Infect Dis Trop Med 2025; 11: e1728

Human metapneumovirus (hMPV): a re-emerging respiratory threat – transmission, clinical features, complications and management

S.N. Aishath, S. Kannan, F. Razana, A. Sheeza

School of Medicine, The Maldives National University, Male', Maldives

ABSTRACT:

Human metapneumovirus (hMPV) is a globally prevalent yet underrecognized respiratory pathogen that disproportionately affects high-risk populations. Between 2024 and January 2025, numerous hMPV clinical cases were recorded in China, India, and other Asian countries. Despite near-universal childhood exposure, diagnostic challenges persist due to clinical overlap with other respiratory viruses. This paper reviews the current understanding of its virology and transmission, noting a resurgence in the post-COVID-19 era. In the absence of specific antivirals or vaccines, the rising incidence highlights the urgent need for enhanced surveillance, clinical vigilance, and targeted research efforts.

Keywords: Human metapneumovirus, hMPV, Virology, Transmission, Complications, Management.

INTRODUCTION

Since its discovery in 2001, the human metapneumovirus (hMPV) has been identified as one of the leading respiratory pathogens, particularly affecting vulnerable groups such as young children, the elderly and immunocompromised individuals[1-7]. Many hMPV cases have been frequently reported from China, India, Italy, Malaysia, and Kazakhstan in 2024 and 2025[1]. Initially, this virus was classified in the *Paramyxoviridae* family; it was later reclassified in 2016 as a member of the *Pneumoviridae* family within the genus *Metapneumovirus*[2,5]. The peak incidence of hMPV occurs in infants aged 6 to 12 months[3], affecting approximately half of all children below 2 and nearly all by age 5, with possible reinfection occurring later in adulthood[2]. The symptoms can range from mild respiratory illness to bronchiolitis and pneumonia, occasionally requiring hospitalization. Whereas infected adults typically remain asymptomatic or mildly symptomatic, immunocompromised individuals and those with underlying medical conditions were found to be at a higher risk of developing severe pneumonia[1-7]. During the past decade, the global prevalence of respiratory tract infections caused by hMPV had increased from 5-15%[2,4] up to 20%, with some regions reaching 43%[2]. In 2018 alone, an estimated 11.1 million cases of hMPV-associated acute lower respiratory tract infections were reported in children under 5[4]. Despite this increasing trend of hMPV infections, it remains underdiagnosed due to a lack of routine testing and its co-circulation with other respiratory pathogens, such as respiratory syncytial virus (RSV). Recent outbreaks, including the 2024 outbreak in China, further highlight the public health threat posed by the virus[5].

HMPV GENOME, VIRAL PROTEINS, AND MORPHOLOGY

The hMPV is enveloped by lipid, encasing negative-sense, single-stranded RNA at its core. This ge-

Corresponding Author: Kannan Subbaram, MSc, Ph.D; e-mail: kannan.subbaram@mnu.edu.mv

nome comprises eight genes that encode nine distinct proteins, all of which play vital roles in facilitating host cell infection. These include the nucleoprotein (N), phosphoprotein (P), large RNA-dependent RNA polymerase (L), matrix protein (M), M2-1 and M2-2 regulatory proteins, and three surface glycoproteins: the attachment protein (G), small hydrophobic protein (SH) and fusion protein (F) (Figure 1). Based on genetic variations in the glycoproteins, hMPVs are distinguished into two major genotypes (A and B), which are then further divided into four subtypes (A1, A2, B1, and B2)[2,6,7].

The hMPV primarily targets respiratory epithelial cells, where it replicates extensively, leading to cellular necrosis and occasionally the formation of syncytia[2,4]. This disrupts the mucociliary clearance, contributing to airway obstruction[3,4,6]. The key stages of viral replication include attachment to the host cell, fusion with the cell membrane, transcription of its genes, assembly of the new virus particles and their release from the host cell.

This process begins with the attachment of hMPV G or F proteins to the host cell receptors such as glycosaminoglycans[1,2]. Although the G protein facilitates attachment by binding to host cell receptors, it is not essential for viral replication and infection. It is believed, however, to play a role in modulating the host immune response[2]. In contrast, the F protein can independently mediate both viral attachment and membrane fusion, even in the absence of G protein[2,5]. Additionally, the SH protein contributes by interfering with the host's innate immune response, notably through the suppression of nuc-lear factor-κB (NF-κB) and modulation of the fusogenicity of F protein[2]. Following attachment, the virus is internalized *via* endocytosis and subsequently undergoes fusion with the endosomal membrane to release its genome into the host cytoplasm[2,7]. The replicated viral RNA is either incorporated into newly formed viruses or utilized for secondary transcription. Once assembled, the virions then bud from the host cell membrane[2].

HMPV TRANSMISSION

The hMPV, primarily transmitted *via* respiratory droplets, is found worldwide[7] and has a year-round circulation[3]. It has an incubation period ranging from 3 to 6 days, although this may vary between individuals[1]. Like other respiratory viruses, hMPV transmission is amplified in crowded environments such as schools, daycare centres, nursing homes and hospitals[8]. Asymptomatic carriers play a notable role in community transmission as the viral shedding can persist for 7 to 14 days post-infection[9], enabling prolonged infectivity even in the absence of symptoms. Several studies, including those involving healthcare workers, have demonstrated that both symptomatic and asymptomatic individuals contribute to viral spread within domestic and institutional settings[10].

These transmission patterns are supported by evidence from the 2020 SARS-CoV-2 pandemic. During periods of strict public health interventions such as masking, social distancing and mobility restrictions, the incidence of hMPV significantly declined, only to rebound following the relaxation of these measures. This reinforces the need for stringent infection control protocols to reduce viral transmission[6]. Seasonal trends in hMPV circulation are well-documented. In temperate climates, hMPV cases exhibit a seaso-

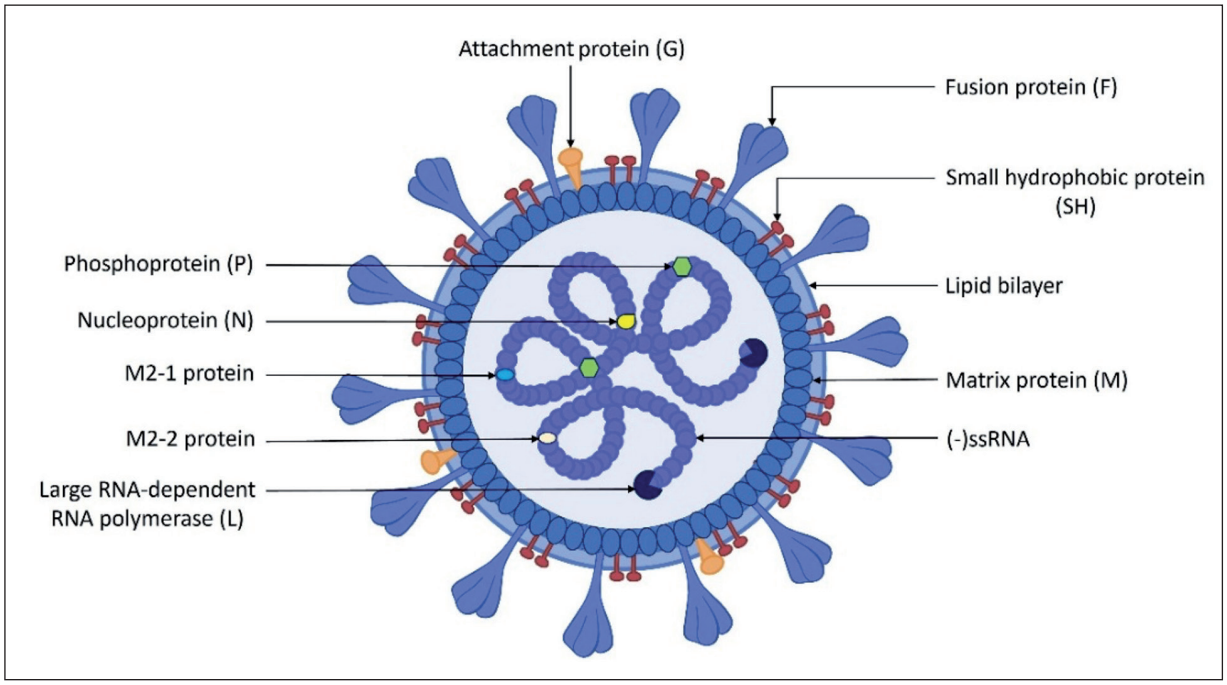

Figure 1. Structural overview of hMPV. Adapted from an icon by Hanna Vega http://book.bionumbers.org/), (https://creativecommons.org/licenses/by-sa/4.0/).

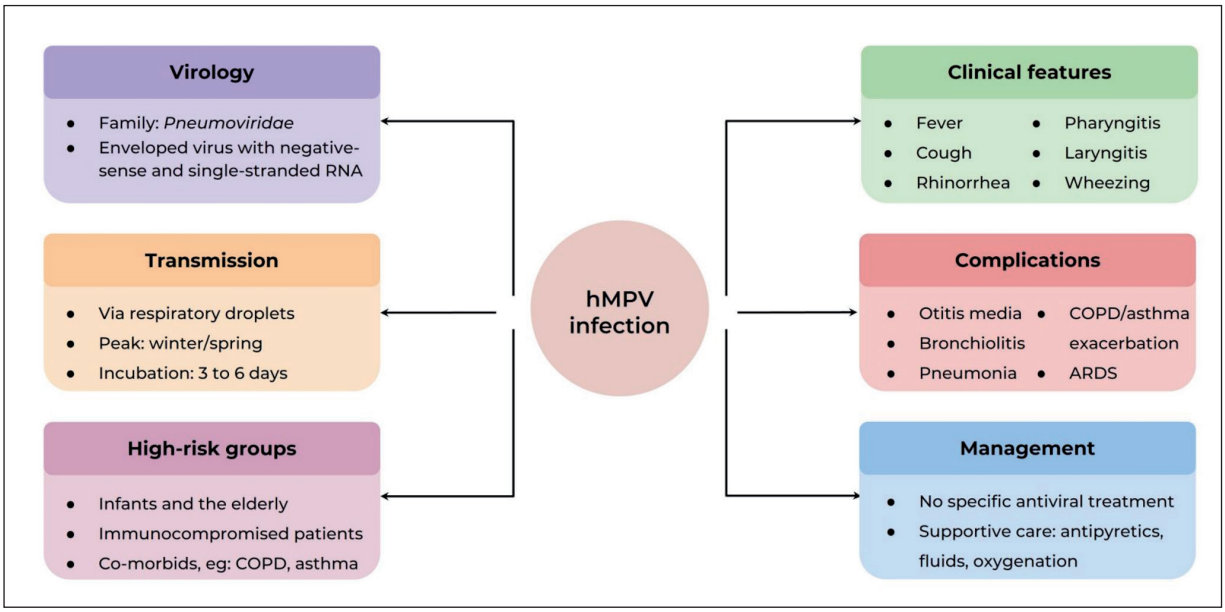

Figure 2. Human metapneumovirus (hMPV) – virology, transmission, clinical features and management.

nal trend, peaking in winter through early spring[1,3,5], preceded by peaks in RSV and influenza, respectively[5]. The seasonal onset occurs between January and March in the northern hemisphere, and from June to July in the southern hemisphere[3]. In tropical regions, cases typically peak in the rainy season along with other respiratory infections[5]. This increase in transmission during colder periods is thought to be due to enhanced viral shedding and increased virus stability in the respiratory secretions[4].

Emerging variants of hMPV, including the A2c lineage, have shown increased transmissibility and virulence. Hence, the rising prevalence of infections may be driven by their ongoing genomic evolution. As mutations accumulate in key antigenic regions, the efficacy of neutralizing antibodies is diminished, facilitating immune evasion and resulting in reinfections even among previously exposed individuals[4,6]. This genetic diversification is further accelerated by the lack of proofreading activity in the hMPV RNA-dependent RNA polymerase, a characteristic common among other RNA viruses with high evolutionary potential[4,7].

EPIDEMIOLOGY

Studies[11] estimate that hMPV accounts for 4-10% of hospitalizations due to acute respiratory infections (ARIs) in children under five years of age, with 10-20 cases per 1,000 children each year. In high-income countries, around 6 out of every 1,000 children in this age group are hospitalized due to hMPV. Co-infections with other respiratory pathogens, RSV and influenza, are observed in up to 16.8% of hMPV cases, often exacerbating disease severity and increasing the demand for hospital-based care[12]. The burden of hMPV is also substantial among older adults. In 2019, global estimates indicated approximately 473,000 hospitalizations for hMPV-associated lower respiratory tract infections in individuals aged ≥65 years. Out of these cases, 185,000 occurred in high-income countries and 288,000 in low- and middle-income countries[13]. More recently, hMPV has re-emerged with notable activity. During 16-22 December 2024, the virus was responsible for 6.2% of all respiratory illness cases and 5.4% of related hospitalizations in China, surpassing other circulating viruses including adenovirus, rhinovirus and SARS-CoV-2[14]. Table 1 summarizes prevalence rates of hMPV in China over the past two decades, highlighting the regional burden.

CLINICAL FEATURES OF HMPV

In both pediatric and adult populations, hMPV infection commonly presents as a mild self-limiting illness[16]. Early symptoms typically include rhinorrhoea, sore throat, a dry cough that may become productive over time, and dysphonia secondary to laryngeal inflammation. Fever is a frequent but variable finding, often accompanied by systemic symptoms such as myalgia, chills, headache and fatigue. These manifestations generally resolve within 1 to 2 weeks[17]. However, in high-risk groups, the infection may progress to involve the lower respiratory tract, resulting in bronchiolitis, pneumonia and, in critical cases, acute respiratory distress syndrome (ARDS)[5].

A cohort study[18] conducted in Finland involving 1,338 children under the age of 13 found that among those infected with hMPV, 97% had cough, 90% experienced rhinitis and 72% presented with fever, with the duration of illness spanning a median of 8 days. Acute otitis media was the most frequent complication, occurring in 61% of children under 3 years of age, although none required hospital admission.

Table 1. Epidemiology of hMPV in China from January 1, 2003, to December 31, 2023[15].

Province	Prevalence (%)	95% Confidence interval
Chongqing	15.88	14.41-17.35
Henan	07.05	5.84-8.62
Tianjin	06.45	3.72-9.18
Jiangsu	06.24	6.02-6.50
Hunan	5.90	5.31-6.45
Zhejiang	5.45	5.00-5.89
Guizhou	5.27	3.55-6.99

The diagnosis of hMPV is often complicated due to its clinical similarity to other respiratory viruses, particularly RSV. Both viruses can cause fever, wheezing, rhinorrhoea, sputum production and cough. However, fever is more commonly observed with hMPV infections than RSV[6]. Asymptomatic infection can also occur, especially among younger adults, though it is less frequently observed in high-risk groups[19].

HMPV COMPLICATIONS

Infection with hMPV can lead to significant complications, particularly in vulnerable populations. In severe cases, patients may require hospitalization and admission to intensive care units (ICUs) for mechanical ventilation, hemodynamic support and management of potential coinfections[6].

Comorbid conditions substantially influence disease severity. In individuals with chronic respiratory diseases such as asthma and chronic obstructive pulmonary disease (COPD), hMPV can exacerbate baseline symptoms, often resulting in repeated hospitalizations. Cardiovascular diseases, including heart failure, may further aggravate respiratory distress[20]. Similarly, metabolic disorders such as diabetes mellitus and obesity are associated with impaired immune responses, reduced viral clearance and worse clinical outcomes (Figure 2). Neurological impairments also elevate the risk of respiratory complications, particularly aspiration pneumonia[12,21].

Immunocompromised individuals face an especially high risk of severe outcomes. In this population, hMPV infections are often marked by prolonged disease courses and a higher incidence of respiratory failure[22]. In one cohort[23] of immunocompromised paediatric patients with hMPV, 23% required ICU admission and/or supplemental oxygen, with neutropenia identified as a common feature among severe cases. Severe lymphopenia (<1,000 lymphocytes/μL), elevated hepatic transaminases, and the presence of bacterial or fungal coinfections have been identified as major contributors to mortality in these patients[6].

Among children, the most common complications necessitating hospitalization are bronchiolitis and pneumonia[3,6]. Coinfection with RSV has been associated with more severe clinical courses, especially in children under two years of age, leading to increased ICU admissions and a 10 times greater need for mechanical ventilation than in children with hMPV infection alone[24]. While hMPV primarily targets the respiratory tract, rare instances of extrapulmonary involvement have also been described. Isolated reports of encephalitis in children with confirmed hMPV infection[25] have raised questions about the virus's potential to disseminate beyond the respiratory system. However, a definitive causal relationship remains uncertain, as hMPV replication is generally restricted to the respiratory epithelium[6].

TREATMENT AND PREVENTION

The management of hMPV infection is primarily supportive, as no specific antiviral therapies are currently available. Treatment strategies are guided by disease severity, with respiratory support constituting the foundation of care. Oxygen supplementation and humidified air can relieve respiratory distress, while bronchodilators may benefit patients with reactive airway components. In severe cases, mechanical ventilation may be required, necessitating close monitoring. Fluid and electrolyte management is essential, especially in individuals at high risk for complications. Symptomatic treatment, including antipyretics for fever and analgesics for myalgia or headache, further supports patient recovery. Decongestants may be considered in select cases, though caution is advised due to potential adverse effects[7].

In the absence of antiviral treatment or an approved vaccine, prevention is critical. Primary prevention relies on infection control measures such as hand hygiene, respiratory etiquette, surface disinfection and limiting exposure to symptomatic individuals. Several vaccine candidates, including live-attenuated, vector-based and subunit formulations, are currently undergoing preclinical and early clinical trials. Secondary prevention involves early identification *via* RT-PCR during seasonal outbreaks to enable timely isolation and reduce transmission, while tertiary prevention focuses on delivering comprehensive supportive care to minimize complications[5,6].

CONCLUSIONS

The hMPV remains an underdiagnosed yet significant cause of respiratory illness, particularly in vulnerable populations. Its clinical resemblance to other respiratory viruses and the lack of routine testing contribute to frequent oversight. With no specific antivirals or licensed vaccines, prevention relies heavily on hygiene, surveillance and public awareness. Its ability to cause severe disease, coupled with increasing prevalence and evolving variants, highlights a pressing need for investment in research, vaccine development and early diagnostic tools. Without timely intervention, hMPV will continue to pose a growing threat, especially in healthcare settings and high-risk individuals.

ORCID ID
Aishath Nur Shathir: 0009-0009-3995-9087
Kannan Subbaram: 0000-0001-8547-0957
Razana Faiz: 0000-0002-9841-4337
Sheeza Ali: 0000-0002-0248-6628

Conflict of Interest
The authors declare that there are no conflicts of interest.

Authors' Contributions
Conceptualization: Dr. Kannan Subbaram.
Writing-original draft: Dr. Aishath Nur Shathir.
Data curation and validation: Dr. Razana Faiz.
Supervision and visualization: Dr. Sheeza Ali.
Writing-review and editing: Dr. Kannan Subbaram, Dr. Aishath Nur Shathir, Dr. Razana Faiz, Dr. Sheeza Ali.

Acknowledgements
The authors thank the School of Medicine and the Maldives National University academic staff for their help in proofreading and grammar correction.

Ethical Approval and Informed Consent
Not applicable.

Funding
The authors received no financial support for the research and publication of this article.

Availability of Data and Materials
Data and materials used for this study are available from the corresponding author upon reasonable request.

AI Disclosure
Authors declare that no form of generative artificial intelligence was used in the writing of this article.

REFERENCES

1. Satapathy T, Satapathy A, Satapathy A, Yadav N, Chandrakar M, Chandrakar K. Recent outbreaks of human metapneumovirus (HMPV): prevention, diagnosis and therapeutic insights. J Drug Delivery Ther 2025; 15: 193-203.
2. Krüger N, Laufer SA, Pillaiyar T. An overview of progress in human metapneumovirus (hMPV) research: structure, function, and therapeutic opportunities. Drug Discov Today 2025; 30: 104364.
3. Wilkhoo HS, Islam AW, Wilkhoo HS, Hussain S, Singh B, Kadam SR. Clinical insights and advancements in human metapneumovirus management and prognosis. Discoveries 2025; 13: e204.
4. Adedokun KA, Adekola SA, Tajudeen A, Bello-Ibiyemi AA, Babandina MM, Magwe EA, Bello A. Rising global threat of human metapneumovirus (hMPV in 2024/2025): pathogenesis, immune dynamics, vulnerabilities in immunocompromised individuals, and lessons from past pandemics. J Rare Dis 2025; 4: 1-20.
5. Gnanasekaran S, Bashar MA, Rajan AK, Prabhat P. Emerging threat of human metapneumovirus (HMPV) and strategies for its containment and control. Infect Genet Evol 2025; 131: 105758.
6. Mohammadi K, Faramarzi S, Yaribash S, Valizadeh Z, Rajabi E, Ghavam M, Samiee R, Karim B, Salehi M, Seifi A, Shafaati M. Human metapneumovirus (hMPV) in 2025: emerging trends and insights from community and hospital-based respiratory panel analyses-a comprehensive review. Virol J 2025; 22: 150.
7. Alotaibi BS, Habib M, Habib A, Syed F, Shah NN, Tantry BA. Human metapneumovirus: a review of epidemiology, pathogenesis, diagnosis, and future prospects. J Pure Appl Microbiol 2025; 19: 1-11.
8. CDC. About Human Metapneumovirus. CDC 2024. Available at: https://www.cdc.gov/human-metapneumovirus/about/index.html
9. Schuster JE, Williams JV. Human metapneumovirus. Pediatr Rev 2013; 34: 558-565.
10. Akingbola A, Adegbesan A, TundeAlao S, Adewole O, Ayikoru C, Benson AE, Shekoni M, Chuku J. Human metapneumovirus: an emerging respiratory pathogen and the urgent need for improved diagnostics, surveillance, and vaccine development. J Pure Appl Microbiol 2025; 57: 304-310.
11. Wang Y, Chen Z, Yan YD, Guo H, Chu C, Liu J, Ding Y, Shao X, Xu J, Ji W. Seasonal distribution and epidemiological characteristics of human metapneumovirus infections in pediatric inpatients in Southeast China. Arch Virol 2013; 158: 417-424.
12. Davis CR, Stockmann C, Pavia AT, Byington CL, Blaschke AJ, Hersh AL, Thorell EA, Korgenski K, Daly J, Ampofo K. Incidence, morbidity, and costs of human metapneumovirus infection in hospitalized children. J Pediatric Infect Dis Soc 2016; 5: 303-311.
13. Kulkarni D, Cong B, Ranjini MJK, Balchandani G, Chen S, Liang J, González Gordon L, Sobanjo-Ter Meulen A, Wang X, Li Y, Osei-Yeboah R, Templeton K, Nair H. The global burden of human metapneumovirus-associated acute respiratory infections in older adults: a systematic review and meta-analysis. Lancet Healthy Longev 2025; 6: 100679.
14. Sah R, Srivastava S, Kumar S, Koteswara Rao GSN, Mehta R, Mohanty A, Sah S, Mehta V, Feehan J, Apostolopoulos V, Rodriguez-Morales AJ. Ongoing hMPV outbreaks in China and other Asian countries. Infez Med 2025; 33: 1-3.
15. Feng Y, He T, Zhang B, Yuan H, Zhou Y. Epidemiology and diagnosis technologies of human metapneumovirus in China: a mini review. Virol J 2024; 21: 59.
16. Zhao H, Feng Q, Feng Z, Zhu Y, Ai J, Xu B, Deng L, Sun Y, Li C, Jin R, Shang Y, Chen X, Xu L, Xie Z. Clinical characteristics and molecular epidemiology of human metapneumovirus in children with acute lower respiratory tract infections in China, 2017 to 2019: a multicentre prospective observational study. Virol Sin 2022; 37: 874-882.
17. Uddin S, Thomas M. Human Metapneumovirus. StatPearls [Internet]. StatPearls Publishing, Treasure Island (FL); 2023.
18. Heikkinen T, Osterback R, Peltola V, Jartti T, Vainionpää R. Human metapneumovirus infections in children. Emerg Infect Dis 2008; 14: 101-106.
19. Walsh EE, Peterson DR, Falsey AR. Human metapneumovirus infections in adults: another piece of the puzzle. Arch Intern Med 2008; 168: 2489-2496.
20. Venkataraman A. Assessing the impact of comorbidities on respiratory virus prevalence across age groups in Washington state. 2024. Available at: https://hdl.handle.net/1773/52009.
21. Shehu MT, Pascual A, Kapinos P, El Khoury MY. Mortality and morbidity of human metapneumovirus infection in the pre-COVID-19 era: the value of the Charlson comorbidity index on outcome prediction. Cureus 2024; 16: e52321.

22. Martinez-Rodriguez C, Banos-Lara MDR. HMPV in immunocompromised patients: frequency and severity in pediatric oncology patients. Pathogens 2020; 9: 51.
23. Chu HY, Renaud C, Ficken E, Thomson B, Kuypers J, Englund JA. Respiratory tract infections due to human metapneumovirus in immunocompromised children. J Pediatr Infect Dis Soc 2014; 3: 286-293.
24. Panda S, Mohakud NK, Pena L, Kumar S. Human metapneumovirus: review of an important respiratory pathogen. Int J Infect Dis 2014; 25: 45-52.
25. Fernández IS, Polo Mr, Muñoz-Almagro C, Carretero LM, Ureña SF, Muñoz AR, Roura RC, Dueñas BP. Human metapneumovirus in the cerebrospinal fluid of a patient with acute encephalitis. Arch Neurol 2012; 69: 649-652.