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Review Article

Global Burden and Clinical Complications of Human Metapneumovirus Associated with Acute Lower Respiratory Infection in Children: A Short Review

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Abstract

Acute respiratory infection (ARI) is a leading cause of morbidity and mortality in children in low and middle-income countries. Human metapneumovirus (HMPV) is a common virus associated with acute lower respiratory infections (ALRIs) in children. We aimed to estimate the global prevalence, hospital admissions, and clinical complications of HMPV-associated ALRI in children. Between 2005 and 2024, we estimated the global burden of human metapneumovirus-associated ALRIs in children from more than 30 studies. We included data for any length of study period. We included data on the proportion of HMPV-positive cases among hospitalized ALRI cases and patient attending outdoor wings with complain of severe or mild respiratory complications. According to estimates, HMPV caused 14.2 million ALRI cases in children under the age of five in 2018, which resulted in 643,000 hospital admissions and 7,700 in-hospital deaths. Children hospitalized with HMPV infection, as compared with those hospitalized without HMPV infection, were older and more likely to receive a diagnosis of pneumonia or asthma, to require supplemental oxygen, and to have a longer stay in the intensive care unit. Fever (97%) and cough (96%) were the most common presenting symptoms of HMPV-associated pneumonia and were also common symptoms of other pathogens. This study describes global prevalence and clinical complications of HMPV associated ALRIs in children. Clinical features did not reliably distinguish HMPV-associated ALRI from other respiratory infections.

Keywords

Human Metapneumovirus (HMPV), Acute Lower Respiratory Infections (ALRIs), Global Burden, Pneumonia

1. Introduction

Human metapneumovirus (HMPV) is an important cause of ARI across all ages [1], with manifestations ranging from a mild upper respiratory tract infection to a lower respiratory tract infection (LRTI), including croup, bronchiolitis, and pneumonia. Younger children and older adults are most likely to experience severe disease [2]. The recent spike in HMPV cases in China, together with increased monitoring in neighboring countries such as Malaysia, India, Indonesia, Bangladesh, and Vietnam, has brought respiratory viruses that have long been in circulation but have frequently been eclipsed by new pandemics back into the spotlight [3]. The virus was first characterized by the team of Pr Osterhaus in

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2001, although retrospective serological studies have revealed the existence of HMPV antibodies among the human population from as early as the 1950s [4]. Two retrospective Canadian studies detected HMPV in specimens collected from patients with respiratory illness between 1993 and 2019 and a US study detected HMPV in specimens from 1976 to 2001 [4, 5]. HMPV belongs to the Pneumovirinae subfamily of the family Paramyxoviridae. the genus Metapneumovirus includes the two viral species HMPV and avian pneumovirus (APV) [6].

HMPV can cause both upper and lower respiratory diseases in people of all ages, with young children, older adults, and those with weakened immune systems being most vulnerable. However, the risk of severe illness is higher for people who are younger than five or older than 65 [7]. There is no vaccine or specific antiviral treatment for HMPV; treatment primarily involves managing symptoms. Like other similar viruses, HMPV usually spreads from person to person through droplets from coughing and sneezing, through human contact such as hugging or kissing, and through touching surfaces and objects contaminated with the virus and then the mouth, nose or eyes [8].

Researchers first identified HMPV from stored nasopharyngeal samples from 28 children with respiratory illness by using electron microscopy and random reverse transcription-polymerase chain reaction (RT-PCR) techniques [6]. HMPV is a negative-sense, non-segmented, single-stranded RNA virus. The genome is about 13,000 nucleotides in length and is composed of eight genes encoding for nine proteins: 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 protein [6, 9].

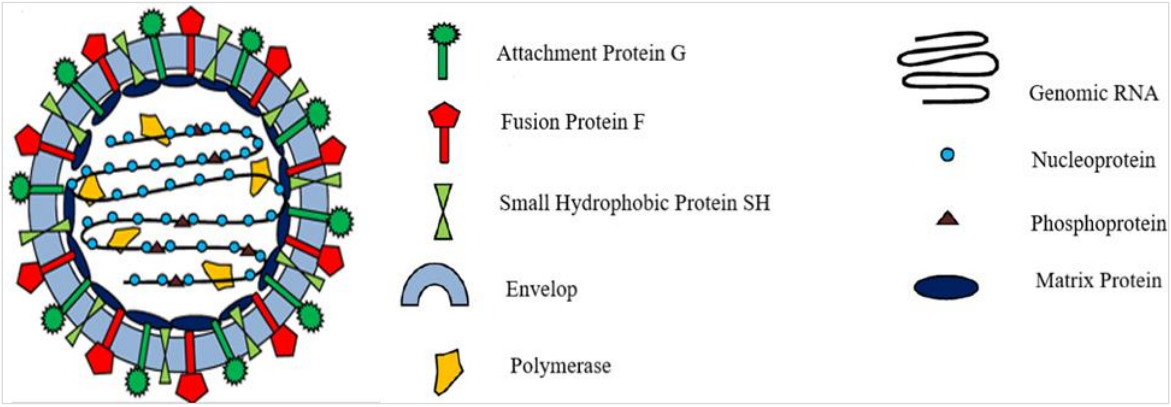

Figure 1. *Schematic representation of HMPV and of hRSV viral particle [6].*

HMPV usually causes symptoms similar to the common cold that last roughly 2-5 days and go away on their own. Its symptoms include cough, fever, nasal congestion, shortness of breath and fatigue, with an incubation period of 3 to 6 days. Most children who get infected with HMPV are age 5 or younger. A small number of children (5-16%) infected will develop a LRTI such as pneumonia. Clinical symptoms of HMPV infection may progress to bronchitis or pneumonia and are similar to other viruses that cause upper and lower respiratory infections. HMPV-positive children are more likely than HMPV-negative children to require supplemental oxygen, had a longer mean stay in the intensive care unit (ICU), and were more likely to undergo chest radiography [10].

Effective prevention remains key to managing HMPV, with measures like hand washing, mask use in crowded spaces, and isolation when sick reducing transmission via droplets, contact, and surfaces. Improving healthcare access, transparent communication, and adequate resource allocation are essential to support vulnerable populations and sustain public trust. Though HMPV may not require urgent vaccine development, its seasonal impact highlights the need for global collaboration to advance research on antiviral therapies and respiratory infections. In this study, we aimed to describe the epidemiology and worldwide prevalence of HMPV infection to circulate knowledge among people regarding this comparatively less known cause of respiratory infection.

2. Epidemiology and Global Burden

In 2018, among children younger than 5 years globally, there were an estimated 14·2 million HMPV-associated ALRI cases [11]. Reports from China show an unusual increase of HMPV cases, particularly among children under the age of 14, amid the typical winter surge of respiratory diseases. In December 2024, the virus became one of the top three causes of outpatient flu-like illnesses and hospitalizations for severe respiratory infections in northern Chinese provinces. Malaysia has also reported a significant rise in HMPV cases, with a 45% year-on-year increase from 225 cases in 2023 to 327 cases in 2024. An Indian newspaper reported at least

seven cases in Gujarat state of India, primarily affecting infants and senior citizens [3]. According to a study conducted in Peru, total of 539 samples belonging to patients with a clinical context suggestive of an acute respiratory tract infection were analyzed. Of these samples, 73 were positively identified using RT-PCR for HMPV. This finding establishes a prevalence of 13.54% for HMPV in the population studied [11]. HMPV was identified in 19 (10.9%) samples as the third major cause of RTI in Saudi Arabia, Riyadh province [12]. HMPV was first reported and found to be a significant cause of childhood ARI causing morbidity in Bangladesh in 2007 [5].

Multiple different strains of HMPV typically co-circulate and their relative distribution varies both within and between communities. 70% of HMPV isolates were genotype A, but a switch to predominantly type B infections occurred next winter. For samples with information on clinical presentations, 26% of HMPV infections were from subjects with lower respiratory tract presentations. Around 13% of HMPV infections were associated with upper respiratory tract symptoms or disease, comparable with other respiratory virus infections [6]. In Bangladesh, on the basis of sequence diversity and virus neutralization titers, it has been shown that there are two major HMPV serotypes and that there are no major antigenic differences between these serotypes [13].

3. Methods

1. Search strategy & selection criteria

Different electronic websites, databases, and journals, including MEDLINE (through PubMed), EMBASE, Scopus were searched to detect published articles on human metapneumovirus. Additionally, the first 5 pages of the Google Scholar search engine were manually screened for relevant articles. The keywords used for searching articles were: human metapneumovirus, acute respiratory infection, children and global prevalence. The language of the articles that were reviewed was limited to English.

We included studies that reported HMPV positive cases and hospitalized ALRI cases with complain of severe or mild respiratory complications in children younger than 5 years. We excluded studies: those in which HMPV was not the primary outcome; and those only including elderly population with high-risk conditions.

2. Statistical analysis

The statistical analysis was performed by using the Microsoft Excel and IBM SPSS Statistics 22 software. Demographic and clinical data were compared with the use of a Pearson chi-square test. The analysis included: pie chart, cluster bar and frequency table presenting global prevalence of HMPV, comparison of clinical features and demographic analysis of the patients respectively.

4. Result

A total of 30 studies were screened. This study found 250 research articles on HMPV associated ALRI infection by using the previously mentioned search terms (Figure 2). 110 articles were screened and found eligible for further investigation. Based on the inclusion criteria, 30 of the 110 articles were eventually chosen. Of these, 4 studies were analyzed. The included studies were conducted between 2005 and 2024. Among 30 studies, 5 were done in community settings and the remaining studies were done in health-care settings, including outpatient clinics and inpatient hospital settings. This section summarizes the findings from our retrieved articles. Findings are showed in pie chart, cluster bar and bi-variate table.

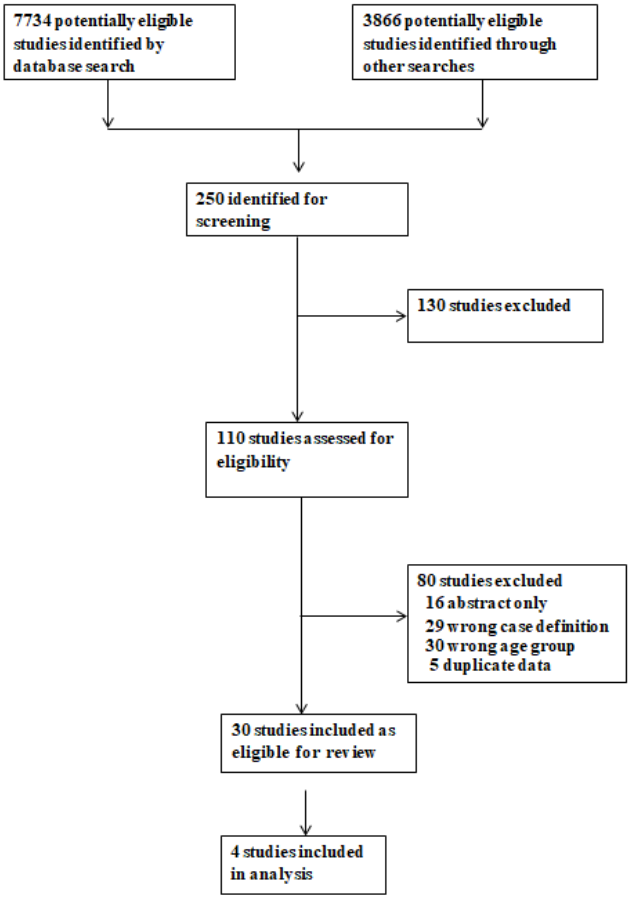

Figure 2. *Study selection procedure.*

1. Global Prevalence of HMPV infection

We estimated the regional and global burden of HMPV associated ALRI infections in children. We accommodated data regarding population-based rates of HMPV infection in children in different countries worldwide (see figure 3).

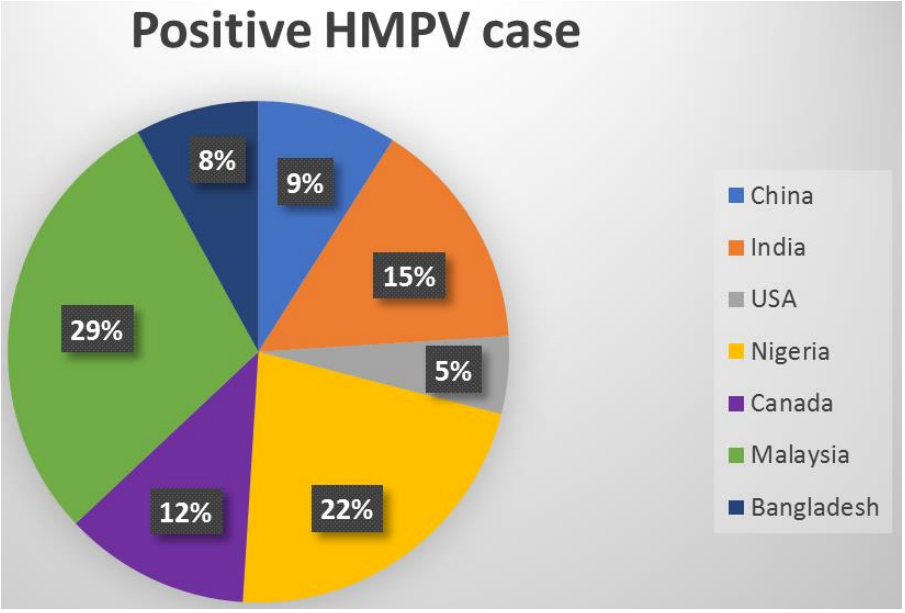

Figure 3. *Pie chart shows the global prevalence of HMPV virus.*

Based on the detection of HMPV by PCR and immunofluorescence method, out of the total number of respiratory samples which were tested, the prevalence of HMPV was found 9% in China, 15% in India, 5% in USA, 22% in Nigeria, 12% in Canada, 29% in Malaysia and 8% in Bangladesh [5, 14-19].

2. Demographic Surveillance

HMPV was detected in 200 of 3490 hospitalized children (6%) and 446 of 5812 children (8%) evaluated in outpatient clinics (Table 1). HMPV-positive inpatients were significantly older than HMPV-negative inpatients (median age, 13 months vs. 6 months; P<0.001). However, among hospitalized children, those who were HMPV-positive were more likely than those who were HMPV-negative to have high-risk coexisting conditions (40% vs. 30%, P=0.002). HMPV-positive children were more likely than HMPV-negative children to require supplemental oxygen (53% vs. 36%, P<0.001).

Table 1. *Demographic characteristics of children with and without HMPV infection.*

Characteristics	Inpatients			Outpatients		
	HMPV-Positive (N=200)	HMPV-Negative (N=3290)	P value	HMPV-Positive (N=446)	HMPV-Negative (N=5812)	P value
Age- m						
Median	13	6	<0.001	17	16	0.61
Interquartile range	5-26	1-19		8-32	8-32	
Age group			<0.001			0.59
<6 m	56 (28%)	1614 (49%)		71 (16%)	1036 (18%)	
6-11m	39 (20%)	443 (13%)		96 (22%)	1148 (20%)	
12-23m	49 (24%)	605 (18%)		114 (26%)	1524 (26%)	
24-35m	27 (14%)	291 (9%)		77 (17%)	892 (15%)	
36-54m	29 (14%)	337 (10%)		88 (20%)	1212 (21%)	
Sex			0.16			0.35
Male	105 (52%)	1892 (58%)		248 (56%)	3099 (53%)	
Female	95 (48%)	1398 (42%)		198 (44%)	2713 (47%)	

Characteristics	Inpatients			Outpatients		
High-risk condition	81 (40%)	990 (30%)	0.002			0.81
Premature birth	48 (24%)	513 (16%)	0.006	39 (9%)	585 (10%)	0.34
Asthma	61 (30%)	677 (21%)	<0.001	83 (19%)	1084 (18%)	0.98
Chronic Lung disease	20 (10%)	182 (6%)	0.009	1 (<1)	70 (1%)	0.06
Supplemental oxygen	106 (53%)	1178 (36%)	<0.001	-	-	

Source: Adapted from Edwards et al. 2013; New England Journal of Medicine [20].
*Outpatients were defined as children seen in the emergency department or outpatient clinic. P values were calculated by means of the Pearson chi-square test, except for the median age, which was calculated by means of the Wilcoxon rank-sum test. As race, history of premature birth and insurance status did not differ between groups, the variables have been excluded.

3. Hospital admissions:

We have accommodated data of surveillance of hospitalized children (IPD), children at outpatient clinics (OPD) and children in emergency departments (ED) from November through May in the years from 2005 to 2024 [21, 22]. The rate of HMPV-associated OPD visits was 55 per 1000 children less than 5 years of age. Children 6 to 11 months of age had the highest rate, at 726. Rates of OPD visits associated with HMPV infection were 554 among children who were 12 to 23 months old, and 291 among those who were 24 to 59 months old. Children less than 6 months old had been found greater number of hospitalization rate with HMPV associated complication (see figure 4).

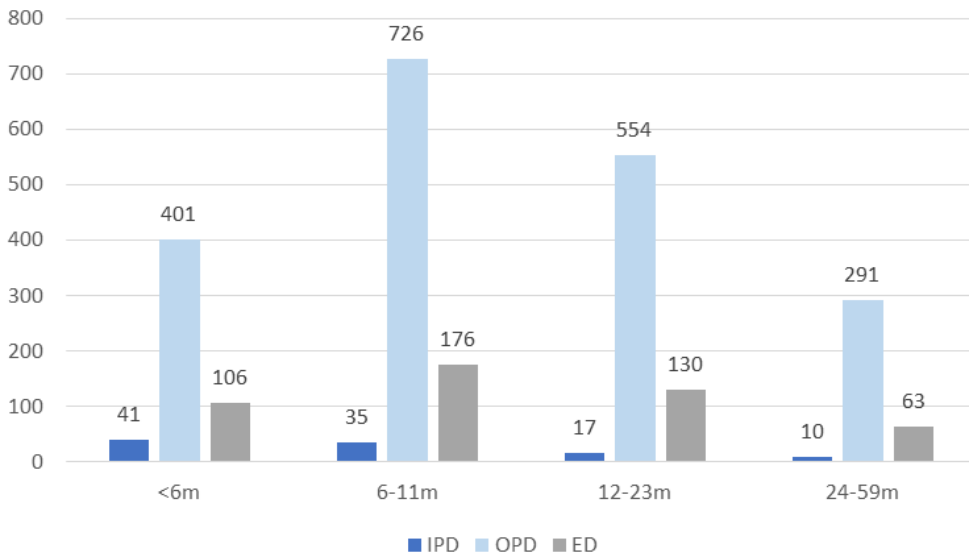

Figure 4. *Rates of patients attending in IPD, OPD and ED for treatment of HMPV infection.*

4. Seasonal Distribution

HMPV infection was found in 10% of all specimens from patients with acute respiratory disease in April, with the majority of HMPV infections (82%) occurring between January and April. The spring and winter seasons—January to March in the northern hemisphere and June to July in the southern hemisphere—are when outbreaks generally happen. According to a recent study, the RSV and influenza infection seasons are followed by March and April, when the peak of HMPV seasonal cases occurs [23].

5. Clinical complications

In a study the clinical features of HMPV infection in children, were compared with pneumonia caused by RSV and other viruses [24, 25]. Children with HMPV infection were found to have a cough (96%), dyspnea (64%), retractions (42%), documented wheezing (39%), and a white blood cell count >15 × 103 (13%) less than those with RSV pneumonia 99%, 77%, 53%, 51%, and 17%, respectively (see Figure 5).

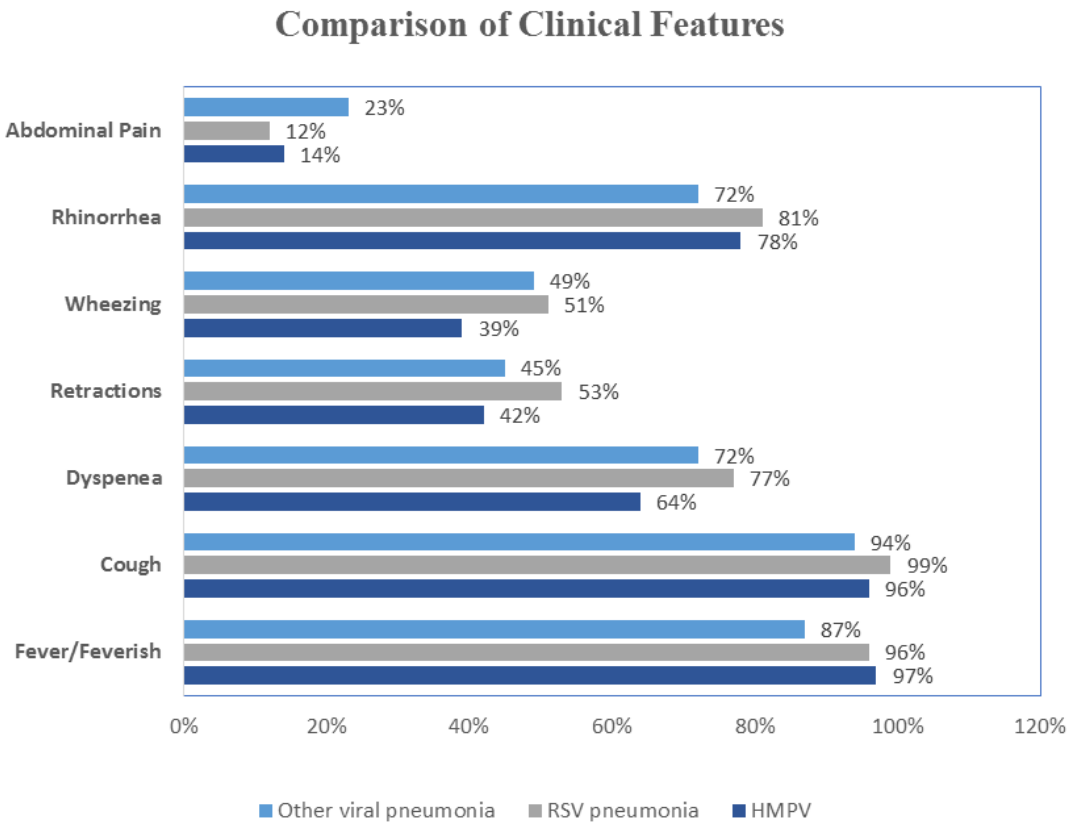

Figure 5. *Clinical features of Hospitalized Children with HMPV Compared with RSV Pneumonia & Other Viral Pneumonia.*

5. Discussion

HMPV is frequently associated with acute respiratory illness in young children and adults that requires medical attention [2-4], and HMPV infection represents a substantial health care burden among both inpatients and outpatients [23]. Our findings show that among children who were younger than 5 years of age, the annual rate of hospitalization associated with HMPV was 1 per 1000 children, which is the same as the rates of hospitalization associated with influenza virus [24]. The rates of HMPV-associated clinic and ED visits were highest among children 6 to 11 months of age, in contrast to rates for HMPV-associated hospitalization, which were highest among children less than 6 months old. Furthermore, the rate of HMPV-associated outpatient visits among older children remained similar to the rate among young infants. This pattern is in contrast to that for RSV infection, for which outpatient rates decreased markedly after 1 year of age [22].

Similar to respiratory syncytial virus and influenza, we found that the HMPV-associated ALRI hospital admission rate was much higher in infants than older children [25]. The high burden in infants could be due to the immaturity of infants' immune systems and decaying maternal antibodies during the first several months of life. In this cohort, 40% of children hospitalized with HMPV infection had underlying high-risk conditions, including premature birth and asthma, whereas only 22% of outpatient children with HMPV infection had a high-risk condition [10]. Other reports have also identified a substantial number of children with high-risk conditions who were hospitalized with HMPV infection [1-5]. The clinical features of HMPV infection are similar to those of infections due to other respiratory viruses [23]. However, compared to children without detectable HMPV infection, hospitalized children with HMPV infection were more likely to need supplemental oxygen and to stay in the intensive care unit for longer periods of time. This could be due to underlying problems that made them more susceptible to more severe disease.

Although the peak of HMPV detection varied from year to year, the prevalence of HMPV overlapped with the circulation of other common respiratory viruses [8]. This finding underscores the strength of a multiyear study in delineating the epidemiologic features of HMPV. The consistently high HMPV-associated ALRI hospital admission rate among infants across different settings highlights the importance of developing safe and effective maternal HMPV vaccines, particularly for infants.

6. Conclusion

HMPV infection is responsible for a considerable proportion of adult cases of pneumonia and pediatric cases of acute

bronchiolitis. Even though diagnostics and our understanding of the etiology of HMPV have advanced significantly over the past decade, there is currently no approved treatment or vaccine for the virus. Because several treatment and vaccination strategies have demonstrated encouraging outcomes in animals, we are optimistic that they will soon be put into clinical trials.

Abbreviations

HMPV	Human Metapneumovirus
ALRI	Acute Lower Respiratory Infection
IPD	Inpatient Department
OPD	Outdoor Patient Department
ED	Emergency Department
RSV	Respiratory Syncytial Virus

Author Contributions

Shamsun Nahar Ahmed: Conceptualization, Formal Analysis, Investigation, Methodology, Project administration, Resources, Writing – original draft, Writing – review & editing

DebJyoti Mukharjee: Formal Analysis, Methodology, Writing – review & editing

Shameem Akhter: Conceptualization, Supervision

Conflicts of Interest

The authors declare no conflicts of interest.

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