Journal of Epidemiology and Global Health (2025) 15:38
https://doi.org/10.1007/s44197-025-00380-3

RESEARCH ARTICLE

Epidemiological and Clinical Characteristics of Human Metapneumovirus-Associated Acute Respiratory Tract Infection Cases in the Pudong New Area, Shanghai, from 2014 to 2023

Yanhong Ding[1,2] · **Li Zhang**[2] · **Xiao Wang**[2] · **Rongxin Wu**[2] · **Anran Zhang**[2] · **Bing Zhao**[2] · **Chuchu Ye**[2]

Received: 18 January 2025 / Accepted: 21 February 2025

Abstract

Background This study characterized Human metapneumovirus (HMPV) infection epidemiology and clinical features in patients with acute respiratory infections (ARIs) in Pudong New Area, Shanghai, China, compared by pre- and post-COVID-19 periods.

Methods Between January 2014 and December 2023, the basic and clinical information, as well as respiratory tract specimens from ARIs, were collected at 14 sentinel hospitals in Shanghai Pudong. Specimens were tested for HMPV and other respiratory pathogens. The positivity rates were analyzed by age, period (pre- and post-COVID-19), season, and case type. Clinical characteristics of HMPV-infected versus non-infected cases were compared.

Results 14,488 ARI patients were enrolled, with a 1.77% HMPV-positive rate (257/14,488). Among the age groups, the highest positive rate was 5.39% (11 /204) in the 6–11-month age group, and all the HMPV-positive cases in the 6–11-month-old age group were inpatients. Among the < 6 months old, 1–2 years old, 3–5 years old, 6–14 years old, 15–64 years old, and ≥ 65 years old groups, the positivity rates were 1.92% (6/313), 2.92% (23/788), 2.21% (33/1494), 1.08% (25/2311), 1.4 6% (94/6443) and 2.21% (65/2935), respectively. HMPV-positive patients showed higher proportions of cough ($p < 0.001$), runny nose ($p = 0.048$), and sore throat ($p = 0.0175$) than HMPV-negative patients in children. Compared to HMPV-negative patients, there was a significant difference in pneumonia diagnosis in both children and adults ($p < 0.001$, $p = 0.004$). Before COVID-19, HMPV infection peaks occurred mainly in February and March. In October 2023, a significant peak (4.37%, 10/229) was observed.

Conclusions Young children and elderly individuals are at higher risk for HMPV infection, with a reversal of seasonal patterns observed post-COVID-19. Surveillance of HMPV in children and the elderly is crucial for future epidemic Preparedness.

Keywords Human metapneumovirus · Acute respiratory infections · Seasonal patterns

1 Introduction

Human metapneumovirus (HMPV) is a prevalent pathogen that is responsible for acute respiratory infections (ARIs) across various demographic groups, including children, adults, elderly individuals, and immunocompromised individuals [1]. In 2018, it was estimated that approximately 11.1 million cases of acute lower respiratory infections globally were attributable to HMPV, leading to approximately 502,000 hospitalizations and 113,000 fatalities [2]. In hospitalized patients younger than five years of age, 5 to 7% of acute respiratory infections worldwide can be attributed to infections caused by HMPV [3]. The most frequently observed clinical manifestations of HMPV infection include infections of both the upper and lower respiratory tracts [4].

Yanhong Ding, Li Zhang, and Xiao Wang contributed equally to this work.

✉ Bing Zhao
zerg8424@hotmail.com

✉ Chuchu Ye
cynthia-cloth@163.com

1 School of Public Health, Dali University, Dali, Yunnan, China

2 Shanghai Pudong New Area Center for Disease Control and Prevention (Shanghai Pudong New Area Health Supervision Institute), Shanghai, China

Published online: 10 March 2025

Patients testing positive for HMPV would mostly present with flu-like symptoms [5], with a lack of specificity in clinical symptoms.

Epidemiological studies play a crucial role in delineating the prevalence of HMPV within the population, thereby aiding in the identification of high-risk groups and facilitating the formulation of focused prevention and control strategies. Several studies on the prevalence of HMPV infection in children have been reported nationally and internationally [6–8]; despite research analyzing the epidemiology of HMPV in children, these studies have typically involved single-population analyses based on data from a limited number of hospitals. There is a lack of studies investigating HMPV infection in ARIs through multicentre surveillance.

In addition, owing to the implementation of nonpharmaceutical interventions (NPIs), the positivity rates and seasonal patterns of most respiratory viruses have changed globally during the COVID-19 pandemic [9–13]. The changing epidemiological patterns have the potential to lead to widespread severe outbreaks among children, particularly those with underlying medical conditions [14]. There are few studies on the seasonal changes of HMPV in the Pudong New Area before and after the COVID-19 period, and these need to be supplemented.

In this study, a comparative analysis of confirmed HMPV patients was conducted based on 10 years of ARI surveillance data from Pudong New Area, Shanghai, China, from 2014 to 2023. Our study aims to investigate HMPV in all populations with ARIs through multicentre surveillance. This approach is designed to explore the epidemiological trends and clinical characteristics of HMPV, thereby providing a reference for developing disease prevention policies and guiding clinical practice.

2 Materials and Methods

2.1 Ethical Approval

The data analysis and protocols of this study were reviewed and approved by the Medical Ethics Committee of Shanghai Pudong New Area Center for Disease Control and Prevention.

2.2 Case Definition and Sources

This study was based on data obtained from the Comprehensive Surveillance of Acute Respiratory Infections in the Pudong New Area, which was implemented by the Shanghai Pudong New Area Center for Disease Control and Prevention. The survey enrolled ARI patients of all ages, including both outpatients and inpatients, from 14 sentinel hospitals in Shanghai Pudong. The inclusion criteria for ARI patients were as follows: (1) acute onset within 10 days; (2) at least one of the following symptoms/signs: sore throat, cough, expectoration, nasal congestion, runny nose, chest pain, tachypnoea, or abnormal pulmonary breath sounds; and (3) with or without fever. The exclusion criterion was confirmed diagnosis of a noninfectious respiratory disease, such as asthma and respiratory tumors. All the participating hospitals conducted patient enrolment and specimen collection in accordance with the monitoring implementation plan formulated by the Shanghai Pudong New Area Center for Disease Control and Prevention (Pudong CDC). Before and during the surveillance was carried out, all healthcare workers participating in surveillance work in the sentinel hospitals had accepted training to be qualified for recruiting patients and sample collection.

2.3 Questionnaire Investigation and Specimen Collection

The attending physician selected enrolled patients who met the criteria for ARI based on their self-reported symptoms during the visit. All participating hospitals carried out patient enrolment and specimen collection according to the monitoring implementation plan formulated by the Shanghai Pudong New Area Center for Disease Control and Prevention (Pudong CDC). For each enrolled patient, basic and clinical information was recorded via a questionnaire developed by the Pudong CDC, and throat swabs or sputum were collected and stored in 2 mL of viral transport media (VTM, Yocon, Beijing, China), which was transported at 2 °C–8 °C within 24 h to the Pudong CDC for laboratory testing. The samples that could not be transported immediately were stored temporarily at −20 °C. The parents/guardians of the participants in this study were required to provide brief verbal consent during patient enrolment, which was recorded in each questionnaire by the physician.

2.4 Laboratory Method

Each specimen was tested within 24 h of collection by polymerase chain reaction (PCR) for viral pathogens: HMPV, influenza virus (IFV), (including subtypes A, B, and C), human rhinovirus (HRV), para-influenza virus (PIV), (including subtypes 1–4), adenovirus (ADV), respiratory syncytial virus (RSV), (including subtypes A and B), human coronavirus (HCoV), (including 229E, OC43, NL63, and HKU1), human bocavirus (HBoV). Additionally, testing for SARS-CoV-2 was also conducted on patients enrolled between 2020 and 2023. Real-time reverse transcription polymerase chain reaction (RT-PCR) was performed using a LightCycler 480 II Real-Time Fluorescent PCR Instrument (Roche, Switzerland) and a RespiFinder SMART 22 FAST Kit (RespiFinder, Lot: PF2500-SF, Netherlands). If not examined within 48 h, the collected specimens were stored at −70 °C until tested.

2.5 Statistical Analysis

The respiratory surveillance questionnaires were entered into the integrated surveillance platform after data quality control by public health physicians from Pudong CDC.

The chi-square test was utilized to assess the differences in positivity rates across various cases, sexes, age groups, and clinical features. To compare categorical data, the chi-square and Fisher's exact tests were used, as appropriate. Wilcoxon's test was used to compare continuous variables. Two-tailed p-values less than 0.05 were considered statistically significant. All the analyses were conducted in R version 4.3.3 (R Core Team, R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria).

3 Results

3.1 Demographic Characteristics

A total of 14,488 patients with ARIs were enrolled in this study from 2014 to 2023. The median age of the patients with ARIs was 31 years (interquartile range [IQR], 8–60 years), and the male-to-female sex ratio was 1.21 (7922:6566). Of these, 65.81% of the patients were outpatients (9535/14,488), and 34.19% were inpatients (4953/14,488, Table 1). The proportion of ARI patients aged < 6 months was 2.16% (313/14,488), aged 6–11 months was 1.41% (204/14,488), aged 1 ~ 2 years was 5.44% (788/14,488), aged 3 ~ 5 years was 10.31% (1494/14,488), aged 6–14 years was 15.98% (2311/14,488), aged 15–64 years was 44.8% (6443/14,488), and aged ≥ 65 years 20.26% (2935/14,488, Table 1).

3.2 Positive Rates with HMPV

Of the 14,488 patients, 257 (1.77%) were positive for HMPV. Thereinto, 137 were identified from outpatient settings, and 120 were from inpatient settings. A significantly higher rate of HMPV positivity was found among inpatients than among outpatients (1.44% vs. 2.42%, $p < 0.001$).

The HMPV-positivity rate was 1.62% and 1.96% for males and females. There were no significant gender differences in the positivity rate of HMPV ($p = 0.1284$). Regarding age groups, the highest percentage of HMPV-positivity was observed in the 6–11 months old age group (5.39%, 11/204), while the lowest positivity rate was observed among the 6–14 years old age group (1.08%, 25/2311). Among the < 6 months old, 1–2 years old, 3–5 years old, 15–64 years old, and ≥ 65 years old groups, the positivity rates were 1.92% (6/313), 2.92% (23/788), 2.21% (33/1494), 1.46% (94/6443) and 2.21% (65/2935), respectively. The age distribution of HMPV infections significantly differed ($p < 0.001$, Table 2).

There were no significant differences between genders in either HMPV-positive outpatients (1.22% in males vs. 1.67% in females, $p = 0.060$) or HMPV-positive inpatients (2.28% in males vs. 2.64% in females, $p = 0.409$). Among the outpatients, the HMPV-positivity rate significantly differed among the different age groups ($p < 0.001$). Among the inpatients, the HMPV-positivity rate also differed significantly across age groups (1.59% in the < 6-month-old group, 8.66% in the 6–11-month-old group, 4.77% in the 1–2-year-old group, 2.21% in

Table 1 Characteristics of the population comprising enrolled patients with ARIs

Characteristics	Total n = 14,488 (n, %)	No. of outpatient cases n = 9535 (n, %)	No. of inpatient cases n = 4953 (n, %)
Gender			
Male	7922 (54.63)	4935 (51.76)	2987 (60.31)
Female	6566 (45.12)	4600 (48.24)	1966 (39.69)
Age (years, median, IQR*)	31.00 (8.00, 60.00)	28.00 (8.00,45.00)	54.00 (5.00,73.00)
Age group			
< 6 months old	313 (2.16)	62 (0.65)	251 (5.07)
6 ~ 11 months old	204 (1.41)	77 (0.81)	127 (2.56)
1 ~ 2 years	788 (5.44)	411 (4.31)	377 (7.61)
3 ~ 5 years old	1494 (10.31)	996 (10.45)	498 (10.05)
6–14 years old	2311 (15.98)	1759 (18.45)	552 (11.14)
15–64 years old	6443 (44.48)	5236 (54.91)	1207 (24.37)
≥ 65 years old	2935 (20.26)	994 (10.42)	1941 (39.19)

*IQR interquartile range

Table 2 Positivity rates of HMPV for different cases

Characteristics	Total			Outpatient			Inpatient		
	All	Positive for HMPV	Positivity rate (%)	All	Positive for HMPV	Positivity rate (%)	All	Positive for HMPV	Positivity rate (%)
Sex									
Female	7922	128	1.62	4935	60	1.22	2987	68	2.28
Male	6566	129	1.96	4600	77	1.67	1966	52	2.64
Age group									
< 6 m[a]	313	6	1.92	62	2	3.23	251	4	1.59
6 ~ 11 m	204	11	5.39	77	0	0	127	11	8.66
1 ~ 2 y[b]	788	23	2.92	411	5	1.22	377	18	4.77
3 ~ 5 y	1494	33	2.21	996	22	2.21	498	11	2.21
6–14 y	2311	25	1.08	1759	14	0.8	552	11	1.99
15–64 y	6443	94	1.46	5236	71	1.36	1207	23	1.91
≥ 65 y	2935	65	2.21	994	23	2.31	1941	42	2.16
Year									
Period 1									
2014	1026	26	2.53	670	22	3.28	356	4	1.12
2015	1135	30	2.64	820	19	2.32	315	11	3.49
2016	1320	31	2.35	716	14	1.96	604	17	2.81
2017	1292	33	2.55	756	14	1.85	536	19	3.54
2018	1709	42	2.46	1288	25	1.94	421	17	4.04
2019	1724	44	2.55	1043	20	1.92	681	24	3.52
Period 2									
2020	1046	5	0.48	817	4	0.49	229	1	0.44
2021	1617	6	0.37	1087	5	0.46	530	1	0.19
2022	797	3	0.38	590	2	0.34	207	1	0.48
Period 3									
2023	2822	37	1.31	1748	12	0.69	1074	25	2.33
Total	14,488	257	1.77	9535	137	1.44	4953	120	2.42

In the tables of this article, a "m" means months old, and b "y" means years old

the 3–5-year-old group, 1.99% in the 6–14-year-old group, 1.91% in the 15–64-year-old group, and 2.16% in the ≥ 65-year-old group ($p < 0.001$); Table 2).

The period 2014–2023 is divided into three phases based on when the prevention and control of new crown outbreaks occur: period 1 (2014–2019), period 2 (2020–2022), period 3 (2023). The HMPV positivity rate was 2.46–2.64% during the period 1, 0.37–0.48% during the period 2, 1.31% During the period 3. Compared to period 2, the positivity rate in period 3 (2023) has increased. Among outpatients, the annual positivity rate varied from 3.28% to 1.85% during the period 1, varied from 0.49% to 0.34% during the period 2, and was 0.69% during the period 3. Among inpatients, the positivity rate varied from 1.12 to 3.52% during period 1, varied from 0.19% to 0.48% during period 2, and was 2.33%, during period 3 (Table 2).

3.3 Changes in Seasonality of HMPV due to COVID-19 Pandemic

During period 1, large peaks of HMPV positivity occurred in February 2014 (11.63%, 10/86), March 2015 (9.48%, 11/116), March 2016 (7.59%, 12/158), February 2017 (6.96%, 8/115), April 2018 (8.49%, 9/106) and March 2019 (7.74%, 13/168). During period 2, HMPV positivity rates and seasonal patterns changed due to the impact of the COVID-19 pandemic. From 2020 to 2022, these large peaks disappeared. During period 3, a large peak occurred in October (4.37%, 10/229) (Fig. 1).

During period 1, the typical HMPV outbreak seasons were identified as spring and winter (Fig. 2a, b). During period 2, the seasonal patterns of HMPV disappeared. In 2023 (period 3), the HMPV outbreak seasons were

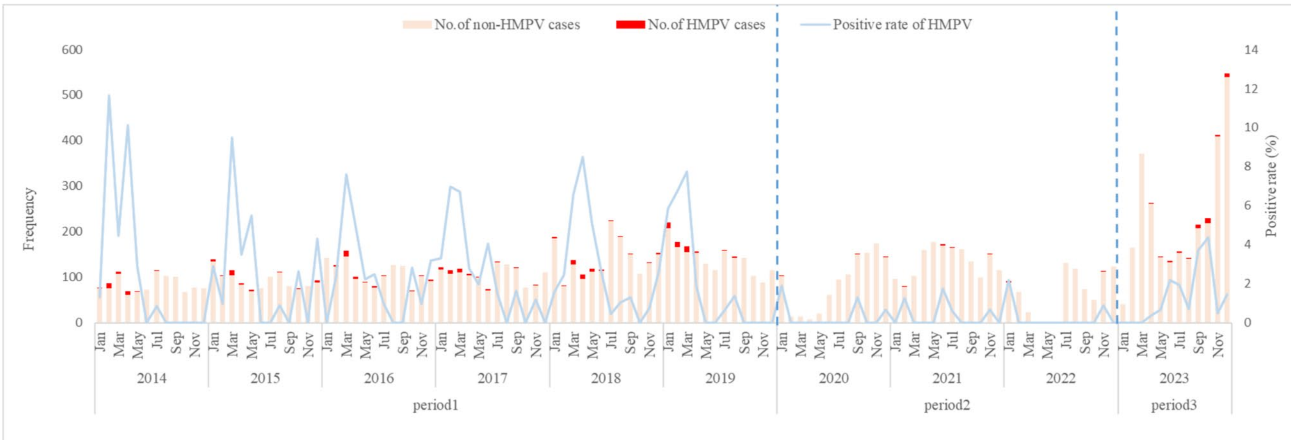

Fig. 1 Temporal distribution of HMPV positive cases

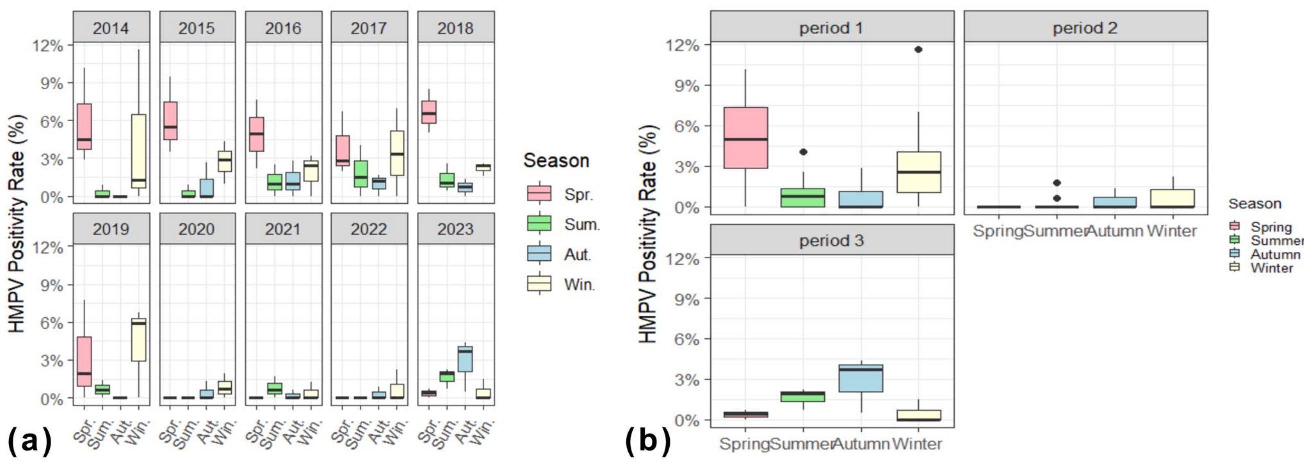

Fig. 2 **a** Seasonal distribution of human metapneumovirus infections in patients with acute respiratory infections, 2014 to 2023; **b** Seasonal distribution of human metapneumovirus infections in patients with acute respiratory infections, period 1 to period 3

identified as summer and autumn, thus indicating reverse seasonality (Fig. 2a, b).

3.4 Clinical Characteristics of Patients with HMPV

The main clinical features of HMPV-positive patients included cough (82.88%, 213/257), fever (67.32%, 173/257), expectoration (42.80%, 110/257), and sore throat (32.68%, 84/257). The main diagnosis for HMPV-positive patients was upper respiratory tract infection (36.19%, 93/257) and pneumonia (33.85%, 87/257, Table 3).

In our study, Clinical characteristics of HMPV-infected versus non-infected cases were compared according to age distribution. Among the children, the main clinical features of HMPV-positive patients included cough (88.78%, 87/98), Fever (75.51%, 74/98), and sore throat (24.49%, 24/98). In adults, the main clinical features of HMPV-positive patients were fever (77.53%, 69/89), cough (75.31%, 67/89), and expectoration (48.31%, 43/89). In the elderly, the main clinical features of HMPV-positive patients were cough (84.29%, 59/70), expectoration (62.86%, 44/70), and Fever (42.86%, 30/70), In addition, a higher number of older people felt breathlessness (21.43%, 15/70, Table 3).

Compared with non-infected cases, a significant difference in the occurrence of cough ($p < 0.001$), runny nose ($p = 0.048$), and Sore throat ($p = 0.0175$) in children. In adults, there was a significant difference in the frequency of expectoration ($p < 0.001$) occurrence. Among elderly patients, no significant differences in clinical symptoms were observed between HMPV-infected cases and non-infected cases. A significant difference in the diagnosis of pneumonia was noted between children and adults ($p < 0.001$, $p = 0.004$, Table 3).

Table 3 Clinical characteristics of patients with HMPV

Clinical features	HMPV-positive n = 257 (n, %)	0–14y n = 98 (n, %)	*p*	15–64y n = 89 (n, %)	*p*	≥ 65y n = 70 (n, %)	*p*
Fever	173 (67.32)	74 (75.51)	0.2367	69 (77.53)	1	30 (42.86)	1
Cough	213 (82.88)	87 (88.78)	< 0.001	67 (75.31)	0.28	59 (84.29)	0.678
Runny nose	59 (22.96)	22 (22.45)	0.048	28 (31.46)	0.2	9 (12.86)	0.871
Sore throat	84 (32.68)	24 (24.49)	0.0175	42 (47.19)	0.66	18 (25.71)	0.168
Expectoration	110 (42.80)	23 (23.47)	0.118	43 (48.31)	< 0.001	44 (62.86)	0.102
Chest pain	3 (1.17)	0 (0.00)	1	0 (0.00)	0.19	3 (4.29)	1
Headache	33 (12.84)	1 (1.02)	0.521	28 (31.46)	0.41	4 (5.71)	1
Dyspnea	3 (1.17)	1 (1.02)	0.426	2 (2.25)	0.2	0 (0.00)	0.074
Breathlessness	23 (8.95)	5 (5.10)	0.205	3 (3.37)	0.74	15 (21.43)	0.617
Weakness	37 (14.40)	2 (2.04)	0.686	30 (33.71)	0.62	5 (7.14)	0.663
Abdominal pain	1 (0.39)	1 (1.02)	1	0 (0.00)	1	0 (0.00)	1
Diarrhea	3 (1.17)	3 (3.06)	0.242	0 (0.00)	1	0 (0.00)	1
Clinical diagnosis							
URTI	93 (36.19)	30 (30.61)	0.263	49 (55.06)	0.669	14 (20.00)	0.607
Pneumonia	87 (33.85)	43 (43.88)	< 0.001	22 (24.72)	0.004	22 (31.43)	0.718

**URTI* upper respiratory tract infection

3.5 Positive Rates of Other Respiratory Viruses and HMPV Co-infection

In the analysis of 14,488 specimens, IFV was the most commonly detected respiratory virus (15.33%, 2221/14488), followed by HRV (4.42%, 640/14,488), HPIV (3.31%, 479/14488), HCoV (3.29%, 477/14488), RSV (2.66%, 385/14488), HAdV (2.35%, 340/14488), HBoV (0.68%, 99/14488). During 2020 to 2023, the detective proportion of SARS-CoV-2 was 2.53% (159/6282). Of the 257 patients who were detected HMPV positive, 77.43% (199/257) patients had no other pathogens positive, 20.23% (52/257) were co-infected with one additional virus, and 2.33% (6/257) were infected with ≥ 3 viruses. Specifically, the most frequent co-infection combinations were HMPV + HRV, accounting for 36.21% (21/58) of all co-infection samples, of which the main clinical features were cough (19/21, 90.48%), sore throat (11/21, 52.38%), fever (9/21, 42.86%), and expectoration (9/21, 42.86%). HMPV + IFV accounted for 20.69% (12/58) of all co-infection samples, of which the main clinical features were cough (9/12, 75%), sore throat (5/12, 41.67%), fever (6/12, 50%) and expectoration (6/12, 50%). HMPV + HCoV accounted for 15.52% (9/58) of all co-infection samples, of which the main clinical features were cough (8/9, 88.89%), and fever (5/9, 55.56%).

4 Discussion

Viruses are the most frequent cause of respiratory infections [15]. HMPV was first discovered in 2001 in the Netherlands [15]; since then, HMPV has been associated with acute respiratory disease in individuals of all ages worldwide. In this study, a comparative analysis of confirmed HMPV patients was conducted based on 10 years of ARI surveillance data from Pudong New Area, Shanghai, China, from 2014–2023.

In this 10-year study, 257 of 14,488 (1.77%) patients were positive for HMPV. In previous studies, HMPV was detected in approximately 2.24% of ARI cases from January 2009 to June 2021 in nine provinces [16]. In our study, during the pre-COVID-19 pandemic period, the positivity rate was 2.46–2.64% from 2014 to 2019.our results were similar to previous reports [16]. During 2022, the positivity rates decreased significantly due to the impact of the COVID-19 pandemic in Shanghai. In 2023 (period 3), the positivity rate was 1.31%; compared with that in period 2, the positivity rate in period 3 was higher. These findings are consistent with those of a previous study [17].

We found there was no significant difference in HMPV positivity rates between male and female patients ($p = 0.1284$), which is consistent with the findings of a previous study [8]. In our study, HMPV-positive cases occurred more frequently in patients aged 6–11 months old, 1–2 years old, 3–5 years old, and ≥ 65 years old than in patients aged 6–14 years old and 15–64 years old, which is consistent with the findings many previous studies [14, 18, 19]. In summary, HMPV positivity rates were lower in individuals aged 6–14 and 15–64 years old. Children under 5 years of age are most susceptible to HMPV infection [16], and most HMPV-positive subjects are younger than 12 months of age [7]. As children grow older, their increased contact with the outside world may lead to higher exposure to HMPV. Therefore, greater attention should be paid to preventing HMPV infection in this age group.

Specifically, the HMPV positive rate was highest in children aged 6–11 months old and all the HMPV positive cases in the age group of 6–11 months old were inpatients. This finding may be attributed to maternal immunity against HMPV, which wanes over time, potentially explaining why a significant portion, but not all, of children aged 6–11 months are hospitalized. In one study, the estimated annual burden of outpatient visits associated with HMPV infection was 55 clinic visits and 13 emergency department visits per 1000 children [6], thus indicating a considerable clinical and economic burden. HMPV infection is associated with a substantial burden of hospitalizations and outpatient visits among children throughout the first 5 years of life, especially during the first year [6]. It has been confirmed that a history of prematurity, particular age groups, and the presence of chronic diseases increases the risk of severe LRTI among children infected with HMPV and RSV [5, 20]. In adults, the patients who tested positive for hMPV were mostly aged ≥ 65 years [5]. Therefore, more attention to HMPV-associated ARI among young children and older adults was needed, highlighting the importance of antiviral treatments and vaccines for preventing and managing HMPV infections in these vulnerable groups [21, 22].

In this study, the changes in the seasonal patterns of HMPV in patients with ARIs were also researched before and during the COVID-19 pandemic. In our study, seasonal peaks of HMPV were detected. During period 1, large peaks in HMPV cases occurred in February 2014 (11.63%, 10/86), March 2015 (9.48%, 11/116), March 2016 (7.59%, 12/158), February 2017 (6.96%, 8/115), April 2018 (8.49%, 9/106) and March 2019 (7.74%, 13/168). This finding indicates that HMPV circulated primarily during the spring and winter in Shanghai from 2014 to 2019. The prevalence of HMPV in temperate climates typically peaks at the end of winter or in early spring [14, 18]. The seasonal distribution of HMPV infections mainly occurs in cold months, and HMPV infections overlap with each other in temperate regions of China [19]. We found that the seasonal pattern of HMPV was similar to that reported in previous studies. During period 2, the seasonal patterns of HMPV were altered due to the impact of the COVID-19 pandemic. Additionally, the typical peaks in HMPV activity, which were previously observed, disappeared as a result of the disruption. During period 3, a large peak occurred in October (4.37%, 10/229). This pattern is similar to previous reports from other areas [13, 16, 23, 24]. In response to the COVID-19 pandemic, NPIs have been implemented worldwide since 2020, including travel restrictions, school closures, social distancing, wearing face masks, handwashing, etc. The implementation of NPIs has largely disrupted not only the prevalence of SARS-CoV-2 but also that of other respiratory viruses. As a result, the prevalence of respiratory viruses has changed significantly in many countries [9–11, 25–27]. For example, in the Netherlands, a higher positive rate of RSV infection was reported during the summers of 2021 and 2022. Similarly, in Australia and New Zealand, the pattern of RSV (Respiratory Syncytial Virus) activity suggests that resurgences of these non-COVID-19 viruses could occur outside the traditional season and with a greater impact. The changing epidemiological patterns have the potential to lead to widespread severe outbreaks among children, particularly those with underlying medical conditions who may experience more severe symptoms [14]. Surveillance of HMPV is essential to provide a sound basis for future epidemic prevention and treatment strategies.

In our study, among all the clinical features recorded, fever (67.32%, 173/257), cough (82.88%, 213/257), expectoration (42.80%, 110/257) and sore throat (32.68%, 84/257) were the most frequent symptoms among HMPV-positive patients. In our study, Clinical characteristics of HMPV-infected versus non-infected cases were compared according to age distribution. Compared with non-infected cases, significant difference in the occurrence of cough, runny nose, and sore throat in children. In adults, there was a significant difference in the frequency of expectoration occurrence. similar to those reported previously [8, 16].

In previous studies, the most frequently observed clinical manifestations of HMPV infection include infections of both the upper and lower respiratory tracts [4]. Our study showed that 36.19% (93/257) and 33.85% (87/257) of HMPV-positive patients were diagnosed with upper respiratory tract infection and pneumonia, respectively. In our study, a significant difference in the diagnosis of pneumonia was noted between children and adults. In previous studies, the most frequent diagnoses of HMPV infection were pneumonitis and bronchiolitis [4, 8, 16]. HMPV is an important cause of pneumonia in adults [28]. It's similar to these reports.

This study has several limitations. First, the data collection was limited to patients with ARIs from 14 hospitals in Shanghai, eastern China, potentially introducing selection bias. Conducting a larger multicentre research trial would greatly contribute to the control, prevention, and treatment of respiratory viral infections in the future. Second, the rigorous enforcement of NPIs during the early phase of the COVID-19 pandemic resulted in a lower enrolment of patients with ARIs, potentially skewing the analysis of their temporal distribution. Determining changes in the seasonal patterns of HMPV is challenging because of the potential influences of various factors.

Despite these limitations, in Shanghai, which is an international metropolis and the most important political, economic, and cultural center in China, our study in 14,488 patients with ARI reflected the epidemiological characteristics and clinical characteristics of HMPV, playing a positive role in the prevention and diagnosis of HMPV infections in the region.

5 Conclusions

The findings of the present study revealed that young children and elderly individuals are at increased risk of HMPV infection, and the opposite pattern of HMPV infection was observed after the COVID-19 pandemic. Surveillance of HMPV is essential to provide a sound basis for future epidemic prevention and treatment strategies.

Acknowledgements We appreciate the support of all the sentinel hospitals and colleagues who have been involved in the surveillance over the years in the Pudong New Area Center for Disease Control and Prevention. Thank Chuchu Ye for the guidance on this article.

Author Contributions Conceptualization: Y.H.D, L.Z, X. W, R.X.W, A.R.Z, B. Z, C.C. Y; Data curation: Y.H.D, L. Z, X.W; Formal analysis: Y.H.D; Methodology: Y.H.D, L. Z, X.W, R.X.W, A.R. Z, B. Z, C.C.Y; Project administration: C.C.Y, L.Z, B.Z, X.W; Writing-original draft: Y.H. D; Writing-review & editing: Y.H. D, C.C. Y, L. Z, X.W; Resources and Supervision: C.C.Y, All authors have read and agreed to the published version of the manuscript.

Funding Key Disciplines (GWVI-11.1–02 Infectious Diseases) supported by Shanghai Municipal Health Commission (2023–2025). Pudong New Area Science and Technology Development-Innovation fund (No.PKJ2023-Y73).The Investigator-initiated Trial Program of Shanghai Pudong New Area Health Commission (the Cohort Study Program) (2025-PWDL-18).

Data Availability The data sets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Conflict of Interest The authors declare no competing interests.

References

1. Esposito S, Mastrolia M. Metapneumovirus infections and respiratory complications. Semin Respir Crit Care Med. 2016;37:512–21. https://doi.org/10.1055/s-0036-1584800.
2. Wang X, Li Y, Deloria-Knoll M, Madhi SA, Cohen C, Ali A, et al. Global burden of acute lower respiratory infection associated with human metapneumovirus in children under 5 years in 2018: a systematic review and modelling study. Lancet Glob Health. 2021;9:e33-43. https://doi.org/10.1016/S2214-109X(20)30393-4.
3. Van Den Hoogen BG, Osterhaus DME, Fouchier RAM. Clinical impact and diagnosis of human metapneumovirus infection. Pediatr Infect Dis J. 2004;23:S25-32. https://doi.org/10.1097/01.inf.0000108190.09824.e8.
4. Howard LM, Edwards KM, Zhu Y, Griffin MR, Weinberg GA, Szilagyi PG, et al. Clinical features of human metapneumovirus infection in ambulatory children aged 5–13 years. J Pediatr Infect Dis Soc. 2018;7:165–8. https://doi.org/10.1093/jpids/pix012.
5. Khan A, Khanna V, Majumdar K. Demographics, clinical presentation and outcome of metapneumovirus infection in adults: a case series analysis at scarborough general hospital, United Kingdom. Cureus. 2024. https://doi.org/10.7759/cureus.73292.
6. Edwards KM, Zhu Y, Griffin MR, Weinberg GA, Hall CB, Szilagyi PG, et al. Burden of human metapneumovirus infection in young children. N Engl J Med. 2013;368:633–43. https://doi.org/10.1056/NEJMoa1204630.
7. Yousafzai MT, Ibrahim R, Thobani R, Aziz F, Ali A. Human metapneumovirus in hospitalized children less than 5 years of age in Pakistan. J Med Virol. 2018;90:1027–32. https://doi.org/10.1002/jmv.25044.
8. Zhang L, Liu W, Liu D, Chen D, Tan W, Qiu S, et al. Epidemiological and clinical features of human metapneumovirus in hospitalised paediatric patients with acute respiratory illness: a cross-sectional study in Southern China, from 2013 to 2016. BMJ Open. 2018;8: e019308. https://doi.org/10.1136/bmjopen-2017-019308.
9. Li ZJ, Yu LJ, Zhang HY, Shan CX, Lu QB, Zhang XA, et al. Broad impacts of coronavirus disease 2019 (COVID-19) pandemic on acute respiratory infections in China: an observational study. Clin Infect Dis. 2022;75:e1054–62. https://doi.org/10.1093/cid/ciab942.
10. Olsen SJ, Winn AK, Budd AP, Prill MM, Steel J, Midgley CM, et al. Changes in influenza and other respiratory virus activity during the COVID-19 pandemic—United States, 2020–2021. MMWR Morb Mortal Wkly Rep. 2021;70:1013–9. https://doi.org/10.15585/mmwr.mm7029a1.
11. Groves HE, Piché-Renaud P-P, Peci A, Farrar DS, Buckrell S, Bancej C, et al. The impact of the COVID-19 pandemic on influenza, respiratory syncytial virus, and other seasonal respiratory virus circulation in Canada: a population-based study. Lancet Reg Health Am. 2021;1: 100015. https://doi.org/10.1016/j.lana.2021.100015.
12. Olsen SJ, Azziz-Baumgartner E, Budd AP, Brammer L, Sullivan S, Pineda RF, et al. Decreased influenza activity during the COVID-19 pandemic—United States, Australia, Chile, and South Africa, 2020. Am J Transpl. 2020;20:3681–5. https://doi.org/10.1111/ajt.16381.

13. Ye C, Tian Y, Huo D, Zhang T, Zhang L, Zhao B, et al. Changes in epidemics of respiratory viral infections resulted from the COVID-19 pandemic in Shanghai. J Med Virol. 2024;96: e70034. https://doi.org/10.1002/jmv.70034.
14. Kuang L, Xu T, Wang C, Xie J, Zhang Y, Guo M, et al. Changes in the epidemiological patterns of respiratory syncytial virus and human metapneumovirus infection among pediatric patients and their correlation with severe cases: a long-term retrospective study. Front Cell Infect Microbiol. 2024;14:1435294. https://doi.org/10.3389/fcimb.2024.1435294.
15. Van Den Hoogen BG, De Jong JC, Groen J, Kuiken T, De Groot R, Fouchier RAM, et al. A newly discovered human pneumovirus isolated from young children with respiratory tract disease. Nat Med. 2001;7:719–24. https://doi.org/10.1038/89098.
16. Cui A, Xie Z, Xu J, Hu K, Zhu R, Li Z, et al. Comparative analysis of the clinical and epidemiological characteristics of human influenza virus versus human respiratory syncytial virus versus human metapneumovirus infection in nine provinces of China during 2009–2021. J Med Virol. 2022;94:5894–903. https://doi.org/10.1002/jmv.28073.
17. Maggi F, Pifferi M, Vatteroni M, Fornai C, Tempestini E, Anzilotti S, et al. Human metapneumovirus associated with respiratory tract infections in a 3-year study of nasal swabs from infants in Italy. J Clin Microbiol. 2003;41:2987–91. https://doi.org/10.1128/JCM.41.7.2987-2991.2003.
18. Ji W, Chen Y, Han S, Dai B, Li K, Li S, et al. Clinical and epidemiological characteristics of 96 pediatric human metapneumovirus infections in Henan, China after COVID-19 pandemic: a retrospective analysis. Virol J. 2024;21:100. https://doi.org/10.1186/s12985-024-02376-0.
19. Xie Z, Zhu Z, Xu J, Mao N, Cui A, Wang W, et al. Seasonal and genetic characteristics of human metapneumovirus circulating—Henan Province, China, 2017–2023. China CDC Wkly. 2024;6:450–6. https://doi.org/10.46234/ccdcw2024.087.
20. Williams JV, Maitre N. Human metapneumovirus in the preterm neonate: current perspectives. Res Rep Neonatol. 2016;6:41–9. https://doi.org/10.2147/RRN.S76270.
21. Aminisani N, Wood T, Jelley L, Wong C, Sue HQ. The burden of human metapneumovirus-and influenza-associated hospitalizations in adults in New Zealand, 2012–2015. J Infect Dis. 2024;230:933–43. https://doi.org/10.1093/infdis/jiae064.
22. Loubet P, Mathieu P, Lenzi N, Galtier F, Lainé F, Lesieur Z, et al. Characteristics of human metapneumovirus infection in adults hospitalized for community-acquired influenza-like illness in France, 2012–2018: a retrospective observational study. Clin Microbiol Infect. 2021;27:127.e1-127.e6. https://doi.org/10.1016/j.cmi.2020.04.005.
23. Billard M, Van De Ven PM, Baraldi B, Kragten-Tabatabaie L, Bont LJ, Wildenbeest JG. International changes in respiratory syncytial virus (RSV) epidemiology during the COVID-19 pandemic: association with school closures. Influenza Other Respir Viruses. 2022;16:926–36. https://doi.org/10.1111/irv.12998.
24. O'Neill G, Taylor J, Kok J, Dwyer D, Dilcher M, Hua H, et al. Circulation of influenza and other respiratory viruses during the COVID-19 pandemic in Australia and New Zealand, 2020–2021. West Pac Surveill Response J. 2023;14:13–22. https://doi.org/10.5365/wpsar.2023.14.3.948.
25. van den Hoogen BG, van Doornum GJJ, Fockens JC, Cornelissen JJ, Beyer WEP, de Groot R, et al. Prevalence and clinical symptoms of human metapneumovirus infection in hospitalized patients. J Infect Dis. 2003;188:1571–7. https://doi.org/10.1086/379200.
26. Li Z-J, Zhang H-Y, Ren L-L, Lu Q-B, Ren X, Zhang C-H, et al. Etiological and epidemiological features of acute respiratory infections in China. Nat Commun. 2021;12:5026. https://doi.org/10.1038/s41467-021-25120-6.
27. Kume Y, Hashimoto K, Chishiki M, Norito S, Suwa R, Ono T, et al. Changes in virus detection in hospitalized children before and after the severe acute respiratory syndrome coronavirus 2 pandemic. Influenza Other Respir Viruses. 2022;16:837–41. https://doi.org/10.1111/irv.12995.
28. Johnstone J, Majumdar SR, Fox JD, Marrie TJ. Human metapneumovirus pneumonia in adults: results of a prospective study. Clin Infect Dis. 2008;46:571–4. https://doi.org/10.1086/526776.