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Original Article

Retrospective analysis of human metapneumovirus in hospitalized and outpatient children: Insights from a four-year experience in Türkiye

Furkan Kalaycı[1], Aslinur Özkaya Parlakay[2], Ayça Çırak[1], Ece Karaköse[1], Kaan Çelebier[1], Metin Yiğit[1,3]

[1]Department of Pediatrics, Ankara Bilkent City Hospital, Ankara, Türkiye
[2]Department of Pediatric Infectious Disease, Ankara Bilkent City Hospital, Yildirim Beyazit University, Ankara, Türkiye
[3]Department of Pediatrics, Yildirim Beyazit University, Ankara, Türkiye

ABSTRACT

Objective: Human metapneumovirus (hMPV), particularly affecting children under five, is a significant viral agent associated with a wide range of respiratory illnesses, from mild upper respiratory infections to severe lower respiratory tract involvement. This study aimed to evaluate the clinical characteristics, severity indicators, and seasonal distribution of hMPV infections over a four-year period in one of Türkiye's largest pediatric hospitals, and to assess the potential epidemic risk in the national context.

Material and Methods: This retrospective study included 345 pediatric patients diagnosed with hMPV between January 2021 and December 2024. Demographic data, clinical findings, hospitalization status, respiratory support requirements, imaging results, and outcomes were analyzed.

Results: The median age was four years; 44.6% of patients were hospitalized, and 9.2% required intensive care. Common symptoms included cough (84.1%), fever (65.8%), and rhinorrhea (59.7%). Hypoxia, tachypnea, and pulmonary infiltrates were significantly associated with hospitalization ($p<0.001$). Four patients died, three without known comorbidities. The highest case count occurred in 2022, followed by a marked decline in 2023–2024, consistent with global trends.

Conclusion: Although generally considered mild, hMPV infection can result in severe disease and mortality, even in healthy children. These findings highlight the importance of early risk identification and integration of hMPV into respiratory infection surveillance and public health strategies. No significant outbreak was observed in Türkiye during the study period.

Keywords: Children, human metapneumovirus, respiratory tract infections

INTRODUCTION

Human metapneumovirus (hMPV), first identified in 2001, affects individuals of all age groups but is particularly prevalent among children under five years of age (1). As a major viral agent of respiratory infections, hMPV can present with a wide clinical spectrum, including bronchiolitis, pneumonia, and upper respiratory tract infections (1). Although hMPV infections can occur year-round, they are most commonly observed during the winter months (2).

The most commonly observed symptoms of hMPV infections include cough, fever, nasal discharge, tachypnea, and hypoxia. However, these manifestations closely resemble those of other viral respiratory infections, thereby limiting their diagnostic specificity (2). The clinical presentation can vary widely, ranging from mild upper respiratory tract infections to severe lower respiratory tract involvement (1). It has been reported that approximately 15% of community-acquired pneumonias requiring hospitalization in children are attributable to hMPV (3). Therefore, identifying risk factors that may predict the severity of illness is critical for effective patient management.

Since its discovery, outbreaks of hMPV among children have been reported at various times (4). Notably, recent reports have indicated significant increases in hMPV cases in the northern provinces of China, which are being closely monitored due to potential public health implications (5). This surge not only highlights the importance of public health preparedness but also contributes to growing societal concern. The increasing number of cases underscores the need for robust epidemiological surveillance of hMPV.

The aim of this study was to evaluate hMPV cases detected over the past four years at one of Türkiye's largest children's

Correspondence Address:
Furkan Kalaycı
e-mail: drfurkankalayci@gmail.com

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hospitals, to elucidate their clinical characteristics, and to assess the potential epidemic risk in the country from an epidemiological perspective.

MATERIALS and METHODS

This study was conducted at Ankara Bilkent City Hospital, Children's Hospital. The study population included patients who presented to the center between January 2021 and December 2024 and were diagnosed with hMPV at the time of presentation. Data from both hospitalized patients and those managed on an outpatient basis were retrospectively analyzed. Cases in which samples were improperly collected or multiple viral or bacterial agents were detected in the same nasopharyngeal swab were excluded. Additionally, individuals presenting for reasons unrelated to respiratory symptoms or asymptomatic patients sampled for other indications were not included.

Data for this study were obtained from the electronic medical record system of Ankara Bilkent City Hospital, Children's Hospital. The retrospectively analyzed data included patients' ages, genders, dates and seasons of presentation; symptoms (fever, cough, nasal discharge, tachypnea, hypoxia); histories of chronic diseases; hospitalization status and location (general pediatric unit or pediatric intensive care unit); length of hospital stay; need for respiratory support [invasive mechanical ventilation (IMV), non-invasive mechanical ventilation (NIMV), and high-flow nasal cannula (HFNC)]; and laboratory findings. IMV and NIMV were administered in the pediatric intensive care unit. As chest radiographs were not routinely obtained upon admission, only those available were assessed. The radiographic evaluations were conducted by pediatricians. Radiographs of patients with chronic conditions were compared with previous images in the system, and new pathological findings were assessed.

Patients with chronic diseases were categorized into five subgroups based on their underlying conditions: (1) the Asthma/Wheezy Infant Group, including patients diagnosed and followed by the pediatric allergy clinic for asthma or its variants, regardless of regular inhaler use; (2) the Immunodeficiency Group, comprising patients with primary immunodeficiencies, those undergoing chemotherapy for hematologic malignancies or solid tumors, patients receiving pulse steroid or biological agent therapy, and bone marrow transplant recipients under immunosuppression; (3) the Cardiac Disease Group, which includes patients with cyanotic congenital heart diseases (e.g., Tetralogy of Fallot, Truncus Arteriosus) or other cardiac conditions associated with hemodynamic instability (e.g., myocarditis, cardiomyopathy, heart failure); (4) the Neurological and Neurometabolic Diseases Group, consisting of patients with severe neurodevelopmental impairment affecting swallowing function, including cerebral palsy, neuromuscular disorders (e.g., spinal muscular atrophy, Duchenne muscular dystrophy), sequelae of hypoxic ischemic encephalopathy, intracranial hemorrhage, or hydrocephalus, and neurometabolic disorders with significant neurological involvement (e.g., MSUD, lysosomal storage diseases, Dravet syndrome, West syndrome); and (5) the Chronic Pulmonary Disease Group, encompassing patients with structural or functional pulmonary disorders, such as bronchopulmonary dysplasia, cystic fibrosis, congenital diaphragmatic hernia, respiratory distress syndrome, pulmonary sequestration, pulmonary hemosiderosis, sequelae of congenital pneumonia, genetically undefined interstitial lung diseases, and a history of tracheoesophageal fistula or esophageal atresia surgery.

Multiplex RT-PCR Analysis

Respiratory viruses were identified using the multiplex real-time PCR (mPCR) assay (Rotor-Gene Q, QIAGEN, Germantown, Maryland, United States). This technique facilitates the detection of various pathogens, including IFV, hRSV, hCoV (Corana 229E, OC43, NL63, HKU1, SARS-COV2), hPIV, hMPV, hRV, EV, hBoV, hAdV, and human parechovirus. Additionally, bacterial pathogens including Mycoplasma pneumoniae, Bordetella pertussis, Chlamydophila pneumoniae, Haemophilus influenzae, and Streptococcus pneumoniae were also detected.

Statistical Analysis and Ethics

The Statistical Package for the Social Sciences (SPSS) 23.0 (Chicago, Illinois, USA) was implemented for the statistical analysis. The Kolmogorov-Smirnov test and the examination of histograms were used to evaluate the compliance of numerical and continuous variables with normal distribution. Numerical data with a normal distribution were expressed as the mean and standard deviation (SD), while data with a non-normal distribution were expressed as the median and interquartile range (IQR). Percentages (%) and numbers (n) were used to express categorical variables. The Mann-Whitney U test was used to compare continuous variables that did not meet the normal distribution. The Kruskal-Wallis test evaluated continuous variables from many groups that did not fit into the normal distribution. Categorical variables were analyzed with the Pearson chi-square or Fisher's Exact Test. When comparing more than one group, p values were calculated using the Bonferroni correction. The significance level was established at $p<0.050$.

RESULTS

Among 40.610 patients tested using mPCR, hMPV was detected in 371 individuals. Twenty-six patients presenting with non-respiratory symptoms were excluded, resulting in a final study population of 345 patients. The median age of the study group was 4 years (IQR: 3–7), with 59.4% being male. The median age was 3 years (IQR: 3–5) for hospitalized patients and 6 years (IQR: 4–8) for outpatients. A total of 50.1% of the cases occurred in 2022, and 68.7% of patients presented during the winter season (Figure 1).

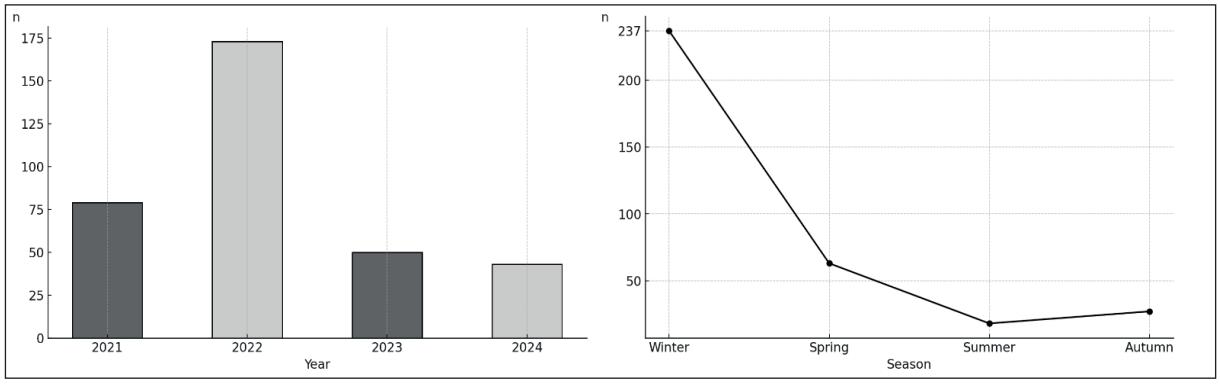

Figure 1: Distribution of metapneumovirus infections by years and seasons.

Table I: Demographic, laboratory, and chest x-ray findings in patients with and without chronic disease

	With Chronic Disease	Without Chronic Disease	Total	p
Number of patients (n)	82	263	345	-
Age*	5 (4-9)	4 (3-7)	4 (3-7)	<0.001
Gender† Male Female	 50(61) 32 (39)	 154 (58.8) 109 (41.2)	 205 (59.4) 140 (40.6)	0.899
Hospitalization† General pediatric unit Pediatric intensive care unit (PICU)	43 (52.4) 30 (69.7) 13 (30.3)	111 (42.4) 92 (88.9) 19 (11.1)	154 (44.6) 122 (55.4) 32 (20.6)	0.098
Respiratory support† Invasive mechanical ventilation Non-invasive mechanical ventilation High-flow nasal cannula (HFNC) Oxygen mask	 5 (11.6) 6 (14) 7 (16.3) 25 (58.1)	 6 (5.4) 8 (7.2) 18 (16.3) 79 (71.1)	 11 (7.2) 14 (9) 25 (16.2) 104 (67.6)	0.254
Length of hospital stay* General pediatric unit (days) Pediatric intensive care unit (PICU) (days) Total (days)	 7 (4-11) 4 (3-9) 8 (4-14)	 6 (4-10) 6 (3-9) 5 (1-9)	 6 (3-9.5) 4.5 (3-9) 7 (4-11)	 0.626 0.125 0.128
Laboratory parameters†	63 (76.8)	154 (58.6)	217 (62.9)	-
White blood cell (WBC) (×10⁶/L)*	8760 (5877-12150)	9655 (7217-12822)	9350(6870-12675)	0.361
Platelet count (PLT) (×10⁹/L)*	302 (228-398)	336 (279-472)	334 (260-444)	0.615
C-reactive protein (CRP) (mg/L)*	3.00 (1-14)	1.70 (1-5)	2 (1-6.5)	0.120
Absolute neutrophil count (ANC) (×10⁶/L)*	4340 (2615-6925)	4410 (2805-6752)	4410 (2755-6740)	0.157
Absolute lymphocyte count (ALC) (×10⁶/L)*	2750 (1380-3982)	3425 (2085-4952)	3160 (1920-4835)	0.161
Neutrophil-to-lymphocyte ratio (NLR)*	1.77 (0.97-3.79)	1.25 (0.69-3.75)	1.37 (0.74-3.70)	0.247
Alanine aminotransferase (ALT) (U/L)*	25 (18-36)	20 (15-27)	21 (15-28)	0.221
Aspartate aminotransferase (AST) (U/L)*	43 (31-56)	38 (32-51)	39 (32-51)	0.305
Lactate dehydrogenase (LDH) (U/L)*	349 (310-454)	352 (294-405)	350 (299-408)	0.142
Pulmonary infiltration† Present Absent	66 (80.5) 46 (69.7) 20 (30.3)	182 (69.2) 104 (57.1) 78 (42.9)	248 (71.9) 150 (60.4) 98 (39.6)	0.061

:** *median (IQR) (Mann-Whitney U test)* , **†:** *n(%) (Pearson chi-square),* ***White blood cell (WBC): *6600–15.600×10⁶/L,* ***Platelet count (PLT):*** *240–520 ×10⁹/L,* ***C-reactive protein (CRP):*** *<5 mg/L,* ***Absolute neutrophil count (ANC):*** *1500–8500 ×10⁶/L,* ***Absolute lymphocyte count (ALC):*** *1500–7000 ×10⁶/L,* ***Alanine aminotransferase (ALT):*** *0–41 U/L,* ***Aspartate aminotransferase (AST):*** *0–73 U/L, Lactate dehydrogenase (LDH): 0–470 U/L*

When evaluating the distribution of symptoms, 84.1% of patients (n=290) presented with cough, 65.8% (n=227) with fever, and 59.7% (n=206) with nasal discharge. Additionally, 45.5% (n=157) exhibited tachypnea, and 30.1% (n=104) showed decreased oxygen saturation (SpO_2). Overall, 44.6% of patients (n=155) were hospitalized, of whom 20.6% (n=32) required admission to the pediatric intensive care unit. At presentation, 3.2% (n=11) required IMV, 4.1% (n=14) required NIV, and 7.2% (n=25) received HFNC

support. The median total length of hospital stay was 7 days (IQR: 4–11). The median duration of stay in the general pediatric unit was 6 days (IQR: 3–9.5), while the median intensive care unit stay was 4.5 days (IQR: 3–9). Four patients died, one of whom had underlying neurological and neurometabolic disorders, while the remaining three had no chronic conditions.

According to imaging findings, 71.9% of patients (n=248) underwent chest radiography, among whom 60.4% (n=150) showed pulmonary infiltration; however, no complications such as lobar consolidation, pleural effusion, or pneumothorax were observed. Laboratory evaluations revealed a median white blood cell count of 9.350 ($\times 10^6$/L) (IQR: 6.870–12.675), a median platelet count of 334 ($\times 10^9$/L) (IQR: 260–444), a median CRP level of 2 mg/L (IQR: 1–6.5), and a median ALT level of 21 U/L (IQR: 15–28.75) (Table I).

Patients were categorized into two groups based on the presence of chronic diseases. The majority, 76.2% (n=263), had no history of chronic conditions, while 23.8% (n=82) had at least one chronic disease. Among those with chronic conditions, 31.7% (n=26) had neurological or neurometabolic disorders, 23.2% (n=19) had asthma or a history of wheezing in infancy, 22% (n=18) had immunodeficiency, 13.4% (n=11) had chronic lung disease, and 9.7% (n=8) had cardiac disease.

Among patients without chronic diseases, the median age of hospitalized individuals was significantly lower than that of outpatients (p<0.001). No significant association was observed between hospitalization and variables such as gender, fever, nasal discharge, or cough (p=0.998, p=0.671, p=0.393, p=0.123, respectively). However, hospitalization was significantly associated with the presence of tachypnea, low SpO_2, and pulmonary infiltration (p<0.001 for each). No statistically significant differences were found between the groups in terms of laboratory parameters.

Similarly, among patients with chronic diseases, the median age of hospitalized children was significantly lower than that of non-hospitalized patients (p<0.001). No statistically significant association was found between hospitalization and variables such as gender, fever, nasal discharge, or cough (p=0.899, p=0.129, p=0.206, p=0.863, respectively). However, hospitalization was significantly associated with tachypnea, low SpO_2, and pulmonary infiltration (p<0.001 for each).

Hospitalized patients comprised 55.1% (n=154) of the study group. When these patients were subdivided based on the presence of chronic diseases, it was found that younger children with chronic diseases had a higher hospitalization rate (p<0.001). No statistically significant differences were found between the two groups in terms of intensive care admission rates and length of stay (p=0.098, p=0.125, respectively). Additionally, no significant differences were observed between the groups concerning gender, fever, cough, nasal discharge, tachypnea and lung infiltration (p=0.922, p=0.531, p=0.470, p=0.086, p=0.179, p=0.061,respectively).

DISCUSSION

Despite being identified relatively recently, hMPV is generally regarded as a less severe pathogen compared to other viral agents responsible for lower respiratory tract infections (LRTIs) in children. Nevertheless, although often overshadowed by more prominent pathogens such as IFV and RSV, hMPV has been shown to cause serious clinical outcomes, including the need for intensive care and even death. This study analyzes four years of clinical data on hMPV infections from one of the largest children's hospitals in Türkiye, assessing recent epidemic risks and providing a comprehensive clinical evaluation of hMPV cases nationwide. The findings shed light on the current epidemiological landscape in Türkiye and offer guidance for evaluating global risks and developing management strategies for hMPV.

Studies conducted in various countries have reported that hMPV infections are more frequently observed in children under five years of age (4,6–8). A pediatric study involving patients under five indicated that hospitalizations were most common in those under one year of age (9), while another study reported this threshold as under three years (6,10). In the present study, the median age of all patients was four years, and that of hospitalized patients was three years, consistent with the literature. Moreover, hospitalization rates were found to increase as age decreased, regardless of the presence of chronic conditions. Globally, hMPV accounts for approximately 11% of LRTIs in children under five and 4–13% of hospitalizations due to LRTIs (6,11,12). Although hMPV can affect all pediatric age groups, it is particularly prevalent among children under five and may lead to hospitalization, necessitating careful surveillance. As with other viral respiratory pathogens, prevention and control strategies for hMPV should be developed and integrated into public health programs.

In human metapneumovirus, as with other viral respiratory pathogens, symptoms such as fever, cough, shortness of breath, nasal discharge, and hypoxia are commonly observed (13,14). Clinical presentation may range from mild fever and cough to severe bronchiolitis and pneumonia (6). Due to the similarity of symptoms, distinguishing hMPV infections from other respiratory infections has been reported to be challenging (15,16). Fever and cough are consistently described as the most common symptoms in the literature (16). Similarly, in the present study, these two symptoms were the most frequently observed. The absence of a significant association between fever, cough, nasal discharge, and either a history of chronic disease or hospitalization suggests that these symptoms alone are insufficient to predict disease severity. In contrast, the significant association between tachypnea, decreased SpO_2, and hospitalization highlights the importance of considering all clinical signs and findings collectively during patient evaluation.

In one study, infiltration was observed in 8% of patients with hMPV infection on chest radiographs, while a review reported

this rate as 26.4% (16,17). A study conducted in China found an infiltration rate of 75.2% (18). In the present study, this rate was 60.4%. Pulmonary infiltration was found to be significantly associated with hospitalization, regardless of the presence of chronic disease. The wide variation in reported rates may be attributed to methodological differences, including patient selection and imaging criteria. Nevertheless, the high rate observed in this cohort suggests that hMPV can be a serious pathogen affecting the lower respiratory tract. Moreover, the strong association between pulmonary infiltration and hospitalization indicates that radiographic findings may serve as a useful predictor of disease severity.

In the literature, reported rates of PICU admission among patients with hMPV infection vary considerably. For example, in one study involving 78 patients, 64.1% (n=50) were hospitalized, but only two required PICU care (19). In a U.S.-based cohort study, 6% (n=12) of 200 hMPV-positive patients were admitted to the PICU, and 4% (n=8) were intubated (10). In contrast, a study of 145 patients reported no PICU admissions (18), while another study reported a PICU admission rate of 11.4% (6). In the present cohort, 9.2% of patients (n=32) required pediatric intensive care, and 3.2% (n=11) underwent intubation. These findings indicate that severe clinical presentations can occur in children with hMPV infection. The PICU admission rate observed in this study was higher than in some previous reports, possibly due to differences in patient demographics, underlying disease profiles, access to healthcare services, and diagnostic or therapeutic approaches. Therefore, careful assessment of individual risk factors and early implementation of intervention strategies are critical in the management of pediatric hMPV cases. Notably, the intubation rate was similar to those reported in the literature, suggesting that the higher PICU admission rate may be attributable to an increased need for NIV rather than IMV. The potential role of NIV in reducing the need for IMV should also be considered.

In the present study, four patients died following hMPV infection, three of whom had no underlying chronic conditions. In the literature, mortality has typically been reported in the context of co-infections, secondary bacterial infections, or serious chronic illnesses (20). However, fatal cases involving isolated hMPV infection, as observed in this study, have rarely been reported. Although limited in number, these findings suggest that hMPV infection can, in some instances, lead to complications requiring intensive care and even result in death. This underscores the need for vigilant clinical monitoring and risk stratification, particularly given that severe outcomes may occur even in previously healthy children.

Various studies have reported that hMPV infections most commonly occur during the winter season (2,21). Consistently, in the present study, the highest number of cases was recorded during the winter months, followed by spring. Outbreaks associated with hMPV in children have been reported in Norway (2002–2003), Korea (2007), and Switzerland (2021) (1). Additionally, significant increases in case numbers were observed in China and several European countries in 2022; however, reported rates declined markedly in 2023 and 2024 (5,22,23). Although a rise in cases was noted in China towards the end of 2024, the World Health Organization did not classify this as an unusual outbreak or pandemic threat (23). In this Turkish cohort, the peak number of cases was observed in 2022, followed by a notable decline in 2023 and 2024. These findings suggest that no clinically significant epidemic occurred during the study period, and the seasonal distribution of cases was consistent with global trends.

This study has several limitations. First, due to its retrospective design and single-center setting, the findings may not be representative of the general population. In addition, infection control measures implemented during and after the SARS-CoV-2 pandemic may have influenced the observed prevalence of hMPV. Although some pathogens and co-infections were excluded using multiplex PCR, the absence of sputum culture data limited the ability to rule out secondary bacterial infections. Furthermore, conducting the study in the capital city may not fully reflect the socioeconomic disparities and inequalities in healthcare access present across the country, potentially limiting the generalizability of the findings to the broader Turkish population. Nevertheless, despite these limitations, this study—conducted in one of the largest pediatric centers in Türkiye and based on a large patient cohort—offers valuable insights into the clinical course and management of hMPV infections and supports the development of effective public health strategies.

CONCLUSION

In conclusion, hMPV is a common viral pathogen, particularly affecting children under five years of age. Clinical symptoms alone are insufficient to predict disease severity; however, SpO_2, tachypnea, and pulmonary infiltrations at presentation have been identified as significant risk factors for hospitalization. Although often perceived as a mild virus, the notable proportion of patients requiring intensive care, along with four reported deaths—three of which occurred in previously healthy children—suggests that hMPV can follow a severe and potentially fatal course. These findings underscore the importance of not underestimating hMPV as a respiratory pathogen and highlight the need for its inclusion in diagnostic, monitoring, and preventive health strategies. Despite recent concerns about epidemic risk, a decrease in case numbers compared to previous years was observed. Nonetheless, given that this decline may be temporary and viral circulation patterns can fluctuate over time, the continuation of effective surveillance and prevention strategies remains essential.

Ethics committee approval

This study was conducted in accordance with the Helsinki Declaration Principles. This study was conducted in accordance

with the Declaration of Helsinki and received ethical approval from the Ethics Committee of Ankara Bilkent City Hospital (24.04.2024/141).

Contribution of the authors

Study conception and design: **FK, MY, AOP;** data collection: **EK, AC, KC;** analysis and interpretation of results: **FK,MY;** draft manuscript preparation: **FK, KC;** All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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