

Threats of Human Metapneumovirus (HMPV): Analysis of different phase

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Abstract

Respiratory diseases are one of the most public causes of passing rates and health complications worldwide. Human Metapneumovirus (HMPV) is a respiratory pathogen and can affect both the upper and or lower airways and may spot a life-threatening risk with specific and nonspecific symptoms. Nevertheless, the prevalence and rigorousness of HMPV exposure in children remain unexplored in developing nations. A detailed analysis related to effect of HMPV based on age, gender, patient type (inpatient/outpatient), clinical characteristics, patients with chronic disorders, before corona pandemic and after corona pandemic-19, medical history of prematurity and climate conditions in varies countries. Intense cough and significant feverish symptoms were the most common HMPV clinical characteristics features observed in affected children lesser than 5 years and whereas in adult cases additionally followed by sore throat etc. Increased cognizance of HMPV's influence on public healthiness is indispensable to advance investigation, comprehensive vaccine development, and diminish pathological morbidity and mortality internationally. Our outcomes infer that developed and industrialized countries should support developing nations in augmenting their research infrastructures. Further investigations on the diagnostic features of HMPV should be accomplished recurrently for anticipation and containment about this pathogen.

Keywords: Acute Respiratory Tract Infections, Bronchiolitis, Human Metapneumovirus, Pneumonia.

Introduction

Acute Respiratory tract infection (ARI) are a foremost Infectious diseases cause of morbidity and mortality internationally. Respiratory tract illness is the second prominent cause of death among offspring under 5 years old, irrespective of the region. ARI are categorized into upper respiratory tract infections (URI) and lower respiratory tract infection (LRI) [1]. In 2021, the global amount of fresh cases of URI was about 12.8 billion, upsetting regardless gender of all generations with weakened immune systems. URI comprises the nose, sinuses, pharynx, larynx, and the primary airways [2].

According to the United States of America data, Influenza, Pneumonia and Influenza-Like Illnesses (ILI) are the 6th leading cause of death approximately 45,000 annually.

Whereas in Netherlands, the frequency of ARI is 5,445 patients per year [1].

In developing countries, nearly 95% loss of life due to broad range of ARI's and utmost ARI's contribution leads to one-third of all deaths globally. The highest proportions of critical ARIs are found in Southeast Asia and Africa regions. South Asian counties like Bangladesh, India, and Nepal account for 40% of the worldwide death due to ARIs. In the year 2016, there were 68.06 million patients suffered with LRIs. Pneumonia and bronchiolitis are the crucial components leads to ARI related demise in youngsters [3].

Virus microorganisms are part of the most predominant pathogens instigating ARIs in both young children and adults. Though, the causative agents of numerous RTIs persist mysterious. Influenza virus, Respiratory

Syncytial Virus (RSV), coronavirus, bocavirus, human rhinovirus, human respiratory syncytial virus (hRSV) and human HMPV are the treated as key roots of acute viral respiratory contaminations. In Thailand, from the review article it was observed that, from January 2015 to December 2019, RSV was acknowledged as the leading source of bronchiolitis and Influenza viruses were most frequently identified in children with pneumonia (15.52%) [4].

Unlike the influenza virus, which characteristically sees a couple of strains circulating universally each year, outbreaks of HMPV appear to occur on a further localized scale. The strains of HMPV diverge from one community to another. It was observed that, strains found in one zone may meticulously resemble those spotted in other areas in different time periods [5]. It was originally revealed as a novel microorganism (year 2001) from a nasopharyngeal specimen among youngsters with LRIs in the Netherlands. In Latin America, HMPV was first noticed in children lesser than three years in north-east Brazil [6].

With reference to morphological investigations, HMPV is a single-stranded RNA microorganism with negative orientation which copies in the cytoplasm. This virus is a species within the Metapneumovirus genus categorized under the Pneumoviridae family [7]. The genetic structure of the virus is about 13.35 kb nucleotides in size. HMPV has two crucial genotypes labelled A and B. Each genotype distributed into subclasses comprising of A1, A2, B1, B2 with year to year inconsistency. This virus portrays as threads and sphere-shaped with lengths that varies from 150 to 600 nm [8].

The infected HMPV patient's dendritic cell gets obstructed and weakens T-cell stimulation, ensuing in unfinished virus clearance and an improved probability of recurring infection. Hence, virus infected cases do not accomplish permanent immunity [9]. Its

infection can be either symptomatic or asymptomatic.

The clinical physiognomies are challenging to distinguish HMPV disorder from those of influenza-like symptoms. LTIs due to HMPV can lead to severe cough, sore throat, wheezing, pneumonia, bronchiolitis, and often associated with severe fever and muscle pain, and nausea. Epidemic statistics has revealed that the prevalence of HMPV varies between 1.5% and 43%, subject to the population group and geographic locality. HMPV cases tend to be more common during the winter and spring months, often concurring with hRSV outbreaks [10-14].

HMPV has been spotted in various continents. Weather also considerably influences the seasonality of HMPV in tropical regions. In temperate countries, with the highest frequency of occurrence of HMPV between during the months of autumn and spring. Along with the number of showery days, it is vital to scrutinize other significant factors in a tropical climate, such as relative moistness, hotness, and rainfall, to better comprehend their influence on the predominance of HMPV and its seasonality [15].

In general, HMPV classically emerges over the winter months to next summer. However, HMPV went overlooked for 2 years amid the COVID-19 pandemic, only to return in the fall of 2022, an era normally not associated with epidemics. The non-pharmaceutical involvements familiarized following COVID-19, lowers the propaganda of HMPV, leading to a lessening in acquired resistance [16-17].

Long-term scrutiny data have not yet been completely analyzed to describe the molecular evolutionary trajectory of HMPV. Baseline material on HMPV, comprising disease burden, evolutionary behaviors, and clinical structures, is vital for evaluating the impact of therapeutic or precautionary strategies on public health [18].

Presently, there is no operative antiviral agents'/ antibody therapies handling for HMPV infections and no vaccine endures for this virus. The key encounters for the therapeutic and methodical societies lie in understanding the illness progression of HMPV-related syndromes and emerging a safe and operative vaccine to defend against infection and disease instigated by this newly acknowledged respiratory virus [19].

Discussion on Clinical Indexes

HMPV is recognized as one of the leading causes respiratory pathogen that affects both the upper and lower respiratory tracts in children. Unlike adults, youngsters infrequently remain asymptomatic, although numerous medical reports tend to emphasis on labelling the most severe indicators detected in clinical admissions. The predominance of severe cases among patients in paediatric care proposes that normal infection provides limited immunity of defence against the illness. However, it is essential to note that no cross-protection is perceived between dissimilar strains of the virus. A child had infected with 2 episodes of HMPV within a month, each caused by a dissimilar strain [20].

The findings of [21] exhibited that kindergarten youngsters with a Prematurity in their medical history endured superior severity HMPV i Pathogen exposure, as specified by clinical evaluations of wheezing, Chest wall retractions, oxygen therapy, and tachypnea. Notably, the higher clinical severity was associated with better healthcare resource consumption, ensuing in a twofold rise in hospitalization period matched with HMPV

infected cases but no medical history of prematurity.

Additionally, the rigorousness of the infection manifest in healthcare depend not only on the patient's age but also on the infecting strain, climate condition and population of the country. Finding of HMPV infection is classically relying on clinical evidence, which can range from rhino pharyngitis to fever, acute bronchiolitis, Bronchopneumonia and Myalgia, with some cases are in need of intensive care service.

In the forthcoming paragraphs, a detailed analysis related to effect of HMPV based on age, gender, patient type (inpatient/outpatient), clinical characteristics, patients with chronic disorders, before corona pandemic and after corona pandemic-19, medical history of prematurity and climate conditions in varies countries. In this article, review has been done on the research published from the following countries - United States, Taiwan, China, Brazil, Nepal, India, Australia, Pakistan, Vietnam, Spain, and Senegal.

Table 1 provides an overview of the medical characteristics associated with HMPV in West Virginia and Idaho states of United States from 2011 to 2012 with respect to number of cases and in terms of percentage [22, 23].

Table 2 summarizes medical outcomes of HMPV in Taiwan during the period 2013-23 [24]. It was observed that patients visited hospital with fever ($>38^{\circ}\text{C}$) proceeding with cough rhinorrhoea, inflamed throat, pneumonia.

Table 1. Medical Outcomes of HMPV in West Virginia and Idaho States of United States

Medical syndrome	West Virginia		Idaho	
	No.*	(%)	No.*	(%)
Tussis	25	(89)	29	(100)
New findings on chest	22	(79)	16	(55)
New or increased sputum/Productive cough	12	(43)	11	(38)
Dyspnea	4	(14)	8	(28)
Runny nose	3	(11)	4	(14)

Sore throat	1	(4)	1	(3)
Fever >100°F (37.8°C)	11	(39)	7	(24)
Positive radiographic imaging for pneumonia	18	(78)	7	(35)

Table 2. Medical Outcomes of HMPV in Taiwan during the Period 2013-23

Medical syndrome	Total	Percentage	Medical syndrome	Total	Percentage
Fever	64	56.1%	Sore throat	16	14.0%
Cough	51	44.7%	Headache	12	10.5%
Rhinorrhea	24	21.1%	Pneumonia	11	9.6%
Myalgia	9	7.9%	Malaise	5	4.4%
Acute bronchiolitis	8	7.0%	Vomiting	4	3.5%
Pneumonia	6	5.3%	Acute obstructive laryngitis	4	3.5%
Acute bronchitis	3	2.6%	Diarrhea	2	1.8%
Coryza	3	2.6%	Acute tonsillitis	2	1.8%
Acute pharyngitis	3	2.6%	CNS symptoms	2	1.8%

Dissemination of HMPV infection among different populations with respect to gender, age and patient type in Tertiary Care Hospital

- Kathmandu of Nepal as shown in Table 3 [1].

Table 3. Rates of HMPV Infection - Kathmandu of Nepal, according Gender, Age and Patient Type

Variable		Total cases	+ ve cases (%)
Sex	Female	46	6 (13)
	Male	59	8 (13.6)
Age Group	< 3	32	7 (21.9)
	3–5	45	6 (13.3)
	6–15	28	1 (3.6)
Patient Type	Out-patient	90	12 (13.3)
	In-patient	15	2 (13.3)

From Beijing Friendship hospital (China) during the period Apr. 2017 to Mar. 2019, received 2,848 samples & 176 specimens were

HMPV positive [25]. Clinical manifest of 176 HMPV-infected patients are illustrated in Table 4 & 5.

Table 4. Medical Outcomes of HMPV in Beijing, China during the Period 2017-19

Clinical Characteristics	Age in years	
	0 to 4 (n = 139)	5 to 14 (n = 37)
Cough	133	36
Fever	126	35
Rhinorrhea	82	8
Nasal obstruction	41	6
Shiver	17	4
Vomit	14	2
Sneeze	30	3
Diarrhea	6	0

HMPV infected patients under the age of 4 were suffered from respiratory signs than

patients aged between 5 and 14 years, such as rhinorrhoea and nasal obstruction.

Table 5. Rates of HMPV Infection - in Beijing, China, According Gender and Age

Variable	Patient count	HMPV +ve cases
Male	1574	107
Female	1274	69
≤ 1	760	42
> 1 to ≤ 2	341	27
> 2 to ≤ 3	609	46
> 3 to ≤ 4	316	24
> 4 to ≤ 5	177	5
> 5 to ≤ 7	266	15
> 7 to ≤ 14	379	17
Total	2848	176

Over the span of Jan.–Dec. 2015, a total number of 127 specimens were acquired from the PIMS Hospital, Islamabad and tested using RT- PCR for finding traces of HMPV. Out of

127 samples, 21 were identified as positive. From the Table 7, it was observed that HMPV infected % was the highest among children > 5 years old [26].

Table 6. Rates of HMPV Infection According Gender and Age

Total no of cases (127)	HMPV positive No. & %
Male count	12 & 17.6
Female count	9 & 15.2
below one year	4 & 14.2
Between 1–2 old	3 & 8.8
above 2–3 old	4 & 23.5
above 3–4 old	3 & 16.7
above 4–5 old	7 & 23.3

The medical complaints commonly allied with HMPV cases suffered temperature with were cough followed by gasping, nausea,

breathing difficulty and increased respiratory rate (Table 7).

Table 7. Clinical Complaints among HMPV Positive Patients

Total no of cases - 127	HMPV affected (21) No. (percentage)
Cough (21)	6 (28.5)
Nasal congestion(104)	18 (17.3)
Sore throat (106)	19 (18)
Wheeze (100)	19 (19)
Tachypnea (96)	18 (18.8)
Short breath (111)	20 (18.0)
Vomiting (5)	1 (20)
Sputum(5)	1 (20)

During the period April 2016 to September 2018, a total number of 206 specimens were diagnosed as positive from the Manipal Institute of Virology, India. Out of 206

HMPV-positive patients, the age group 15–50 had the highest record of positive cases (91) as mentioned in Table 8 [27].

Table 8. HMPV-Positive Patient Demographics from Manipal Institute, India and Clinical Data

Total no. of HMPV positives (n = 206)		
Variables	Count	Percentage (%)
Age in years		
Below 2	1	0.5
2 to lesser than 5 years	26	12.6
5 to lesser than 15 years	75	36.4
15 to lesser than 50 years	91	44.2
50 to lesser than 65 years	13	6.3

Assessment of HMPV findings in Western Australia during the year between 2017 and 2021 [28].

Table 9. HMPV-Positive Patient Demographics from Western Australia, between 2017 and 2021

Year	2017	2018	2019	2020	2021
Virus Detections	508	626	769	182	1879
Age band detections					
<12 months	79	95	97	18	226
1–4 years	107	142	132	23	533
5–15 years	27	51	67	14	182
16–64 years	155	189	229	93	601

During the period between 2017 and 2021, highest cases registered in the year 2021. In the age band, 16–64 years had the highest record of positive cases.

In this research study (Table 10), 2,707 cases with ARIs were scrutinized, including 2,201 with severe acute respiratory infections (SARIs) and 506 with influenza-like illnesses (ILIs). 167 specimens diagnosed with HMPV positive. The analysis has been done with respect to gender and age factors. The prevalence of HMPV was substantially greater in patients with ILIs (9.09%) compared to those with SARIs (5.50%). Females had a

higher infection percentage (7.24%) compared to males (5.37%). HMPV positivity was uppermost among children below 5 years old (7.78%) [29].

In this present study [30] Table 11, 44% of cases were aged 18 to 64 years. Above 65 year old cases was suffering from all respiratory pathogen groups, with 57.0% of HMPV, influenza (51.9%) and RSV (60.9%) cases falling in this age group. Other remarkable threat factors included heart disease (influenza (38.8%), RSV (41.6%) and HMPV (33.0%) and chronic obstructive pulmonary disease (COPD).

Table 10. Rates of HMPV Infection according to Gender and Age

Group	Frequency of enrolled patients (n=2,707)	Frequency of HMPV-positive patients (%) (n=167)
Case group		
ILI	506	46 (9.09)
SARI	121 (5.05)	2,201
Sex		
Male	1,547	83 (5.37)
Female	1,160	84 (7.24)
Age group		
0–4 years	1,774	138 (7.78)

5–17 years	634	26 (4.15)
17–59 years	173	1 (0.58)
60–96 years	134	2 (1.49)
Age (<5 years old)		
<1 year	188	6 (3.19)
1 year	634	54 (8.52)
2 years	278	16 (5.76)
3 years	433	39 (9.01)
4 years	241	23 (9.54)

Table 11. Rates of HMPV Infection with Age above 65 Years

	Influenza (366)	RSV (238)	HMPV (100)	Total
Female gender, No. (%)	193	147	62	404
Age ≥65 y				
Chronic disease(heart disease)	142	99	33	276
Chronic disease(renal disease)	46	39	22	109
Asthma	47	51	20	120
COPD	81	73	32	187
Previous vaccinations, No. (%)				
Influenza	169	143	73	388
Pneumococcal	132	93	58	286

Annual Detection Trends and Seasonal Variability Patterns of HMPV

The seasonal distribution of HMPV infection diverges across constituencies. Figure 1 represents, from the year 2013 to 2023, a total of 121,250 samples were tested

for HMPV in Taiwan, with 114 specimen positive result. The number of Samples investigated annually varied from 9,698 to 12,356. From the graph, it is observed that, HMPV peaking in 2021, with no cases has been reported in 2018–2020 or in 2022 [31].

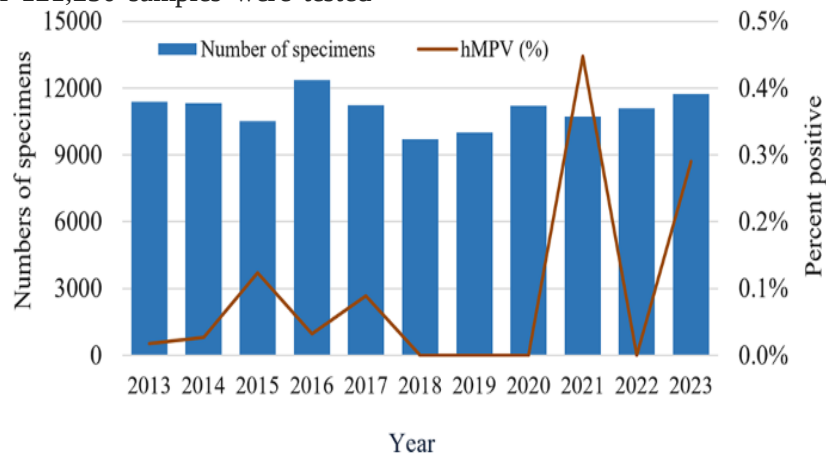


Figure 1. Rates of HMPV Infection during 2013-23

In Taiwan as shown in Figure 2 the predominant cases with HMPV infection showed seasonality, with the utmost prevalence stirring in spring (March - May),

contributing to 47% of cases. Whereas in tropical and subtropical regions, the peak phase contrasts.

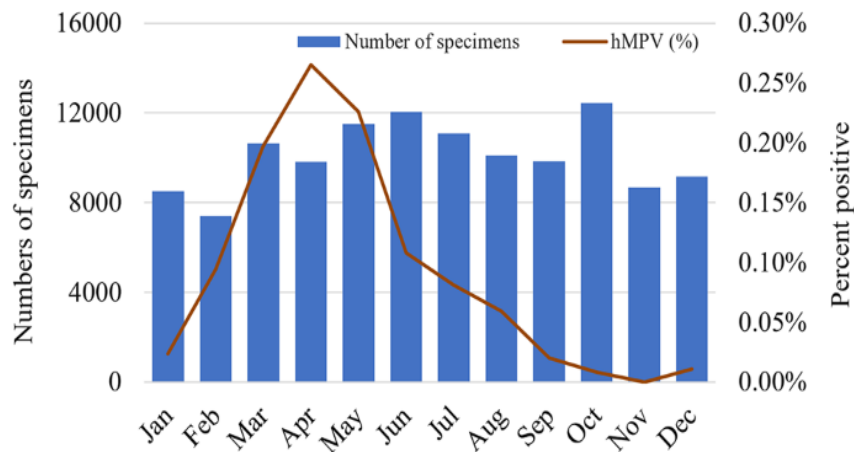


Figure 2. Seasonal Variability Patterns of HMPV in Taiwan

The Figure 3 demonstrates that HMPV infection was greatest prevalent in children < six years old group, identified in 99 (90.8%). The infection was chiefly common in infants, accounting for 43 cases (39.4%). It was also

diagnosed in other age bands: 27.5% in 2-4 year-olds (30 cases) followed by 19.3% in 1-year-olds (21 cases) and 4.6% in 5-6 year-olds (5 cases) [32].

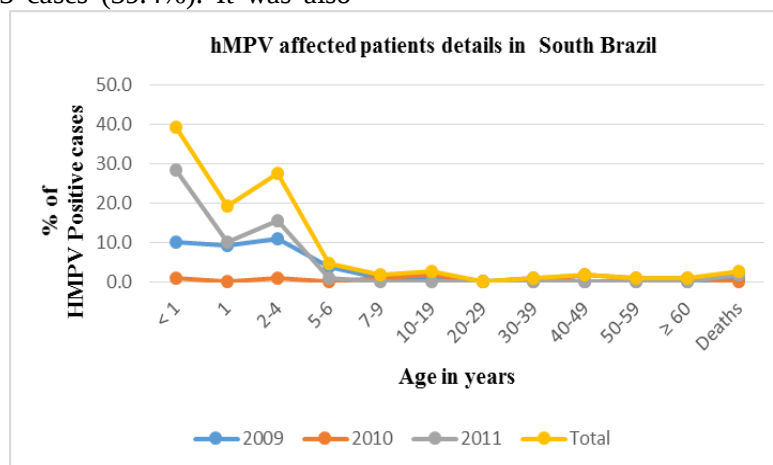


Figure 3. Rates of HMPV Infection according to Age

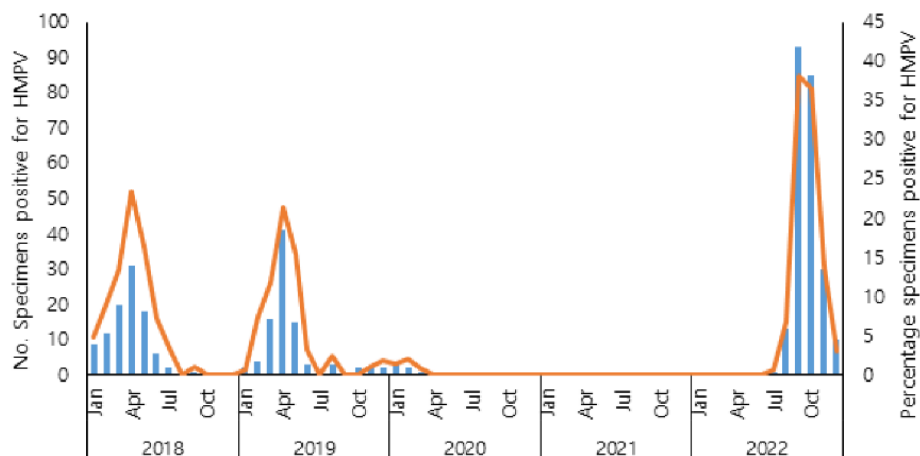


Figure 4. Seasonal Variability Patterns of HMPV in South Brazil

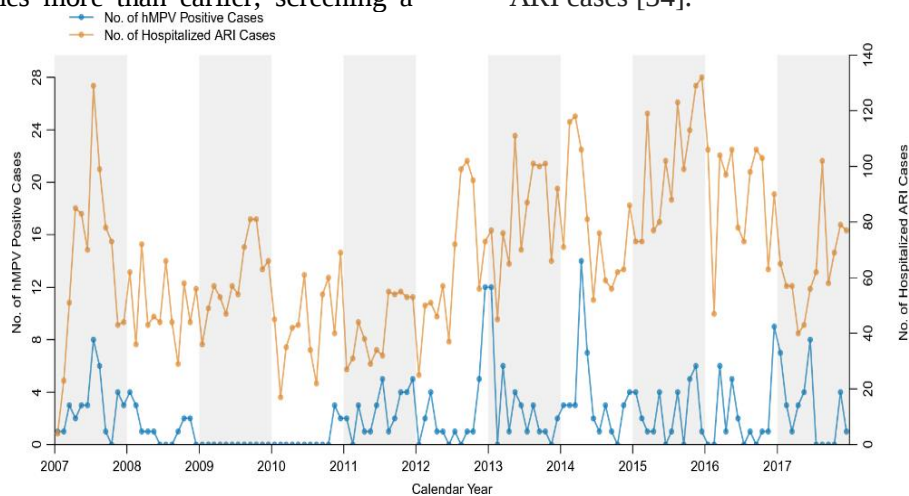
Table 12. Rates of HMPV Cases Earlier and Later COVID-19

Year	Total samples received from paediatric population	Total samples received from adult population	% over paediatric population	% over adult population	% over positive samples
2014-15	3509	2698	1.8	1.5	4.4
2015-16	3958	3587	1.9	2.5	4.6
2016-17	3578	4238	2.7	1.7	4.2
2017-18	3794	5370	5.1	2.6	6.5
2018-19	3912	4584	3.5	2.1	4.9
Total pre-pandemic	23415	25151	2.8	2.1	5
2020-21	12723	3743	1.5	0.2	3.5
2021-22	2786	4445	12.4	0.3	18.3
Total pandemic	15509	8188	3.5	0.2	7.2
Overall	38924	33339	3.1	1.7	5.6

An analysis related to HMPV infection has been done Prior to and post COVID -19. Earlier to the COVID-19, HMPV cases hitting from the month January, reaches peak in the month of April, and then weakening during the summer season. In the midst of the COVID pandemic, HMPV cases were uncommon in 2020, and no cases were reported in 2021, likely due to the non-pharmacological interferences executed for COVID-19. Nevertheless, HMPV remerged in July 2022, with a remarkable growth in cases during the months September and October. The occurrence rate of HMPV later the pandemic was 2.5 times more than earlier, screening a

significant rise. The periodic dissemination of HMPV cases during 2018-22 is revealed in Figure 4. Age status of the patient distribution data revealed a roughly two-fold surge in HMPV cases in the (0–2) age band and (3–5) age band, with a higher than 4.5-fold upsurge in the (6–10) category of age, which was statistically notable (Table 12) [33].

In central Vietnam (Figure 5 and 6), number of HMPV-positive cases noticed through ARI investigation during the period 2007 - 2017 has represented in fig. The blue stripe designates the number of HMPV cases, while the red stripe specifies the number of ARI cases [34].

**Figure 5.** Seasonal Variability Patterns of HMPV in Vietnam

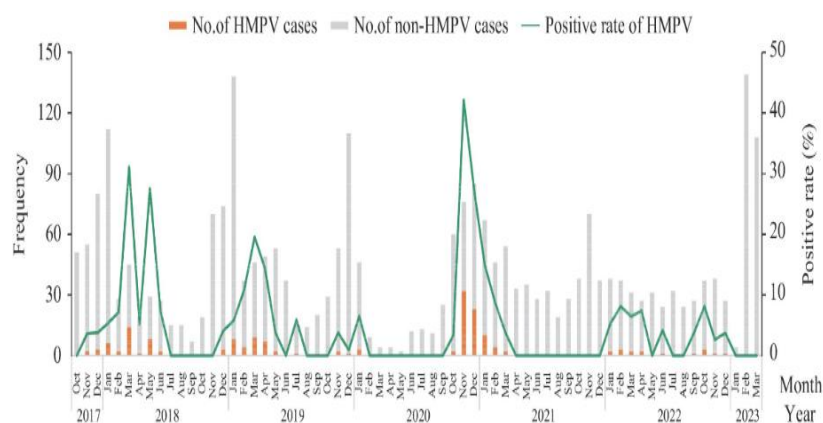


Figure 6. Seasonal Variability Patterns of HMPV in Vietnam

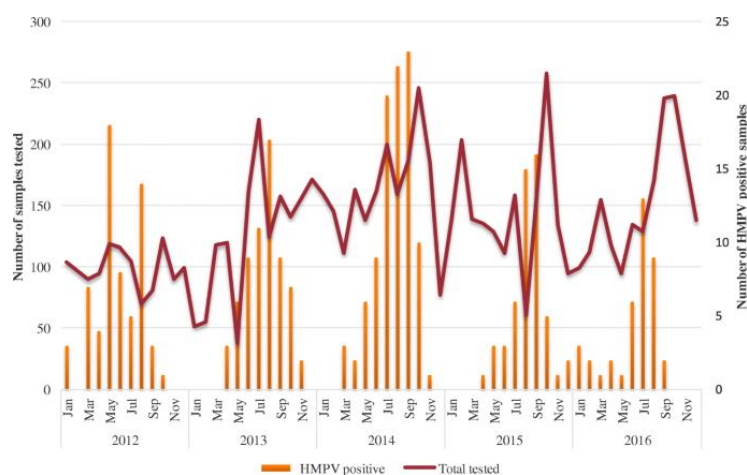


Figure 7. Seasonal Variability Patterns of HMPV in Senegal

The analysis of Senegal monthly temporal distribution for HMPV infection (Figure 7) revealed a clear seasonal pattern. For all years, HMPV infections augmented thoroughly during May to September, topping in the July–August period, excluding in 2012. The higher infection phases align with the monsoon season in Senegal [36].

Promoting Awareness

The threat of HMPV infection rests ongoing partially, due to limited recognition. Respiratory viral infections are often expected to be triggered by influenza viruses and are universally stated to as the "flu." While diagnostics are offered for influenza and potentially RSV, they fail to embrace HMPV. Moreover, new multiplex assays that investigation for HMPV are expensive and may be unapproachable in many hospitals. As a result, HMPV-related syndromes often go

undiagnosed and not reported. It is recommended that struggles in the HMPV field be augmented to address these gaps.

1. Improvement in exploration to disclose the techniques through which the pathogen stimulates a host invulnerable response.
2. Enrich investigation for better measure the burden of HMPV syndrome.
3. Rise consciousness of HMPV among clinicians and clients.
4. Cultivate a budget-friendly investigative assay for HMPV.
5. Advance novel medications and therapies for HMPV.
6. Drive HMPV vaccine growth through medical prosecutions and endorsement.

Allotting new resources and determinations toward vaccine clinical trials could considerably progress the HMPV domain by moving vaccine aspirants past pre-clinical

phases. An accredited and actual vaccine against HMPV would support and prevent plentiful hospitalizations.

Conclusion

HMPV is one of the significant morbidity throughout the world during a specific period based on climate conditions of the zones. It affecting both paediatric and adult with weak immune system. However, during Covid-19 phase, contribution of HMPV has significantly low. Compare with children born with full term affected less from HMPV than children born with prematurity. The medical syndromes of hMPV are very similar to other respiratory diseases (Example influenza-like illnesses (ILIs). A new multiplex assays that investigation for hMPV are expensive and

may be unapproachable in many hospitals. Therefore, hMPV-related syndromes often go undiagnosed and not reported. It is concluded that, it is urged to develop novel medications and therapies for hMPV. Developed nations should support and encourage developing nations to contribute the research toward vaccine for HMPV in future.

Conflict of Interest

There is no conflict of interest.

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