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A BRIEF INFORMATION ABOUT HMPV (Human metapneumovirus): A NEW RESPIRATORY INFECTED VIRUS

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ABSTRACT

Human metapneumovirus is a common respirt (Placeholder1) ory pathogen that affects people of all ages,but is especially prevalent in young children. In 2001,human metapneumovirus was first identified in Netherlands causing clinical symptoms in childern,however serological studies demonstrated that pathogen was already circulating in Netherlands in1958. The complete sequence of the hMPV genome has been elucidated .As the preliminary sequence data for the hMPV genome suggested,the virus is member of the Metapneumovirus genus, a branch of family Paramyxoviridae,and is genetically similar to,through distinct from,the avian pneumovirus at earierly it known as turkey rhinotracheitisvirus.hMPV is the major etiological agent responsible for about 5% to 10% of hospitalizations of children suffering from acute respiratory tract infections. The virus shows toxicity in a vulnerable population, including small children, elderly persons and immunalvanized patients, where it can cause severe infection of the lower respiratory tract. Clinical manifestations range from mild upper respiratory symptoms to serious complications such as bronchiolitis and pneumonia, with special ideas requiring a high-risk population. This review explores the virology, epidemiology, clinical features, diagnostic approaches, treatment options, and prevention strategies for hMPV.

KEYWORDS: *Human metapneumovirus (hMPV), viral pathogenesis, immunocompromised hosts, respiratory infections, molecular diagnostics, therapeutic interventions.*

1. INTRODUCTION

Acute respiratory tract infection (ARI) is a leading cause of morbidity and mortality worldwide. Globally, ARIs were responsible for about 20% of total deaths in children less than 5 years of age in 2000 alone; moreover, about 70% of these deaths occurred in Sub-Saharan Africa and the southern regions of Asia.The risk of pneumonia is higher in children in developing countries (10– 20%, compared to 3–4% in developed countries).ARIs affect children regardless of their economic status, with similar incidence rates in both developed and developing countries, but with a higher mortality rate in developing countries.[1] Human Metapneumovirus (HMPV) is a negative-sense, single-stranded RNA virus belonging to the family Paramyxoviridae and subfamily Pneumovirinae. First identified in 2001 in the Netherlands, HMPV is now recognized as a major cause of respiratory tract infections worldwide.[9]
Clinical symptoms of hMPV- infection can be manifested in both upper and lower respiratory tracts with a predominance for the latter. These symptoms are mainly associated with the appearance of coughing, bronchitis, bronchiolitis and respiratory manifestations related to the absence of airflow.[2]Respiratory tract infections (RTIs) are a leading cause of morbidity and mortality worldwide. For children under the age of 5 years old, RTIs are ranked as the second leading cause of death, regardless of geographical location.[3]Human metapneumovirus (HMPV) is a common cause of respiratory tract infections in children, adults, elderly, and immuno compromised patients. In 2016, it was reclassified from the Paramyxovirdae family to the Pneumoviridae family. This virus is comprised of genetic groups A and B that are each divided into sub-classes consisting of A1, A2, B1, B2 with year to year variability. HMPV was initially discovered in 2001 in the Netherlands but has been found across the globe.

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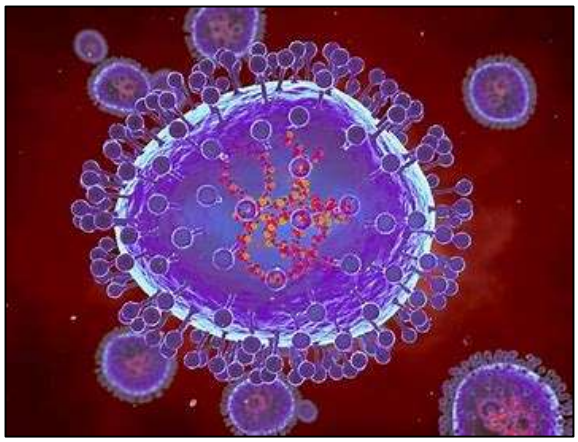

Figure no 1; Structure of hMPV

It is spread predominately by respiratory droplets from those who have been infected with the virus.Infection with HMPV usually occurs by the age of 5 years with reinfection that can occur throughout life. The most predominant clinical scenario caused by HMPV infection is upper and/or lower respiratory tract infections, with lower respiratory tract infections being among the most common. Lower respiratory tract infections due to HMPV can lead to pneumonia, bronchiolitis, as well as acute asthma exacerbations. The mainstay of treatment is supportive care measures with supplemental oxygen, antipyretic agents, and hydration with intravenous fluids if needed[5,6,7,8].Although upper respiratory tract infections are generally less serious, they nonetheless carry significant societal costs in terms of lost work, lost school days, and additional health care costs. For this reason, determining the etiological agents of these infections is important. the first case of the virus has been detected in India's Bengaluru city. "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. 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 bronchopneumoni.[66]

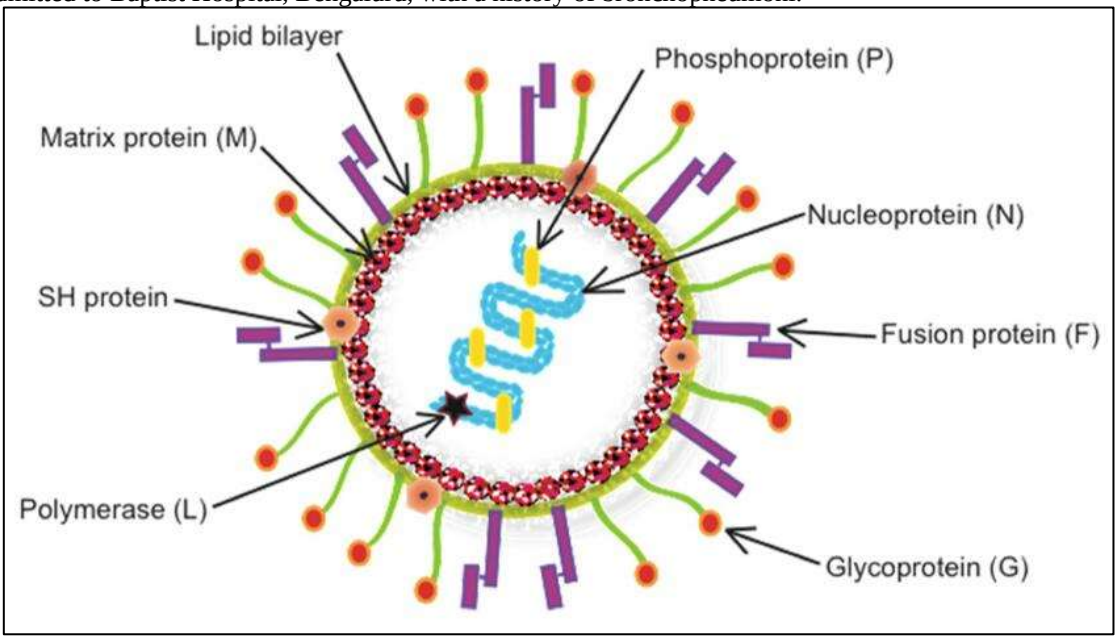

Figure no 2;Inner schematicdiagram of Human metapneumovirus

With decades of research and epidemiological studies, we have been able to establish the importance of known viral pathogens like human respiratory syncytial virus (hRSV), parainfluenza virus, influenza virus, coronavirus, and rhinovirus. However, despite these studies, a substantial proportion of respiratory tract infections still cannot be attributed to any known pathogen.Human metapneumovirus (hMPV) was first discovered in 2001 in the Netherlands, when the virus was isolated from a paediatric patient who had symptoms similar to those of hRSV infection.Since then, hMPV has been detected in 4–16% of patients with ARIs.[1]HMPV is an enveloped, non-segmented, negativestranded virus that belongs to the subfamily Pneumovirinae[10]. Te HMPV genome (nearly 13 kb) contains eight genes that encode nine proteins, namely nucleoprotein (N), phosphoprotein (P), matrix protein (M), fusion protein (F), matrix-2 proteins (M2-1 and M2-2), small hydrophobic (SH) protein, glycoprotein (G), and large (L) polymerase

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protein[11]. According to the genetic features of the F and G genes, HMPV strains prevalent worldwide could be classifed into four genotypes (A1, A2, B1 and B2), and further divided into six lineages (A1, A2a, A2b, A2c, B1, and B2)[12,13].

2. OBJECTIVE

- The primary objective of this review paper is to provide a comprehensive synthesis of the current understanding of Human Metapneumovirus (HMPV), focusing on its epidemiology, molecular biology, clinical impact, diagnostic methods, and therapeutic strategies.
- This paper aims to highlight recent advancements in the identification of HMPV and its associated respiratory diseases, particularly in vulnerable populations such as young children, elderly individuals, and immunocompromised patients.
- Additionally, the review seeks to explore emerging research on potential vaccines and antiviral treatments, identifying knowledge gaps and outlining future research directions to improve prevention and management strategies for HMPV infections.

3.EPIDEMIOLOGY

When HMPV was first described as the causative agent of RTIs in children, it was immediately recognized that at least two genetic lineages of HMPV were circulating in humans.Subsequent phylogenetic analysis of additional sequences obtained for the F and G genes revealed that each of these main lineages, A and B, can be divided into two sublineages: A1 and -2 and B1 and -2 (Fig)[1]. The maximum percent amino acid sequence identity between the F proteins of viruses belonging to lineages A and B was 95 to 97%; in contrast, there was only 30 to 35% identity for G protein sequences.

The similarities between HMPV strains of different lineages are in the same range as that described for the subgroups of AMPV and RSV[(14,15)]. The circulation of the 4 genetic lineages of HMPV was confirmed in studies throughout the world, most notably in long-term retrospective studies conducted in the United States from 1981 to 2001 [(1,3)].

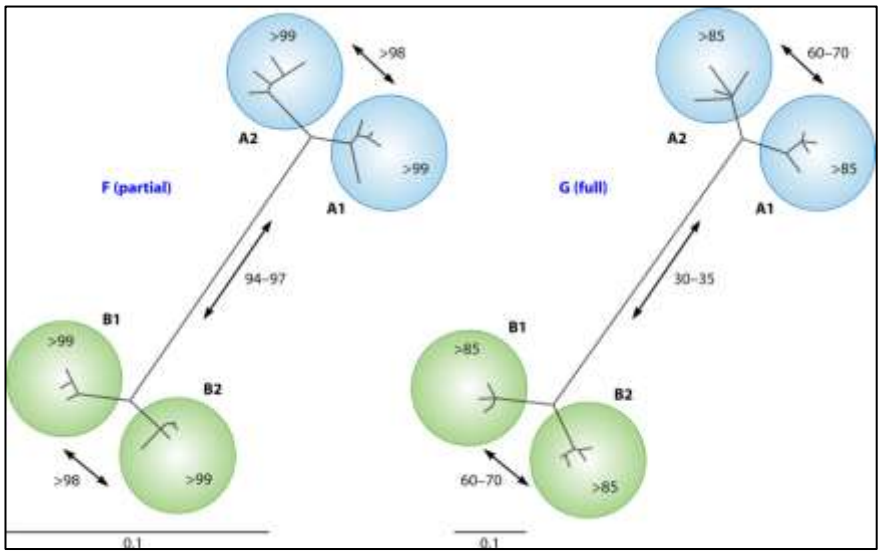

Figure no 3;-Phylogenetic trees for fusion (F) and attachment (G) genes of selected HMPV isolates. For each of the four genetic lineages[1], four representative isolates were selected, and maximum likelihood trees were generated for the G gene (right) and for 451 nucleotides of the F gene (left). Numbers in trees represent percent amino acid identities between virus isolates.

hMPV has been isolated on all continents and has a seasonal distribution.Outbreaks occur mainly in the spring and winter months – January to March in the northern hemisphere and June to July in the southern hemisphere.A recent study reported that the peak of the hMPV seasonal cases is observed between March and April following the RSV and influenza infection seasons.Another study reported that the hMPV infection season overlaps with that of the RSV infection season.[1]Being a respiratory infection, hMPV is transmitted by infectious airborne droplets.[1]Seroprevalence studies have shownthat a high percentage (90–100%) of children have been infected by the time they are 5–10 years old, but re-infection can occur throughout adulthood.[8] This may be due to insufficient immunity acquired during the initial infection and/or due to infection by different viral genotypes. The incubation period varies from individual to individual, but is commonly between 3 and 5 days.During animal experimentation, peak viral titres are seen between days 4 and 5 in BALB/c mice and cotton rats.[1]hMPV is commonly found in the paediatric population, with high susceptibility rates in children less than 2 years old. hMPV infection in adults normally shows only mild flu-like symptoms.
However, in some adult cases (especially elderly adults), severe complications such as chronic obstructive pulmonary disease (COPD) can occur. Dyspnoea is more likely in adults as compared to children. hMPV infection has also been reported in several

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immunocompromised patients, such as lung transplant recipients, patients with haematological malignancies, and hematopoietic stem cell transplant recipients.Two studies found that both genotypes of hMPV (A and B) co-circulated during a typical respiratory virus season,12,and frequent re-infections with different hMPV genotypes occur.[1]

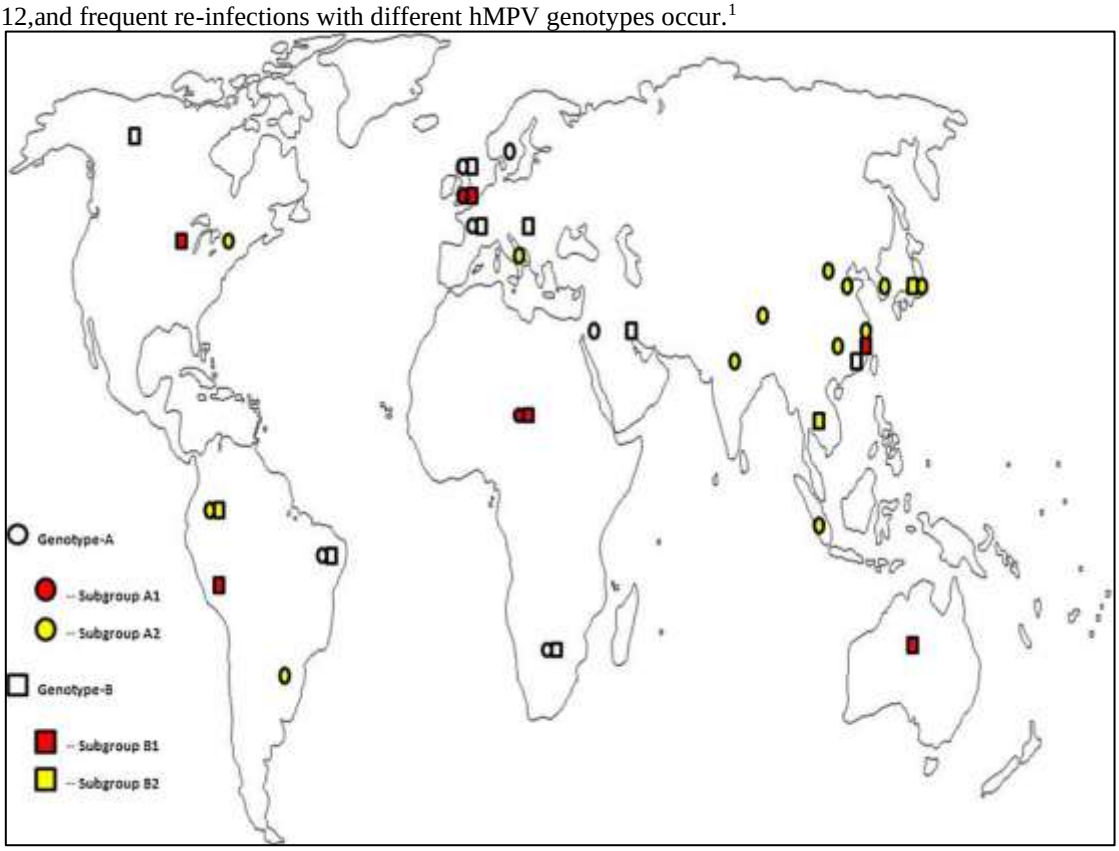

Figure no 4; Geographical distribution of hMPV genotype. Map showing the geographical distribution of hMPV genotypes among humans. Human metapneumovirus isolates are divided into four major subgroups (A1, A2, B1, and B2) and each has its own geographical localization.

Human Metapneumovirus (HMPV) is a significant respiratory pathogen that affects individuals of all ages, particularly young children, the elderly, and those with compromised immune systems. It was discovered in 2001 by Dutch researchers and has since been recognized as a common cause of respiratory infections.HMPV is transmitted through respiratory droplets when an infected person coughs or sneezes. The virus can also survive on surfaces for a limited time, making it possible to contract the infection through contact with contaminated surfaces.[16]

Global Prevalence

HMPV is a leading cause of respiratory tract infections worldwide. It was first discovered in 2001 in the Netherlands and has since been recognized as a significant pathogen .[17] The virus circulates globally, with seasonal peaks in late winter and early spring.[18]

Affected Populations

HMPV primarily affects pediatric populations, elderly individuals, and those with underlying health conditions. Studies estimate that nearly 100% of children are seropositive for HMPV by age five.[17]

Genetic Variability

HMPV is an enveloped, non-segmented, negative-sense RNA virus with two primary subgroups: A and B. These subgroups are further divided into four genetic lineages: A1, A2, B1, and B2.[17]

Recent Outbreaks

Recent surges in HMPV cases have been reported in countries like China and Malaysia, highlighting its potential for widespread outbreaks.[17]

About 40% of children hospitalized with hMPV infection were found to have underlying high risk conditions, like asthma and chronic lung disease·The average annual rate of hospitalization was about three times more in children less than 6 months old (3/1000) compared to children 6 months to 5 years old (1/1000). Nosocomial infection has been reported in several studies as a

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mode of transmission.The annual rate of hospitalization due to hMPV infection is equal to that of influenza and parainfluenza 1, 2, and 3 combined,38 and a recent analysis of an hMPV outbreak in two skilled nursing facilities showed an 11% mortality rate.[1]

Many studies have reported co-infection of hMPV with other respiratory pathogens, including [RSV,rhinovirus or enterovirus, parainfluenza virus,·coronavirus, influenza A,and influenza B. hMPV co-infection has also been reported during an outbreak of severe acute respiratory syndrome (SARS). Studies have also found hMPV co-infection with bacterial pathogens like Streptococcus pneumoniae, Mycoplasma pneumonia, and Chlamydia pneumoniae. However, the interaction of hMPV with these other etiological agents is unclear, as co-infection does not seem to affect hMPV disease severity.[1,20] There are conflicting reports on the association between RSV–hMPV co-infection and disease severity; some studies found that co-infection leads to an increased rate of ICU admission and hospital stay,but others found no association between co-infection and disease severity.[1]

4. ETIOLOGY

Human metapneumovirus is a lipid-enveloped single-stranded, negative-sense non-segmented RNA virus that was reclassified in 2016 from the Paramyxovirdae family to the Pneumoviridae family and the Metapneumovirus genus. It is spread by infectious respiratory droplets. Severe infection with HMPV has been associated with premature birth, immunocompromised status, and underlying chronic pulmonary, neural, or heart disorders.[6,7,21]

1. Virus Classification

HMPV belongs to the family *Pneumoviridae* and the genus *Metapneumovirus*. It is an enveloped, non-segmented, negative-sense RNA virus.[1]

2. Discovery

HMPV was first identified in 2001 by Bernadette G. van den Hoogen and colleagues in the Netherlands.[1]

3. Genetic Structure

HMPV has two primary subgroups, A and B, which are further divided into four genetic lineages: A1, A2, B1, and B2. The virus's genome encodes several structural proteins, including the fusion protein (F), glycoprotein (G), and small hydrophobic protein (SH), which play crucial roles in viral entry and replication.[18,22]

4. Transmission

HMPV is transmitted through respiratory droplets when an infected person coughs or sneezes. The virus can also survive on surfaces for several hours, leading to indirect transmission through contact with contaminated surfaces.[1]

Viruses get enter into body through nose or mouth.The rhinovirus is common virus that cause the common cold,most URIs(upper respiratory infection) are viral infections.Sever infection with HMPV has been associated with premature birth,immunocompromised status,underlying chronic pulmonary,neural or heart disorder.

5. CLASSIFICIACTION AND GENOMIC STRUCTURE

The complete sequence of the hMPV genome has been elucidated.[24.25.26] As the preliminary sequence data for the hMPV genome suggested, the virus is a member of the Metapneumovirus genus, a branch of the family Paramyxoviridae, and is genetically similar to, though distinct from, the avian pneumovirus (previously called turkey rhinotracheitis virus). The family Paramyxoviridae is composed of two subfamilies, one of which is Pneumovirinae, which includes both the Pneumovirus genus and the Metapneumovirus genus .[27]

- **Order:** Mononegavirales
- **Family:**Paramyxoviridae
- **Sub-family:** Paramyxovirinae
- **Genus:**Respirovirus
- **Species:** human parainfluenza types 1 ans 3
- **Genus:**Rubulavirus
- **Species:**Human parainfluenza types 2 and 4
- **Sub-family:**Pneumovirinae
- **Genus:**Pneumovirus
- **Species:**Respiratory syncytial virus
- **Sub group:**A and B
- **Genus:**Human Metapneumovirus
- **Sub group:**A1,A2a,B1, and B2

Figure no 5; Human pathogen of human metapneumovirus

RSV, a pneumovirus, is the most closely related human pathogen to hMPV, and the genomes of the viruses have similar features as well as distinct differences. The negative-strand RNA genomes of both viruses contain open reading frames (ORFs) that encode three putative viral envelope glycoproteins, the F (fusion), G (attachment), and SH (short hydrophobic) proteins, though the order of these genes differs in the two viruses [28,26].

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A.

Family	Genus	Species	Length
Pneumoviridae	Metapnemovirus	HMPV	13,330 nt
	Orthopneumovirus	RSV	15,22 nt

B.

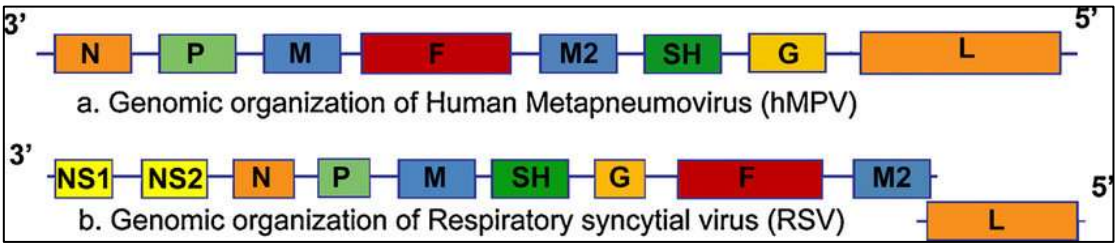

Figure no 6; Genomic maps of the Pneumovirinae. Genomic maps of the negative-sense, single-stranded RNA genomes of hMPV and RSV are displayed in the 3′-to-5′ orientation. In hMPV, the F and M2 genes are 3′ to the SH and G genes, whereas in RSV, the order of these genes is reversed. The RSV genome encodes two nonstructural proteins, NS-1 and NS-2 (shaded), that are not present in the hMPV genome. The M2 genes of both viruses carry two ORFs (M2-1 and M2-2) (not shown). The M2 and L genes overlap in the RSV genome (triangle). The L gene of each virus, encoding the viral RNA-dependent RNA polymerase, comprises two-thirds of the viral genome and is shortened for figure clarity. The genomes are not drawn to scale.

Of these three genes, the F gene is the most highly conserved (33% identity on the amino acid level) between hMPV and RSV. hMPV F contains several features that are conserved among the F proteins of paramyxoviruses, which includes a characteristic distribution of cysteine residues, a putative cleavage site (a distinguishing feature of a fusion proteins), fusion domains, and anchor sequences.[26]

The amino acid identity between the G and SH proteins of hMPV and RSV could not be determined because the predicted amino acid sequences of the corresponding proteins of the two viruses could not be aligned. The putative G protein of hMPV is considerably smaller than the G protein of RSV (236 versus 299 amino acids). Unlike that in RSV, the region of the hMPV genome that encodes the putative G protein also carries an ORF immediately downstream of the G gene (in the same reading frame) and ORFs in the two other reading frames. It is unknown whether these accessory ORFs are expressed as separate proteins or are transcribed as part of the G protein through some RNA-editing event.[26]

The predicted amino acid sequences of the G gene of both hMPV and RSV indicate that these genes encode anchored type II glycoproteins.[26.29]The intracellular amino-terminal cytoplasmic domain of the G protein of both hMPV and RSV is relatively short (~30 amino acids) and is adjacent to the hydrophobic transmembrane domain. RSV G is heavily glycosylated with both O- and N-linked sugars [30], and the predicted amino acid sequence suggests that the same is true for hMPV. Among isolates of RSV, the G gene is the most variable of all RSV genes, and this appears to be the case for the G gene of hMPV.[31] The reasons for the genetic variability of the G gene are not clear, but it may have to do with evasion of the host's immune system by the virus. The SH gene of hMPV encodes a protein (180 amino acids) that is substantially longer than the corresponding protein of RSV (64 amino acids). The function of the SH proteins of both viruses remains unknown.Other than the gene order, the major differences between the genomes of hMPV and RSV are the lack of two nonstructural genes, NS-1 and NS-2, at the 3′ end of the hMPV genome . Because of the gradient of transcription along the RSV genome, NS-1 and NS-2 are transcribed in the greatest molar amounts of all the genes the of the RSV genome. These RSV genes encode an anti-interferon activity.[32] The significance of the lack of NS-1 and NS-2 in the pathogenesis of hMPV is unknown.

6. PATHOPHYSIOLOGY

Human metapneumovirus is spread from person to person via respiratory droplets. The incubation period of HMPV ranges between 3 to 5 days and varies between individuals. After inoculation within the nasopharyngeal mucosa, the virus can rapidly spread into the respiratory tract. HMPV contains approximately eight genes that code for nine different proteins responsible for infecting host cells. With the help of the attachment glycoprotein (G), the fusion glycoprotein (F) is responsible for transmembrane fusion by binding itself to integrins on host cell surfaces in order to facilitate entry into the host cell. Subsequently, the viral nucleocapsid enters the host cell's cytoplasm and undergoes replication. HMPV induces the response of various chemokines and cytokines such as IL-6, IFN-alpha, TNF-alpha, IL-2, and macrophage inflammatory proteins leading to peribronchiolar and perivascular infiltration and inflammation. The inflammatory process also results in monocyte and lymphocyte influx within the airway endothelium. These responses combined lead to pulmonary inflammation causing the respiratory manifestations of cough, mucous production, fever, dyspnea.[5,7,21] .

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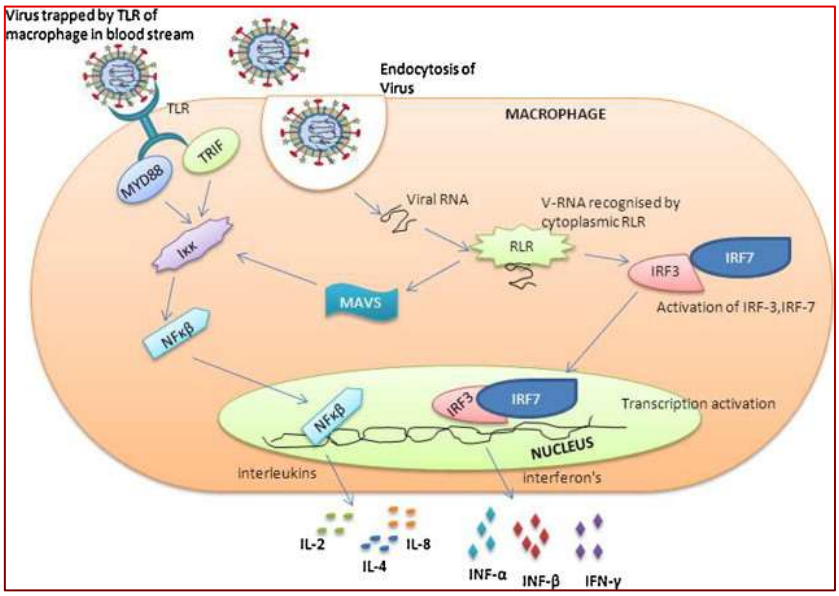

Figure no 7; Molecular events in the pathogenesis of hMPV infection.

7. CLINICAL MANIFESTATIONS OF HMPV INFECTION

The clinical spectrum of HMPV infections ranges from mild upper respiratory symptoms to severe lower respiratory tract infections. Common symptoms include fever, cough, and shortness of breath. In severe cases, HMPV can cause bronchiolitis and pneumonia.[9.19]

Upper Respiratory Tract Infections

Symptoms include cough, nasal congestion, runny nose, and sore throat. These symptoms are often similar to those of the common cold.[33] .The clinical expression of hMPV primarily affects the upper respiratory system, which demonstrates a pattern of symptoms similar to other common respiratory viral infections. Patients usually experience discharge with nose, which is characterized by growth of mucous production and can be associated with productive cough from dry. The path of the nose significantly causes difficulty and discomfort in breathing. People often report throat pain and discomfort, especially when swallowed. The body temperature rise is common, although the pattern of fever may vary significantly in patients. Voice changes, especially the crackshot, often occur due to inflammation of the Laryngeal region. Natural progress of hMPV infection follows a predetermined period, where symptoms usually last from one to two weeks. The immune system or disease prevention system of the human body is a highly complex and efficient process, which fights against viruses, bacteria and other pathogens.[35,36] It is noticeable that although these symptoms are common, their presentation may vary in intensity between different patient population.

Lower Respiratory Tract Infections

HMPV can cause bronchiolitis, pneumonia, and bronchitis. Symptoms include wheezing, difficulty breathing, and chest discomfort[34].Respiratory infection can be promoted to more worrying conditions that have significant impact on breathing and overall health. Among these, bronchiolitis emerged as a particularly anxious condition, especially affecting our youngest patients. When young children are infected with bronchiolitis, their small breathing is full of inflammation and filled with mucous, resulting in difficult breathing that scares both children and parents. Medical teams often have to admit these small patients to hospital, where they can be provided continuous monitoring and support.For people living with chronic obstructive pulmonary disease (COPD), respiratory infections can trigger what we call exacerbation – a period when breathing becomes significantly more difficult than normal.[37-39]

Severe Clinical Manifestations

In severe cases, HMPV can lead to acute respiratory distress syndrome (ARDS) and respiratory failure. Hospitalization may be required for severe cases, especially in young children, the elderly, and immunocompromised individuals.[33]

8. MOLECULAR VIROLOGY

Genome Structure

HMPV has a single-stranded RNA genome of approximately 13.3 kb in length. The genome encodes nine proteins: nucleoprotein (N), phosphoprotein (P), matrix protein (M), fusion protein (F), glycoprotein (G), small hydrophobic protein (SH), polymerase (L), and two non-structural proteins (M2-1 and M2-2).[3]

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Genetic Lineages
HMPV is divided into two primary subgroups, A and B, which are further classified into four genetic lineages: A1, A2, B1, and B2. These lineages exhibit genetic variability, particularly in the G and SH genes.[22]

Viral Proteins
The fusion protein (F) is responsible for viral entry and syncytium formation. The glycoprotein (G) mediates attachment to host cell receptors. The small hydrophobic protein (SH) is involved in modulating the host immune response.[24]

Replication Cycle
HMPV replication occurs in the cytoplasm of infected cells. The virus attaches to the host cell via the G protein, and the F protein facilitates membrane fusion. The viral RNA is then transcribed and replicated by the viral RNA-dependent RNA polymerase (L protein). Newly synthesized viral proteins and RNA are assembled into virions, which are released from the host cell to infect new cells.[40]

Pathogenesis
HMPV targets the respiratory epithelium, causing inflammation and cytokine release. Severe cases often involve bronchiolitis or pneumonia, with histopathological findings showing epithelial damage, mucus plugging, and immune cell infiltration.[23]

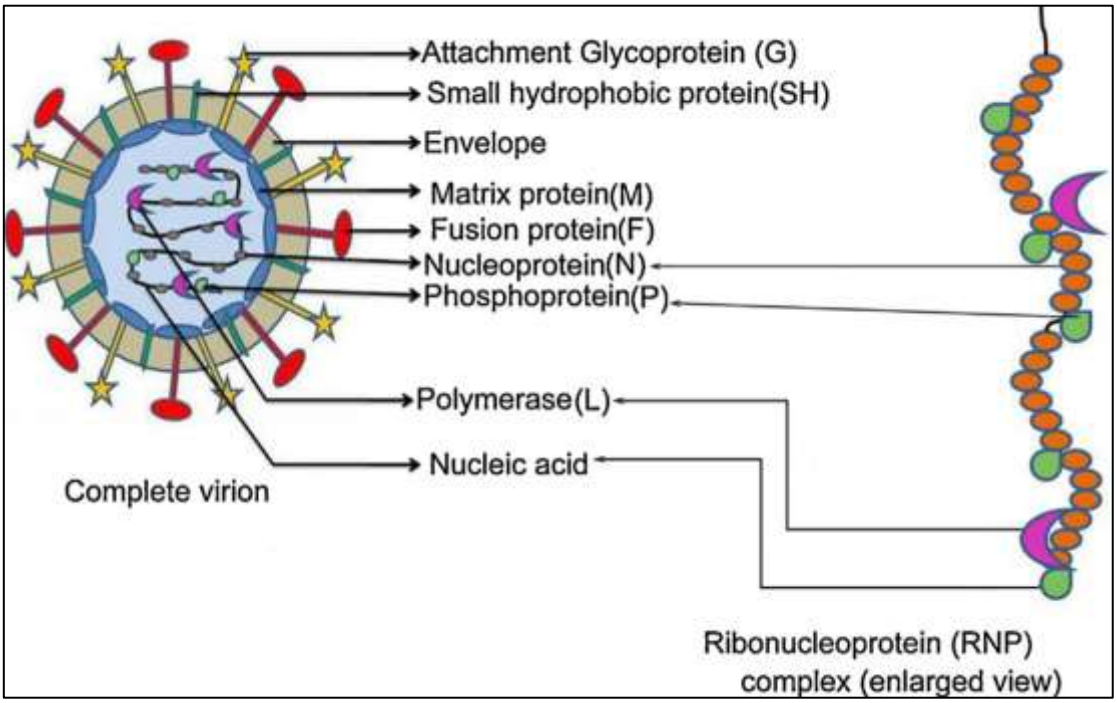

Figure no 8; Schematic diagram of the human metapneumovirus particle and the ribonucleoprotein (RNP) complex.

The hMPV virion is pleomorphic in nature and its size varies from 150 nm to 600 nm.[1]The genomic orientation of hMPV resembles other members of the Paramyxoviridae family.The genome organization of hMPV is quite similar to that of avian pneumovirus (aMPV), particularly type C. The genomes of hMPV and hRSV closely resemble each other, excluding a few differences in the order of the genes and the absence of the non-structural genes from the hMPV genome.For hRSV, the two nonstructural proteins (NS1 and NS2) have been identified as potent multifunctional antagonists of the interferon (IFN) signalling pathways.[41]

The absence of these proteins may be the reason for the difference in level of hostinnate immune response observed during hRSV and hMPV infections[42] .Like other members of the Paramyxoviridae family, hMPV interferes with the host's innate immune system using specific mechanisms. The virus antagonizes cellular responses by regulating pattern recognition receptors,such as toll-like receptor and retinoic acid-inducible gene-like receptors and other signalling molecules.[43] Infection interferes with dendritic cell activity and reduces antigen-specific T cell activation.[44] Thus, virus clearance remains incomplete and the chances of re-infection occurring increase.

9. SYMPTOMS

Following included symptoms of hmpv.[52]

- Cough.

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- Fever.
- Runny or stuffy nose.
- Sore throat.
- Wheezing.
- Shortness of breath (dyspnea).
- Rash.

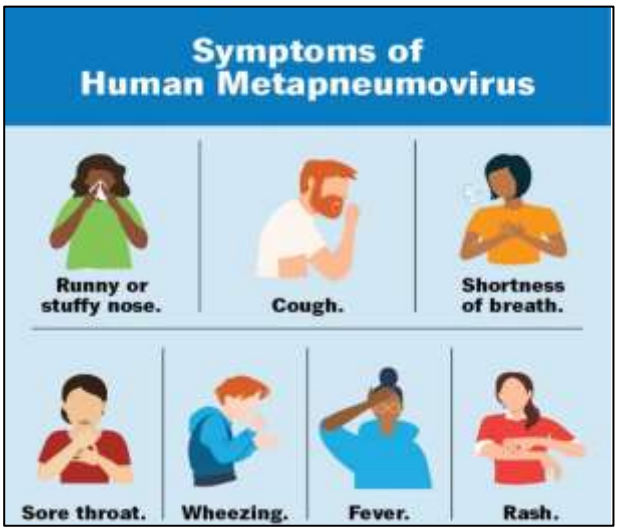

Figure no 9.Symptoms of HMPV

10. DIAGNOSIS

Early diagnosis of HMPV infection will help to develop effective measures against the disease, such as limiting the outbreak and providing timely care for the patients. Since the highly conserved F protein amino acid sequences of HMPV and RSV.[45] Thus a variety of molecular diagnosis methods, probing viral nucleic acids, have been invented for HMPV molecular detection, which mainly include the 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), etc.,

Laboratory Diagnostics

Molecular Testing

RT-PCR (Reverse transcriptase-polymerase chain reaction) on respiratory secretions is the most sensitive method for diagnosing HMPV. It is available as part of a multiplex PCR panel (The BioFire Film Array Respiratory Panel). A multiplex respiratory panel is preferable, as it can also detect co-infection with other pathogens[46]. A multiplex RT-PCR has higher sensitivity than a real time RT-PCR [7].

Serological Testing

Direct immunofluorescence (DFA) or Enzyme-linked immunosorbent assay (ELISA) are other rapid methods to detect the virus on respiratory secretions but lack the sensitivity of PCR. DFA has a sensitivity of only 38% compared to PCR. Direct fluorescent antibody testing can be done on nasopharyngeal aspirates with a turnaround time of approximately three hours.[47]

Clinical Assessment

History-Taking

The clinical assessment of human metapneumovirus (hMPV) infection requires a systematic and comprehensive diagnostic approach that combines careful history-taking with thorough physical examination. Healthcare providers begin by engaging patients in detailed conversations about their illness trajectory, paying particular attention to the temporal progression of symptoms. This patient-centered dialogue helps establish the precise onset and evolution of respiratory manifestations, which typically mirror those of other viral respiratory infections.[48,49]

Physical Examination

Beyond respiratory findings, the physical assessment extends to identifying signs of systemic involvement. This includes checking for lymphadenopathy, examining the oropharynx for inflammation or exudates, and evaluating for signs of dehydration or fatigue. The comprehensive nature of this examination helps clinicians gauge disease severity and distinguish hMPV from other respiratory infections. This structured clinical approach allows healthcare providers to form initial impressions about disease severity and guides decisions about the need for additional diagnostic testing.[50-51]

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X-Ray Method

A chest X-ray uses a focused beam of radiation to look at your heart, lungs and bones. Healthcare providers use chest X-rays to diagnose or treat conditions like pneumonia, emphysema or COPD. Chest X-rays are quick, noninvasive tests. Usually, you'll know the results of your X-ray within one to two days.[52]

11. TREATMENTS

Currently, the treatments available for hMPV infection are primarily supportive.

- ✧ Rest: Adequate rest is important to help the immune system fight the infection.
- ✧ Hydration: Drinking plenty of fluids can help alleviate symptoms like sore throat and dehydration caused by fever.
- ✧ Over-the-counter medications: Pain relievers can help reduce fever and alleviate body aches.
- ✧ Inhalers or nebulizers: For those with wheezing or difficulty breathing, inhalers or nebulized medications may be used to open up the airways.
- ✧ Oxygen therapy: In severe cases, especially for high-risk individuals, supplemental oxygen may be required.[53]
- ✧ Continuous Monitoring of Vital Signs: Regular checks of oxygen levels, heart rate, blood pressure, and respiratory function to detect any signs of deterioration early.
- ✧ Supplemental Oxygen Therapy: Administered via nasal cannulas, masks, or high-flow devices to support adequate oxygen levels in patients with difficulty breathing.
- ✧ Intravenous (IV) Fluids: To prevent dehydration, especially in young children or those unable to drink adequate fluids due to severe symptoms.
- ✧ Mechanical Ventilation: For patients with respiratory failure or severe breathing difficulties, mechanical ventilation provides critical respiratory support.
- ✧ Management of Secondary Complications: Timely identification and treatment of secondary bacterial infections, such as pneumonia, which might arise during severe HMPV cases.[54]

Different Treatment Stratergies;-[63]

Control strategy	Products	Human/animal Model used	Results
Antiviral	Ribavirin	Tissue culture assay	Ribavirin along with intravenous immunoglobulin was found to have antiviral activity against hMPV in vitro.
Antibodies	Monoclonal antibodies	Mice	On immunization in BALB/c mice, showed significantly reduced lung viral titres, decreased histopathological changes, and decreased airway obstruction post challenge with hMPV.
Fusion inhibitors	Inhibitory peptides	Mice	Fusion peptides against heptad repeat A and B domains of F protein gave protection against lethal hMPV intranasal challenge in BALB/c mice. Post-challenge there was a significant decrease in lung viral load, pulmonary inflammation, levels of proinflammatory cytokines, and airway obstruction
Epitope vaccine	T lymphocyte	Mice	Immunization reduced viral load, lung pathology, and expression of Th2-type cytokines (IL-10, IL-4) after hMPV challenge.
VLP	Virus like particles	Mice	Immunization induced cross-protective immunity in mice against both homologous and heterologous strains, along with reduced viral titres in the lungs of immunized animals .

Table no 1; Different Treatments and Stratergies

12. PREVENTION

All following prevention importants for prevent human from hmpv.[54]

a. Wash Your Hands Regularly: Frequent handwashing with soap and water for at least 20 seconds is one of the most effective ways to remove germs and prevent infection. Hand hygiene is especially important after coughing, sneezing, or touching shared surfaces.

b. Avoid Close Contact with Sick Individuals: Limit close interactions, such as hugging or sharing utensils, with people showing signs of respiratory illness. This is particularly crucial for protecting young children, older adults, or those with weakened immune systems.

c. Disinfect Frequently Touched Surfaces: Regularly disinfect high-touch surfaces such as doorknobs, light switches, phones, and toys to minimise the spread of viruses. Use disinfectants proven effective against respiratory viruses.

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d. Practice Respiratory Etiquette: Cover your mouth and nose with a tissue or your elbow when coughing or sneezing. Dispose of tissues immediately and wash your hands to prevent spreading droplets that may carry the virus.
e. Strengthen Your Immune System: Maintaining a healthy lifestyle through balanced nutrition, regular exercise, adequate sleep, and stress management can bolster your immune system, making you more resilient to infections.
f. Stay Home When Sick: If you or your child have symptoms of a respiratory illness, staying home helps prevent spreading the infection to others, especially those who may be more vulnerable.
g. Be Mindful in High-Risk Seasons: HMPV infections typically peak in late winter and early spring, and recent reports of cases in India serve as a timely reminder to stay vigilant. Take extra precautions, such as avoiding crowded spaces and practicing good hygiene, to reduce your exposure risk and protect those around you.

13.FUTURE DIRECTIONS

Research Priority	Description
Vaccine Development	Pursuing live attenuated and subunit vaccines for robust immune responses and safety profiles. Incorporation of novel delivery platforms (e.g., nanoparticles, viral vectors) to enhance vaccine efficacy and administration.
Therapeutic Interventions	Exploration of antiviral agents and immunomodulatory approaches to inhibit viral replication and manage immunopathology. Investigation of combination therapies for enhanced clinical outcomes.
Diagnostic Enhancements	Development of rapid point-of-care tests and identification of reliable biomarkers for disease severity prediction. Creation of severity prediction tools to optimize healthcare resource allocation.
Public Health Implications	Establishment of comprehensive surveillance systems with sophisticated strain tracking mechanisms. Ongoing monitoring of resistance patterns and refinement of hospital preparedness programs. Integration of AI and machine learning in research and surveillance.
Cross-disciplinary Collaboration	Collaboration among virologists, immunologists, clinicians, and public health experts to translate research into practical applications. Global coordination for effective response to respiratory viruses and pandemic threats.
Economic and Environmental Impact	Development of cost-effective prevention and treatment strategies. Sustainable funding mechanisms and consideration of environmental factors influencing viral transmission. Exploration of zoonotic transmission and viral evolution for outbreak prevention.

Table no 2; - Future Directions in Human Metapneumovirus (hMPV) Research[55-64]

CONCLUSION

Human Metapneumovirus (hMPV), a newly identified respiratory virus, has emerged as a significant health concern, particularly affecting vulnerable groups such as young children, the elderly, and immunocompromised individuals. While its clinical manifestations range from mild respiratory symptoms to severe lower respiratory tract infections, the absence of specific antiviral treatments and vaccines presents ongoing challenges. Continued research focusing on improved diagnostics, effective therapeutics, and vaccine development is essential. Public health measures, including hygiene practices and awareness campaigns, play a pivotal role in controlling its spread. Addressing these gaps will be crucial in mitigating the global impact of hMPV and improving public health outcomes.Current diagnostic methods, while improved, still face limitations in terms of speed, accessibility, and cost-effectiveness, especially in resource-limited settings. The development of rapid, point-of-care testing solutions could significantly enhance our ability to identify and respond to hMPV infections promptly.Additionally, the seasonal nature of hMPV infections and its co-circulation with other respiratory viruses complicate both diagnosis and treatment strategies, highlighting the need for more sophisticated approaches to differential diagnosis.The continued evolution of our understanding of host-pathogen interactions, immune responses, and viral genetics will be essential in developing more effective interventions. Furthermore, the lessons learned from recent viral outbreaks emphasize the importance of maintaining robust research programs and public health infrastructure to address both current and emerging respiratory pathogens, including hMPV.[103]

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