



## Research Article

# Metapneumovirus Clinical Course and Outcome in Pediatric Intensive Care Unit in A Tertiary Center in Riyadh, Saudi Arabia

Omar A Abdulmanea\*, Muhammed Nishil Aboo, Reem S Alrasheed, Abdulaziz A Alsoqati

Pediatric Intensive Care Unit, King Fahad Medical City, Riyadh, Saudi Arabia

\*Corresponding author: Omar A Abdulmanea, Pediatric Intensive Care Unit, King Fahad Medical City, Riyadh, Saudi Arabia

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## Abstract

**Background:** Infection is an important cause of morbidity and mortality especially in the respiratory system. Human metapneumovirus (HMPV) belongs to the paramyxovirus family of viruses, and can cause a simple upper respiratory tract infection (URTI) or severe lower respiratory tract infection LRTI which needs intensive care. **Methods:** This is a retrospective, descriptive review of the electronic medical record, for a five-year period between January 2017 until December 2021 which was done for all children aged between 0–14 years old, who were admitted to a tertiary PICU in King Fahad Medical City (KFMC) in Riyadh, Saudi Arabia, with a HMPV infection, which was laboratory-confirmed by polymerase chain reaction on specimens obtained via nasopharyngeal swab. **Results:** 41 patients included in the study period. The age ranged between 3 months to 14 years. The majority of cases 31 [76%] were admitted between November and March. A total of 35(85.4%) children required respiratory support, 7 [17.1%] patients needed vasopressors, 14 [34.1%] patients received blood transfusions and 2 [4.9%] patients needed renal replacement therapy. **Conclusion:** The majority of HMPV cases admitted to PICU were between November to March and had a previous admission to PICU due to other co morbidities. Viral co-infection was present in 21.9% of subjects. We found that the majority of the patients needed respiratory support. One quarter of the patients had acute kidney injury initially, and most of them had improved hemodynamics. However two patients did need renal replacement therapy.

**Keywords:** Human Metapneumovirus; Pediatric Intensive Care Unit; Outcome; Course.

## Introduction

Infection is an important cause of morbidity and mortality especially when it occurs in the respiratory system [1]. Children under 5 years of age often experience three to six episodes of acute respiratory infection per year. The World Health Organization (WHO) categorize respiratory infections as the second most important cause of death in children below 5 years old [2]. Viruses are the main cause of lower respiratory tract infections, especially in infants [3]. There has been an improvement in Virus-detection technology in recent years, after the use of the polymerase chain reaction (PCR) which is now available in many clinical settings and able to detect even co-infection with other viruses [4].

HMPV belongs to the paramyxovirus family, which is similar to respiratory syncytial virus (RSV) and often has a wide spectrum of presentations in infants and children [5]. The human metapneumovirus was discovered in the beginning of 2000 by Dr. Van Den Hoogen [5]. It can range from a simple upper respiratory tract infection URTI to a severe lower respiratory tract infection LRTI, which may need intensive care [6]. Most of the HMPV infections are detected in the winter season, between January to April [7].

HMPV infections cause 4% of pediatric hospitalizations, 15–25% of those need transfer to pediatric intensive care units, with 8–17% requiring mechanical ventilation [8]. The hospitalization due to HMPV may cost around 6000 U.S. dollars per pediatric patient hospitalization [8] Those children with HMPV infections

less than 5 years of age were more likely to need oxygen support and a longer average of stay in the pediatric intensive care unit [4.5 days versus 2 days] than those with a negative HMPV result [8]. Currently, there is no specific treatment or vaccine for HMPV infection [9]. Due to the clinical severity of the infection by Human metapneumovirus, it is important to study the effect of HMPV on the pediatric age group.

In conclusion, we have a lack of knowledge about the impact of human metapneumovirus in a PICU in Saudi Arabia, as the percentage of children in the Saudi Arabian population is high and they are at risk for viral illnesses, especially during the winter seasons and crowded events such as the annual pilgrimage (hajj) and minor pilgrimages (omrah). Therefore, we are looking for improvement in the clinical course and outcome through our study.

## Method

### Study design

In our study we assessed the clinical features and outcomes of the pediatric patients with HMPV infections needing admission to the PICU in King Fahad Medical City (KFMC) in Riyadh, Saudi Arabia. The PICU has a capacity of 20 beds. This is a descriptive, retrospective review of medical records for all children confirmed to have HMPV infection, who were admitted to the PICU during 5 years between January 2017 until December 2021. A total of 41 patients were included. The Institutional Review Board at KFMC approved this study with no: IRB00010471.

### Inclusion and Exclusion criteria

#### Inclusion

All pediatric patients younger than 14 years old, male or female, with or without comorbidities, admitted from January 2017 until December 2021 with a positive human metapneumovirus NPA (nasopharyngeal aspirate) detected by PCR (polymerase chain reaction)

#### Exclusion

Multiple admissions of the patient to PICU in the same hospitalization course, cardiac patients admitted in the cardiac intensive care unit.

### Data collection

Electronic medical records of the 41 patients (via the Epic® and Cortex® systems) were reviewed and analyzed for the following data: sex, age, length of stay, type of respiratory support [HFNC, NIV, invasive mechanical ventilators, HFOV, ECMO, nitric oxide] the length of support, incidence of pneumothorax, plural effusion, inotropes, comorbidities including prematurity, asthma, pneumonia, airway anomalies, GERD, sepsis, congenital heart disease, neurological disorders, immunodeficiency states, AKI, and dysmorphism (e.g. Down syndrome). We collected the data regarding the duration and need for PICU care and respiratory support including the type (invasive, non-invasive positive pressure ventilation and oxygen support), inotropic support, renal replacement therapy and extracorporeal membrane oxygenation and survival outcomes.

### Results

41 patients of HMPV confirmed by PCR were identified during the study period. The data are summarized in the (Tables 1 and 1A). 21 [51%] patients were females. The age was between 3 months to 14 years old with median of 3 years. The PICU stay ranged from 3 to 105 days with median of 14 days. The majority of cases (31[75%] patients) were admitted between the period between November-March. The most common clinical presentations for the patients were cough, shortness of breath and fever with percentages of 97%, 95% and 80% respectively. 28 [68%] of the patients had a previous admission to PICU due to other comorbidities. One of the most common comorbidities was asthma, which was noted in 26 [63.4%] patients, neuromuscular diseases in 21 [51.2%], followed by gastroenterology disease in 18 [43.9%] patients, which was mostly due to gastroesophageal reflux. Other comorbidities included: prematurity 17.1%, chronic lung disease 29.3%, CHD 39%, genetic disorders 43.9% particularly Down syndrome, and immunodeficiency 4.9%. Viral co-infection was present in nine (21.9 %) subjects, mainly with either rhinovirus in four patients (9.7%) or adenovirus in four patients (9.7%). 28 [68.3%] patients used a bronchodilator as a chronic medication, 19 [46.3%] used a steroid inhaler and 14 [34.1%] used anti-reflux medication.

	<b>min - max</b>	<b>Mean ± SD</b>	<b>Median (P25, P75)</b>
Age (month)	3 - 168	54 ± 47	36 (12, 84)
PICU Stay (day)	3 - 105	25 ± 24	14 (10, 36)
Height (cm)	48 - 137	88 ± 27	87 (65, 111)
Weight (Kg)	2.7 - 31	12.5 ± 7.3	11.7 (7, 16)
Body Mass Index(kg/m2)	8.16 - 56.86	16.23 ± 8.73	14.33 (12.08, 15.8)
HNFC duration (day)	1 - 5	3 ± 1	2 (2, 3)
NIV duration (day)	1 - 23	6 ± 6	4 (2, 7)
IMV duration (day)	1 - 36	9 ± 11	5 (2, 9)
HFOV duration (day)	2 - 35	20 ± 14	21 (10, 29)
Nitric oxide duration(day)	3 - 25	16 ± 9	18 (10, 23)
Vasopressor duration	1 - 35	10 ± 12	5 (1, 16)
Renal replacementtherapy duration	2 - 6	4 ± 3	4 (2, 6)

**Table 1:** Descriptive Statistics of the metric data.

A total of 35 (85.4%) children required respiratory support: high-flow nasal cannula in 17 [41.5%] patients, noninvasive mechanical ventilation in 20 (48.8 %) patients, invasive mechanical ventilation via endotracheal intubation in 18 (43.9 %) patients, high-frequency oscillatory ventilation in four(9.8%) patients, while ECMO was not used. 23 [56.1%] patients needed a fluid volume bolus, seven [17.1%] patient needed a vasopressor, 14 [34.1%] patients received blood transfusions and two [4.9%] patients needed renal replacement therapy. We found that the patients with previous co-morbidities had an increased need for the respiratory support when compared with healthy patients. The majority of patients 35 [85.4%] were discharged the home and the remaining six [14.6%] patients died in hospital.

<b>Characteristic</b>	<b>Description</b>	<b>N (%)</b>
Gender	Female	21 (51.2%)
	Male	20 (48.8%)
Clinical signs	Fever	33 (80.5%)
	Shortness of breath	39 (95.1%)
	Cough	40 (97.6%)
	Increase secretion	37 (90.2%)
	Need intubation	19 (46.3%)
	Previous PICU admission	28 (68.3%)
	Other	28 (68.3%)
Chronic lung disease	Prematurity	7 (17.1%)
	Asthma	26 (63.4%)
CHD		16 (39.0%)
Chronic gastroenterology disease		18 (43.9%)
CNS disease		21 (51.2%)
Central: CP		16 [ 39%]

Peripheral , myopathy		5 [12.1%]
Genetic , metabolic disease , mainly Downsyndrome		18 (43.9%)
Renal disease		5 (12.2%)
Immunodeficiency		2 (4.9%)
Failure to thrive		18 (43.9%)
Medications	Immunosuppressor/chemotherapy	2 (4.9%)
	Steroid	19 (46.3%)
	Inhaler	28 (68.3%)
	Anti reflux	14 (34.1%)
Respiratorysupport	Respiratory support	35 (85.4%)
	NIV	20 (48.8%)
	Invasive mechanical ventilation	18 (43.9%)
	HFOV	4 (9.8%)
	Nitric oxide	4 (9.8%)
	Steroid	29 (70.7%)
	Bronchodilator nebulizer	39 (95.1%)
	Chest physiotherapy	35 (85.4%)
	Suction	37 (90.2%)
Hemodynamic support	Fluid boluses	23 (56.1%)
	Vasopressor support	7 (17.1%)
Initial chest x ray :	Pneumonia	39 (95.1%)
	ARDS	13 (31.7%)
Other Treatment modalities	Blood transfusion	14 (34.1%)
	Renal replacement therapy	2 (4.9%)
	Need tracheostomy	4 (9.8%)
Shock		7 (17.1%)
AKI		10 (24.4%)
Secondary infection mainly ADENO , RHINO		19 (46.3%)
Complications	seizure	7 (17.1%)
Survival Outcome	Survived	35 (85.4%)

**Table 1A:** Descriptive Statistics of the non-metric data; PICU: pediatric intensive care unit , HFNC: high flow nasal cannula , NIV: noninvasive mechanical ventilation , IMV: invasive mechanical ventilation , HFOV: high frequency oscillatory ventilator , CHD: congenital heart disease , CNS: central nervous system , CP: cerebral palsy , AKI: acute kidney injury , ARDS: acute respiratory distress syndrome , ADINO: adenovirus , RHINO : rhinovirus.

## Discussion

We reviewed the medical records of 41 patients who were admitted to PICU during 5 years between 2017-2021. The primary objective was to investigate the risk factors, clinical features and outcomes of children admitted to PICU, secondary to a HMPV infection. The median age of these patients was 3 years and the median PICU stay was 2 weeks. Two-thirds of the patients had underlying comorbidities, particularly asthma, prematurity, CHD, neuromuscular disorders, gastroesophageal reflux or Down syndrome all of which may increase the illness severity and the need for the respiratory and hemodynamic support, in comparison to previously-healthy children. The majority of the cases were found to have had a previous PICU admission. Most of the cases use bronchodilators and steroid inhalers as chronic medication for asthma or hyperactive airway disorders. 34 percent used reflux medication for gastroesophageal reflux. We found that most of the patients needed respiratory support, ranging from high-flow nasal cannula with median duration of 2 days, non-invasive ventilation with a median duration of 4 days, to invasive mechanical ventilation, with a median duration of 5 days. None of the patients required ECMO support. Most of the patients needed chest physiotherapy and suction to clear the secretions. Inhaled nitric oxide was used in four patients with diagnosis of pulmonary hypertension.

Thirteen of the patients had acute respiratory distress syndrome; two of which developed a pneumothorax and needed a chest tube insertion. Two patients had a failed extubation; one with severe laryngomalacia and failure to thrive, who needed prolonged ventilation and tracheostomy tube inserted during same admission, who was then discharged on a home ventilator. The second patient, with gastroesophageal reflux, developed severe acute respiratory distress syndrome (ARDS) and needed prolonged ventilation, a tracheostomy tube was inserted during the same admission after the failed extubation. Fifty-four percent of the cases needed fluid volume to be given as a bolus, but 17% needed vasopressors. One quarter of the patients had acute kidney injury initially, and most of them had improved hemodynamics. Two patients needed renal replacement therapy. Co-infections contributed to the severity of disease in 46% of the cases, with the majority related to the viral co-infection mainly with rhinovirus or adenovirus. One fifth of the cases had a hospital-acquired infection, mainly due to ventilator associated infection and sepsis. All of the 6 mortalities in the patient had associated comorbidities such as prematurity, chronic lung disease and had a history of a previous PICU admission. All the six mortalities occurred among patients less than 2 years old, and all had developed a picture of acute respiratory distress syndrome, and septic shock complicated with multi organ failure.

Previous similar study by Holzemer et al when they study Human Metapneumovirus Infection in Hospitalized Children in Children's Hospital of Michigan/Wayne State University. 75.6% of the subjects required respiratory support, 38.9% required pediatric ICU admission and 12.2% developed AKI. A large study done by A. Hahn et al for children under 5 years of age admitted to hospital with respiratory illness or fever in the US showed that children with HMPV infections were more likely to need supplemental oxygen than their HMPV-negative counterparts (53% versus 36%) and had a longer average stay in the pediatric intensive care unit (PICU) [4.5 days versus 2 days]

We do not found similar study in our area study the clinical picture and outcome of human metapneumovirus in children need PICU care.

Our study has several limitations: it's retrospective in nature, a single-center study, and small sample size, all of which may limit the generalization of the results. There is an insufficient number of patients to give a powered analysis of the potential factors that associated with rare outcomes. We think that future prospective and collaborated studies are needed to give better outcome and the effects of HMPV in the pediatric age groups.

## Conclusion

The majority of HMPV cases admitted to PICU between November- March during the years studied, and the majority had experienced previous admissions to the PICU, due to other co morbidities. Viral co-infection was present in 21.9 % of subjects, mainly with rhinovirus and adenovirus. We found the majority of patients needed respiratory support with variable durations. One quarter of the patients had acute kidney injury initially, and most of them improved with improvement in hemodynamics. Two patients needed renal replacement therapy.

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## Conflict of interest

None declared

## ICMJE Statement

Abdulaziz alsoqati was responsible for the organization and coordination of the trial. Omar Abdulmanea was the chief investigator. All authors were responsible for the data analysis and developed the trial design. Omar contributed to the writing of the final manuscript.

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