of both hMPV subgroups A and B were assessed as potential vaccination candidates in a recent study. When tested in mice, the results showed that these VLPs may elicit a strong humoral immune response against both homologous and heterologous strains. Even though the hMPV-VLP vaccination method shows promise, more research is necessary to develop a vaccine that efficiently targets all hMPV subgroups. [28]

The development of a live attenuated vaccine against hMPV infection has significantly progressed since the introduction of plasmid-based reverse genetics techniques. The development of recombinant hMPVs with mutations in the SH, G, or M2-2 genes has advanced research into possible immunization approaches against this virus. [29]

10 . PREVENTION :

HMPV prevention involves general measures to reduce the transmission of respiratory viruses:

- Maintain proper hand hygiene by periodically washing your hands for at least 20 seconds with soap and water.
- When soap and water are unavailable use an alcohol-based hand sanitizer.
- Steer clear of intimate contact with sick people.
- Keep a safe distance away from those who are sneezing or coughing.
- Remain at home if you are ill to prevent infecting others.
- Regularly clean and disinfect surfaces.
- Light switches, doorknobs, and worktops are among the regularly handled items that should be cleaned with a disinfectant.
- Observe the usual vaccination recommendations.
- Although HMPV cannot be prevented with a specific vaccine, being informed about other respiratory viruses Vaccinations, like the flu shot, can lessen the prevalence of respiratory infections in general.
- Masks can help limit exposure to respiratory droplets during flu season or epidemics.

In order to minimize the spread of hMPV, it is critical to put prophylactic measures into place. These tactics ought to include a variety of actions that effectively slow the spread of different respiratory diseases. When coughing or sneezing, for example, it is advised to cover the mouth and nose with a tissue; on the other hand, the upper sleeve may be used. [29, 30]

Maintaining appropriate hand hygiene is crucial after discarding used tissues. This entails spending at least 20 seconds cleaning your hands with soap and water. Additionally, people are cautioned against using unwashed hands to contact their mouth, nose, or eyes because this might spread infections. Apart from practicing personal hygiene, it's a good idea to keep a safe distance from those who are showing signs of disease. By taking these steps, the risk of contracting hMPV and other respiratory infections can be significantly reduced. [30]

11. EXPECTED OUTCOME

A summary of the development of research on the human metapneumovirus (hMPV): Form, purpose, and therapeutic opportunities The Pneumoviridae family includes the human metapneumovirus (hMPV), a serious respiratory pathogen that infects infants, children, the elderly, those with long-term diseases, and people with weakened immune systems. The second most common cause of pneumonia and bronchiolitis in children under five worldwide is hMPV. The lack of hMPV vaccinations or targeted antiviral therapies puts a heavy burden on the world's healthcare system. By analyzing the most recent research on hMPV's life cycle, structure, function, prevention, and available treatments, this review provides an overview of recent developments and scientific discoveries in the field.

As of right now, there are no licensed vaccines or specialized antiviral medications for human metapneumovirus (hMPV). The main goals of treatment include minimizing complications and providing supportive care to reduce symptoms like temperature and pain. Antiviral treatments and vaccines for hMPV are still being researched, and some promising candidates have been found.

Current Management:

Supportive Care: Managing symptoms is the main goal of treatment. This includes taking over-the-counter drugs to treat pain and fever, such as ibuprofen or acetaminophen.

Hydration and Rest: Recovery depends on getting enough sleep and drinking enough water.

No Antibiotics: When it comes to viral illnesses like hMPV, antibiotics are useless.

12. CONCLUSION :

Human metapneumovirus (HMPV) is a disease that is frequently disregarded, although it has significant effects on children and the general public. Given the pathogen's tendency to cause severe respiratory diseases, particularly in at-risk populations, public health interventions should be intensified and monitoring should be raised.

The need for regional and global collaboration in improving monitoring systems, honing diagnostic skills, and creating successful preventive measures is underscored by recent outbreaks seen in China and Malaysia. Furthermore, to reduce the worldwide effects of HMPV infections, continued research into vaccine and antiviral therapy development is crucial.

To effectively address the issues posed by this virus and protect public health, such cooperative initiatives and advances in medical research are necessary.

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