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Research Article

Clinical and Epidemiological Characteristics of Human Metapneumovirus Infection in Children in Kyrgyzstan

Madina Mambetova[1], Zuura Dzholbunova[1], Meerim. Bayalieva[1], Asel Balabasova[2], Zhumagul Anarbaeva[3], Zhanara Asanbekova[4], Poshitha Kondadasula[5]

[1]Department of Pediatric Infectious Diseases, Akhunbaev Kyrgyz State Medical Academy, Bishkek, Kyrgyz Republic.
[2]Republican Clinical Infectious Diseases Hospital, Bishkek, Kyrgyz Republic.
[3]Department of Infectious Diseases, Akhunbaev Kyrgyz State Medical Academy, Bishkek, Kyrgyz Republic.
[4]Department of Propaedeutics of Childhood Diseases, Kyrgyz State Medical Academy named after Akhunbaev, Bishkek, Kyrgyz Republic.
[5]Department of General Medicine, A C Subba Reddy Government Medical College, Nellore, Andhra Pradesh, India.
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I N F O

Corresponding Author:
Madina Mambetova, Department of Pediatric Infectious Diseases, Akhunbaev Kyrgyz State Medical Academy, Bishkek, Kyrgyz Republic.
E-mail Id:
madina365@gmail.com
Orcid Id:
https://orcid.org/0009-0008-5836-7581
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A B S T R A C T

Introduction: Human metapneumovirus (hMPV) has recently emerged as the primary cause of acute respiratory viral infection (ARVI). Like other countries in Central Asia, Kyrgyzstan has experienced a high prevalence of ARVI infections, which sometimes reach epidemic levels. The purpose of this study was to investigate the presence of acute respiratory viruses such as parainfluenza, rhinovirus, adenovirus, respiratory syncytial virus, metapneumovirus, and bocavirus in the etiological structure of ARVI in Kyrgyzstan.

Methods: This cross-sectional study included children diagnosed with ARVIs and divided them into three age groups: Group I (n = 30, 0–12 months), Group II (n = 24, 1–3 years), and Group III (n = 8, 4–7 years). Polymerase chain reaction was performed on nasal secretions collected from children hospitalised for severe ARVIs.

Results: hMPV infection is more common in children under 10 years of age, and the severity of the illness is high, with a mortality rate of 7.0%–10.0% in young children. Several factors, including gestational pregnancy, anaemia, history of ARVIs, and postpartum complications, can affect the severity of the condition. Pneumonia was more common in children in Groups II-III (33.3%, 62.5%, and 50.0%, respectively).

Conclusion: ARVI was the most frequently reported illness among the patients, and the severity of the illness ranged from 70.0–75.0%.

Keywords: Human Metapneumovirus, Acute Respiratory Viral Infections, Epidemiology, Children, Pneumonia

Introduction

Acute respiratory viral infections (ARVI) are a significant public health issue, and viruses account for the majority of these infections in children. Approximately one billion cases are reported annually, accounting for 83.8% of all infectious diseases in children. The severity of ARVI lies in its high incidence of severe forms, presence of comorbidities, and high mortality rate (7.0%–10.0%) in young children. The challenge in treating and preventing ARVI is the numerous respiratory viruses that cause the disease.[1–6]

Human metapneumovirus (hMPV) has recently emerged as the primary cause of ARVI. hMPV was first identified using polymerase chain reaction (PCR) from nasopharyngeal swabs from children. hMPV is classified into two genotypes, hMPV-A and hMPV-B. Genotype A causes blockage in both the lower (36.0%) and upper (5.0%) respiratory tracts and occasionally causes encephalitis in young infants. Studies suggest that hMPV infection is less common in children over 10 years of age, as they are more likely to have been infected at a younger age and to develop antibodies against hMPV.[2,7–9]

Like other countries in Central Asia, Kyrgyzstan has experienced a high prevalence of ARVI infections, which sometimes reach epidemic levels. The purpose of this study was to investigate the presence of acute respiratory viruses such as parainfluenza, rhinovirus, adenovirus, respiratory syncytial virus, metapneumovirus, and bocavirus in the aetiological structure of ARVI in Kyrgyzstan. With severe forms of illnesses causing high death rates, complications, and expensive virological testing, it is crucial to establish diagnostic criteria. The findings of this study can enhance the therapy and treatment outcomes.

Materials and Methods

In this cross-sectional study, 1192 cases of ARVI were analysed, of which 62 (5.2%) had hMPV (RNA). The study was conducted at the Republican Clinical Infectious Diseases Hospital in the Kyrgyz Republic between January 2022 and April 2023 and involved 62 children aged 0–14 years. The children were divided into three age groups: Group I (n = 30, 0–12 months), Group II (n = 24, 1–3 years), and Group III (n = 8, 4–7 years). The majority of cases were found in Groups I and II ($p < 0.05$). Children whose parents did not provide consent or whose medical records were incomplete were excluded from this study.

A molecular genetic examination was conducted on children aged 0–14 years who were hospitalised with a diagnosis of "severe acute respiratory infection" at the Republican Clinical Hospital in Kyrgyzstan. The patients were selected based on the usual World Health Organization case criteria for severe acute respiratory infection, which include having a temperature over 38 °C, along with symptoms such as cough or sore throat, and experiencing shortness of breath and/ or trouble breathing that necessitates hospitalisation. In babies and young children, a respiration rate exceeding 40 breaths per minute, together with indications of danger, such as convulsions, inability to swallow or breastfeed, vomiting, or altered awareness.

Molecular genetic experiments were conducted using the Centers for Disease Control and Prevention procedure for real-time reverse transcription PCR (Artus GmbH, Germany). PCR was performed on nasal secretions collected from children hospitalised for severe ARVIs. In this study, we evaluated the presence of RNA/ DNA from respiratory viruses on the first day of admission to Infectious Diseases Hospital, Kyrgyz Republic.

Statistical analysis, version 11.5 of the Statistical Package for the Social Sciences was employed. The results are presented as mean ± standard deviation and n (%), and a paired t-test was used to evaluate the variations in treatment and outcomes across the participating sites. Statistical significance was set at $p < 0.05$. The study was conducted with the full consent of the patients' parents and was approved by the Bioethics Committee of the IK Akhunbaev Kyrgyz State Medical Academy (Protocol No. 17, dated April 13, 2019).

Results

A higher percentage of females in Group I were affected by the illness (66.7%) than in Group II (58.3%) and Group III (75.0%). The majority of sick children, who were residents of the city, accounted for 70.0%, 79.2%, and 50.0% of the cases in the Chüy region, which could be attributed to overcrowding caused by both internal and external migration. Additionally, 30.6% of sick children living in rural areas sought medical treatment at the Republican Clinical Hospital, bypassing rural territorial facilities.

The highest prevalence of hMPV infection was observed during the autumn-winter season, indicating a seasonal increase (Figure 1).

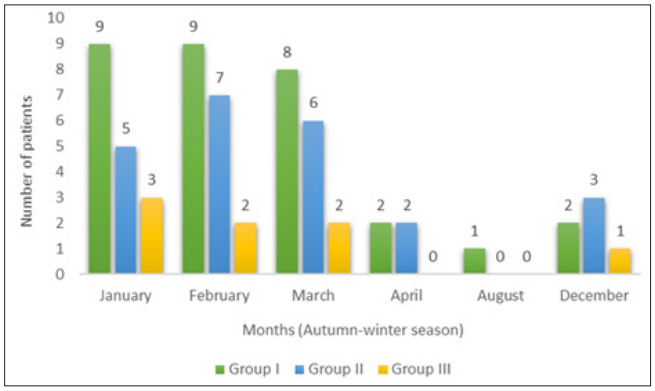

Figure 1.Incidence of hMPV Infection in Children During the Autumn-Winter Season

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Several factors, including gestational pregnancy, anaemia, past history of ARVIs, and postpartum complications can affect the severity of the condition. 50% of the infants experienced an intensified premorbid background due to anaemia. The prevalence of atopic dermatitis, repeated episodes of bronchial obstruction, neonatal hypoxic-ischemic encephalopathy, and convulsive syndrome was higher in the infants (Figure 2).

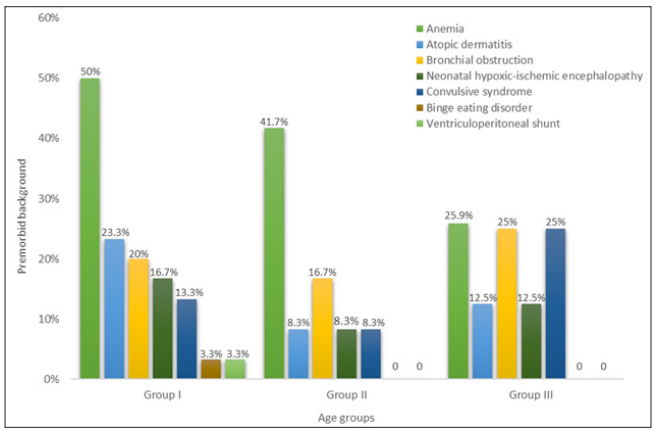

Figure 2.Premorbid Background of Children with hMPV Infection

ARVI was the most frequently reported illness among the patients, with prevalence rates of 56.7%, 79.2%, and 62.5%, respectively. This has an adverse effect on disease progression, and each subsequent hMPV-infected infant had a pre-existing history of health issues and concurrent disorders. Outpatient care was provided to 27 patients (56.7%, 33.3%, and 25.0%, respectively) at family medical centers. Patients in Group I, who received penicillin antibiotics for an average of 4.0 ± 1.3 days, were more likely to seek this treatment. However, when their health worsened, they were transferred to an infectious disease hospital for hospitalisation.

The severity of the illness ranged from 70.0-75.0%, indicating that the most severe forms of the disease were common. Among the 62 hospitalised patients, 67.7% experienced emergency syndrome. The most prevalent syndromes included pneumonia with respiratory failure (46.8%), lower respiratory tract blockage (35.5%), viral croup (12.9%), and convulsive syndrome (14.5%).

The study found that 96.7% of the patients with bronchial obstruction were diagnosed with ARVI in the emergency ward. The percentage of emergency conditions for bronchial obstruction, croup, and convulsive syndrome was 36.6%, 33.3%, and 12.5%, respectively. Pneumonia was more common in children in Groups II-III (33.3%, 62.5%, and 50.0%, respectively). One in four patients was hospitalised at the Republican Clinical Hospital at an advanced stage of the disease.

An in-depth examination of the timing of patient admission in Group I revealed that nearly half of the sick children (53.3%) were admitted to an infectious disease hospital on day 5 ± 1.6 of their illness, indicating a later admission date. Of the total number of newborns, 5 (16.7%) were transported to the hospital by ambulance, but they were promptly transferred to the intensive care unit. The severity of hMPV infections was higher in children within 0–12 months (70.0%) and young children (62.5%) presented in Figure 3. Therefore, the failure of parents and primary-level doctors to accurately assess the severity of the disease, along with delayed presentation and hospitalisation in an infectious disease hospital, played a role in the development of severe illnesses in 67.7% (n = 62) of cases, leading to emergency conditions even before reaching the hospital.

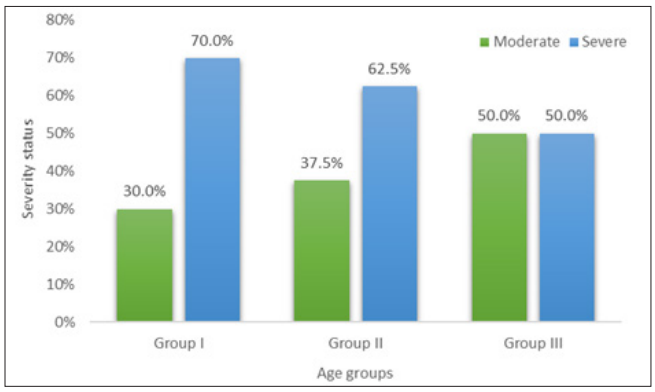

Figure 3.Severity Status in Children with hMPV Infection

In 67.7% of cases, severe signs of intoxication, anxiety, and hemodynamic disruption were detected, including a marbling effect on the skin and recurrent vomiting in 40.3% of cases. These symptoms were reported in age groups I and II with percentages of 70.0%, 62.5%, and 25.0%, respectively. Atypical respiratory syndrome was identified in 54 (82.3%) patients, and the average time from detection to diagnosis was 4.2 ± 0.9 days. The frequency of the clinical signs of hMPV infection is presented in Table 1.

Table 1.Frequency of Clinical Symptoms in Children with hMPV Infection

Clinical Symptoms	Group I (0–12 Months)	Group II (1–3 Years)	Group III (4–7 Years)
Fever	38.8 ± 0.1	38.9 ± 0.1	39.2 ± 0.2
Cough	1.9 ± 0.2	2.0 ± 0.2	3.1 ± 0.5
Catarrh	1.6 ± 0.3	1.2 ± 0.1	1.2 ± 0.1
Vomiting	1.2 ± 0.3	1.7 ± 0.1	1.6 ± 0.1
Diarrhoea	1.5 ± 0.5	-	-

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Conjunctivitis	1.9 ± 0.1	1.8 ± 0.1	1.7 ± 0.1
Rhinitis	2.0 ± 0.1	1.9 ± 0.1	1.8 ± 0.1
Serous otitis media	1.2 ± 0.1	-	-
Dyspnoea	3.2 ± 0.2	1.1 ± 0.1	1.3 ± 0.3*

Values are presented as the mean ± standard deviation, *p < 0.05

Most patients (95.1%, n = 62) experienced coughing, which lasted for an average of 5.5 ± 0.9 days. Eight patients (12.9%) were diagnosed with croup, which is an obstruction of the upper respiratory tract that lasted for an average of 5.0 ± 0.4 days, accompanied by stridor, hoarseness, and mild catarrhal symptoms that lasted 2.4 ± 0.6, 2.9 ± 0.6, and 3.8 ± 0.2 days, respectively.

Obstructive syndrome, which affects the lower respiratory tract, is more frequent in Groups I and II, affecting 43.5% of the 62 patients. Group I patients experienced bronchiolitis in 17.7% of the cases and the occurrence of lower respiratory obstruction pathways in Groups I and II was affected by age-related characteristics of the respiratory system, pre-existing conditions, and hMPV infection in 22.6% of the cases.

A strong positive association (r = +1.0) was found between the intensity and length of intoxication in Group I patients and a moderate positive correlation (r = +0.5) was observed between the duration of shortness of breath and the duration of bed rest. A negative correlation was found between illness severity and the duration of bed rest (r = -0.5).

In Group II, a correlation was observed between fever duration and several indicators. The child's age showed a positive correlation of +1.0, while the duration of bed days of patients had a positive correlation of +0.7. Additionally, there was a negative correlation of -0.5 between disease severity and pyretic fever, as well as a negative correlation of -0.4 between fever duration and the duration of shortness of breath.

Ten patients (16.1 %) experienced intestinal symptoms. Within this group, 70% had one type of symptom, 20% had another, and 10% had a third symptom. Liquid stool occurred three to eight times per day and lasted for an average of 2.7 ± 0.3 days. Nine individuals experienced dyspeptic symptoms, with vomiting occurring, on average, 2.3 ± 0.3 days after the onset of the illness. Obstructive syndrome was observed in 40.0%, 33.3%, and 25.0% of cases, while croup was present in 16.7%, 8.3%, and 12.5% of cases, respectively. However, disseminated intravascular coagulation was more frequently observed in Groups I and II, with prevalence rates of 6.7%, 4.2%, and 0%, respectively.

Of the patients in Group I, 33.3% had bronchiolitis and 3.2% had pulmonary atelectasis. In Group II, 66.7% had pneumonia, and 50.0% of patients in Group III had pneumonia. In Group III, 6.7% of patients had cerebral oedema with a duration of 1.7 ± 0.4 days (Figure 4).

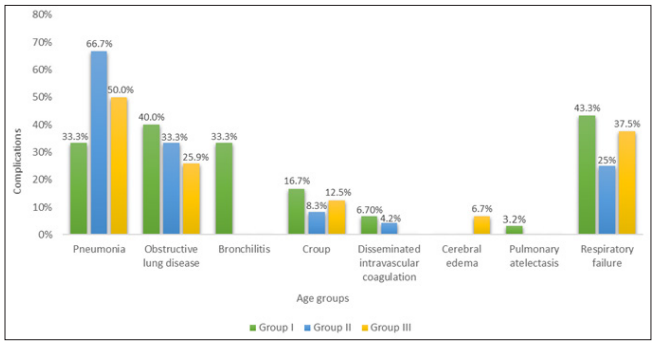

Figure 4.Rate of Complications in Children with hMPV Infection

The patient's peripheral blood sample showed anaemia and minor leukocyte and erythrocyte sedimentation rate alterations upon admission to the infectious disease hospital. Patients diagnosed with pneumonia had high levels of inflammatory markers, such as procalcitonin and C-reactive protein, indicating the need for antibacterial therapy.

Blood coagulation tests showed a decrease in the prothrombin index and an increase in the prothrombin time, as well as hypoproteinaemia, which collectively suggested the development of situational DIC syndrome. Biochemical analyses revealed that the patient's creatinine, urea, and residual nitrogen levels were within normal limits, as were the blood electrolyte compositions of calcium, potassium, sodium, and magnesium levels.

Ultrasound examinations were conducted in 10 patients, revealing diseases of the central nervous system, such as intracranial hypertension, choroid plexus cysts, and hydrocephalus, with a prevalence of 12.8%.

In patients with viral croup (12.9%), adrenaline was administered via a nebuliser on the first day. Corticosteroids were administered to 46.8% of patients with severe croup for 1.6 ± 0.3 days. Humidified oxygen was provided to patients with an average oxygen saturation level of 91.9 ± 2.8 (35.4%), for 2–5 days. Anticonvulsant medication was administered to 8.1% of the participants for 1.9 ± 0.2 days. Cupping therapy was provided to 35.5% of the participants, resulting in hyperthermia for 1.6 ± 0.4 days.

Discussion

hMPV has been detected in humans for at least 50 years.[10] It was discovered by Dutch researchers in both children and adults in 2001.[10] Almost all children have contracted hMPV by the age of five years, as reported in the initial findings.[10] Factors such as the use of continuous cell lines for viral isolation in laboratories where hMPV does not

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replicate efficiently may have contributed to the delay in identifying hMPV.[10] By the time children reach two years of age, 52% of them in Israel have developed antibodies against a specific disease.[11] In the Netherlands and Japan, all children develop these antibodies by the age of 10 years.[10,12]

This study indicates that the hospitalisation rate for children under 3 years of age due to hMPV is similar to the rates for influenza virus and parainfluenza virus types 1, 2, and 3, which affect approximately 1 per 1000 children.[13,14] However, the rate of hospitalisation for respiratory syncytial virus (RSV) was higher at 3 per 1000 children.[15] Therefore, the number of patients requiring hospitalisation due to hMPV was comparable to that of other prevalent respiratory viruses.

In this study, the mean duration of hospitalisation was 6.1 ± 0.1 days, with 88.7% of patients discharged with improvement and 11.3% experiencing full recovery. Forty percent of hospitalised children with hMPV infections had high-risk conditions, such as preterm birth and asthma, while a lower percentage of outpatients with hMPV infections had these conditions. Children with high-risk illnesses were more likely to be hospitalised because of hMPV infection.[16–19] All children were susceptible to hMPV infections and required medical intervention.

All patients received antibiotics for therapy with a duration of 6.0 ± 1.3 days. The most common treatment was single therapy (85.5%), followed by sequential therapy (12.9%), and combination therapy (1.6%). The antibiotics used included broad-spectrum penicillin and third-generation cephalosporins. For obstructive syndrome, patients received inhalation therapy using a salbutamol spacer at a concentration of 66.1% for 3.2 ± 0.6 days. Budesonide was administered to 11.3% of patients with recurrent obstructive syndrome for 1.2 ± 0.3 days. The clinical characteristics of hMPV infection are similar to those of other respiratory viruses; however, hospitalised patients with hMPV infections are more likely to require oxygen and have longer intensive care unit stays.[18,20–22] No fatalities related to hMPV, RSV, or influenza infections in many studies.[15,22] These data suggest that hMPV can cause serious illness, and there have been documented cases of fatal hMPV infections.[23–25]

In this study, among the 44 children studied, 70.9% experienced a progressive onset of illness and 96.7% had elevated temperatures. Only 10.0% of the patients had sub-febrile ranges, 33.3% had febrile ranges, and 50.0% had pyretic hyperthermia. The fever lasted for an average of 3.4 ± 1.0 days, and 14.5% of young children experienced febrile convulsions due to central nervous system damage. Studies suggest that asymptomatic children rarely test positive for hMPV, whereas non-human primates and small-animal species exposed to the virus experience acute respiratory illnesses with similar characteristics to humans.[21,26–28] The prevalence of hMPV coincides with that of other respiratory viruses, emphasising the importance of long-term studies to identify its epidemiological characteristics. Monitoring hMPV activity alongside RSV and influenza viruses throughout the year is crucial to determine the start and persistence of activity.

Although research on the pathophysiology of MPV infections is ongoing, it is known that the virus affects the epithelium of the respiratory tract, causing degenerative changes characterised by numerous eosinophilic inclusions, histiocytes, and multinucleated giant cells.[7,29,30] hMPV infection can result in persistent airway inflammation in children with concurrent bronchopulmonary diseases.

It is important to note that in children in Group III, hMPV infection was less commonly observed due to the existence of established antibodies, indicating a previous hMPV infection. The data we have received align with the findings of contemporary writers.[6,8,9,30]

Conclusion

Among 1192 children diagnosed with ARVI, the incidence of the hMPV infection was 5.2%. The infection caused damage to both the upper and lower respiratory tracts in 12.9% and 66.1% of the cases, respectively. Most infants and young children (67.7%) experienced severe forms of pneumonia, characterised by the development of pneumonia with respiratory failure and emergency syndromes, including croup and obstructive syndromes. Further research is needed to improve the diagnosis and treatment of paediatric hMPV infections.

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Conflicts of Interest: None

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