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ORIGINAL ARTICLE

Outbreak of Parainfluenza Virus During the COVID-19 Pandemic at a University Hospital in Korea

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SUMMARY

Background: **The incidence of respiratory viral diseases including parainfluenza virus (PIV) infection has decreased noticeably due to strict quarantine measures during the COVID-19 pandemic. However, the recent outbreak of PIV in children occurred unexpectedly and the distribution pattern showed prominent differences from before the COVID-19 pandemic. PIV is one of the major viral pathogens related to acute lower respiratory infection in young children and the elderly. Accordingly, the authors intended to identify the incidence and distribution pattern of PIV outbreaks and to contribute to public health by providing information on it.**
Methods: **This study was conducted retrospectively to investigate the incidence and distribution of PIV according to age group, gender, month, and season, and to analyze the co-infections from March 2020 to February 2022. The detection for respiratory microorganisms was performed through FilmArray assay.**
Results: **The overall incidence for at least one respiratory pathogen was 45.9% (665/1,450). PIV was not detected at all from March 2020 to August 2021. However, it was first detected in September 2021 and the rate in the month that followed, October, accounted for 60% (114/190) of the total PIV infections during the entire study period. It also accounted for 44.9% (190/423) of patients with respiratory pathogens from September 2021 to February 2022. It reached the highest proportion at 90.5% (114/126) in October 2021. As for the distribution according to the age groups, group 3 (58.4%) accounted for the highest percentage, followed by group 4 (21.1%). In the PIV positive cases, the overall rate of more than two respiratory pathogens was 32.6% (62/190). The most common pattern of co-infection was PIV3 with rhinovirus/enterovirus (67.7%), followed by PIV3 with adenovirus (8.1%) and PIV3 with rhinovirus/enterovirus and adenovirus (8.1%).**
Conclusions: **The COVID-19 pandemic has brought about many changes in our daily lives. It has been confirmed that the seasonal distribution of PIV was distinctly different from before the COVID-19 pandemic. It is anticipated that this phenomenon will affect the incidence or distribution of other respiratory pathogens and viral epidemiology. Therefore, clinicians should pay attention to these changes in terms of public health.**
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KEYWORDS

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INTRODUCTION

Acute respiratory infection caused by various respiratory microorganisms is the most common infectious disease worldwide. Infection by these microorganisms can lead to more serious problems for immune-compromised patients, the elderly, and children [1].

There are four main kinds of respiratory viruses related to acute lower respiratory infection in young children and the elderly: influenza virus (Flu), parainfluenza virus (PIV), respiratory syncytial virus (RSV), and human metapneumovirus (HMPV) [2]. The molecular genetic testing with increased detection rate is a very useful method for rapid diagnosis for these viruses [1].

Viral factors, human behavioral factors, and environmental parameters like humidity, temperature, and solar radiation have been reported to affect the seasonality of respiratory viral illness [2-5]. The COVID-19 pandemic, which lasted more than two years, has had a profound impact on our lives, including global lockdowns, strict quarantine, mandatory wearing of masks, compulsory social or physical distancing, thorough personal hygiene, etc. [6,7]. As a result, it has been reported that the incidence and distribution patterns of respiratory microorganisms have changed remarkably, in particular, that the incidence of viral diseases has decreased noticeably due to strict quarantine measures during the COVID-19 pandemic [6-14].

However, in 2021, RSV epidemics affecting public health were reported in several countries [15-18], and there were differences from the previous patterns in the magnitude of RSV outbreak and the severity of the disease [18]. In addition, risks of reemergence of non-COVID respiratory viruses including rhinovirus were also reported [19,20].

Several studies have reported a decrease in the incidence of PIV in 2020 and 2021 [6-14]. Nevertheless, the recent outbreak of PIV occurred unexpectedly in children and the distribution pattern showed prominent differences from before the COVID-19 pandemic. PIV is one of the major viral pathogens related to acute lower respiratory infection in children and elderly people. Accordingly, the authors intended to identify the incidence and distribution pattern of the PIV outbreak and to contribute to public health by providing information on it.

MATERIALS AND METHODS

Specimens

From March 2020 to February 2022 during COVID-19 pandemic, 1,450 swabs including nasal, throat, and nasopharyngeal swab samples were collected from patients with acute respiratory symptoms.

FilmArray assay

FilmArray assay was completely automated using FilmArray® Respiratory panel v1.7 (BioFire Diagnostics, Salt Lake City, UT, USA) from cell lysis for nucleic acid extraction to report the result. The pre-treated sample was injected into the pouch through the injection port, and then the pouch was mounted on the FilmArray instrument. Then the test was conducted automatically using the FilmArray assay according to the manufacturer's instructions. FilmArray assay can detect 20 kinds of respiratory microorganisms; coronavirus 229E (CoV 229E), CoV NL63, CoV OC43, CoV HKU1, adenovirus, HMPV, human rhinovirus A/B/C (Rhino)/enteroviruses (Entero), PIV1, PIV2, PIV3, PIV4, RSV, Flu A including three subtypes of Flu A H1, Flu A H1-2009, and Flu A H3, Flu B, *Bordetella pertussis*, *Chlamydophila pneumoniae*, and *Mycoplasma pneumoniae*.

Incidence and distribution of parainfluenza virus

This study was conducted retrospectively to identify the incidence and distribution of PIV according to age, gender, month, and season. The proportion of PIV among the cases in which respiratory microorganisms were detected was investigated. Analyses for co-infection of more than two pathogens with PIV were also conducted.

Statistical analysis

All data were analyzed using Microsoft Excel (2016) (Microsoft Corporation, Redmond, WA, USA) with Analyse-it (ver. 5.50, Analyse-it Software Ltd., Leeds, UK). A p-value of less than 0.05 was considered statistically significant.

RESULTS

Incidence of pathogens causing respiratory infections

There were 1,450 patients in total, of which 812 (56.0%) were male and 638 (44.0%) female; 1,422 were children and adolescents (age group 1 - 5) and 28 were adults (age group 6) (Table 1). The overall incidence for at least one respiratory pathogen was 45.9% (665/1,450) and the incidences for male and female were 44.1% (358/812) and 48.1% (307/638), respectively ($p = 0.140$).

Among the age groups, the highest incidence was identified in group 4 as 65.3% (141/216) and followed by 62.8% (348/554) in group 3 and 49.3% (101/205) in group 2 (Table 1).

Distribution of parainfluenza virus according to the age groups

PIV was not detected at all from March 2020 to August 2021, as the COVID-19 pandemic continued; however, it suddenly began to be detected from September 2021. In October alone, the month that followed, it accounted for 60% (114/190) of PIV positive cases during the entire study period (Figure 1).

When looking at the distribution of PIV according to the age groups, group 3 (58.4%) accounted for the high-

Table 1. Incidence of pathogens causing respiratory infections according to the age groups.

Age group	Age distribution	Positive, n (%)	Negative, n (%)	Total, n
1	≤ 28 days	12 (6.2)	181 (93.8)	193
2	1 - 3 months	101 (49.3)	104 (50.7)	205
3	4 months - 2 years	348 (62.8)	206 (37.2)	554
4	3 - 6 years	141 (65.3)	75 (34.7)	216
5	7 - 18 years	58 (22.8)	196 (77.2)	254
6	≥ 19 years	5 (17.9)	23 (82.1)	28
Total, n (%)		665 (45.9)	785 (54.1)	1,450

Table 2. Incidence of parainfluenza virus according to the age groups and gender.

Age group	Gender	Autumn			Winter			Total, n	
		Sep 2021	Oct 2021	Nov 2021	Dec 2021	Jan 2022	Feb 2022		
1	M	0	0	1	0	0	0	1 (1.1)	2 (1.1)
	F	0	1	0	0	0	0	1 (1.0)	
2	M	0	4	5	3	0	0	12 (12.9)	22 (11.6)
	F	0	4	5	0	1	0	10 (10.3)	
3	M	4	34	11	2	2	1	54 (58.1)	111 (58.4)
	F	4	44	5	1	3	0	57 (58.8)	
4	M	1	9	6	0	0	0	16 (17.2)	40 (21.1)
	F	1	16	6	0	0	1	24 (24.7)	
5	M	0	1	6	2	0	0	9 (9.7)	13 (6.8)
	F	0	0	4	0	0	0	4 (4.1)	
6	M	0	1	0	0	0	0	1 (1.1)	2 (1.1)
	F	0	0	1	0	0	0	1 (1.0)	
Total, n	M	5	49	29	7	2	1	93 (100.0)	190 (100.0)
	F	5	65	21	1	4	1	97 (100.0)	

Table 3. Percentages of parainfluenza virus positive cases.

	Autumn			Winter			Total
	Sep 2021	Oct 2021	Nov 2021	Dec 2021	Jan 2022	Feb 2022	
Total number of tests	37	180	101	67	116	118	619
Positive cases, n	19	126	79	33	89	77	423
Positive rate (%)	51.4	70.0	78.2	49.3	76.7	65.3	68.3
PIV positive cases, n	10	114	50	8	6	2	190
PIV positive rate * (%)	52.6	90.5	63.3	24.2	6.7	2.6	44.9

Abbreviation: PIV - parainfluenza virus.
*** Percentage of parainfluenza virus positive cases among the positive cases for respiratory microorganisms.**

Table 4. Distribution of parainfluenza virus infection with co-infections.

No. of pathogens	Co-infection type	n (%)
2	PIV3 + Rhinovirus/Enterovirus	42 (67.7)
2	PIV3 + Adenovirus	5 (8.1)
2	PIV3 + RSV	2 (3.2)
2	PIV4 + RSV	2 (3.2)
2	PIV4 + Rhinovirus/Enterovirus	1 (1.6)
3	PIV3 + Rhinovirus/Enterovirus + Adenovirus	5 (8.1)
3	PIV3 + Rhinovirus/Enterovirus + RSV	2 (3.2)
4	PIV3 + Rhinovirus/Enterovirus + Adenovirus + RSV	2 (3.2)
4	PIV3 + PIV4 + Rhinovirus/Enterovirus + Adenovirus	1 (1.6)
Total, n (%)		62 (100.0)

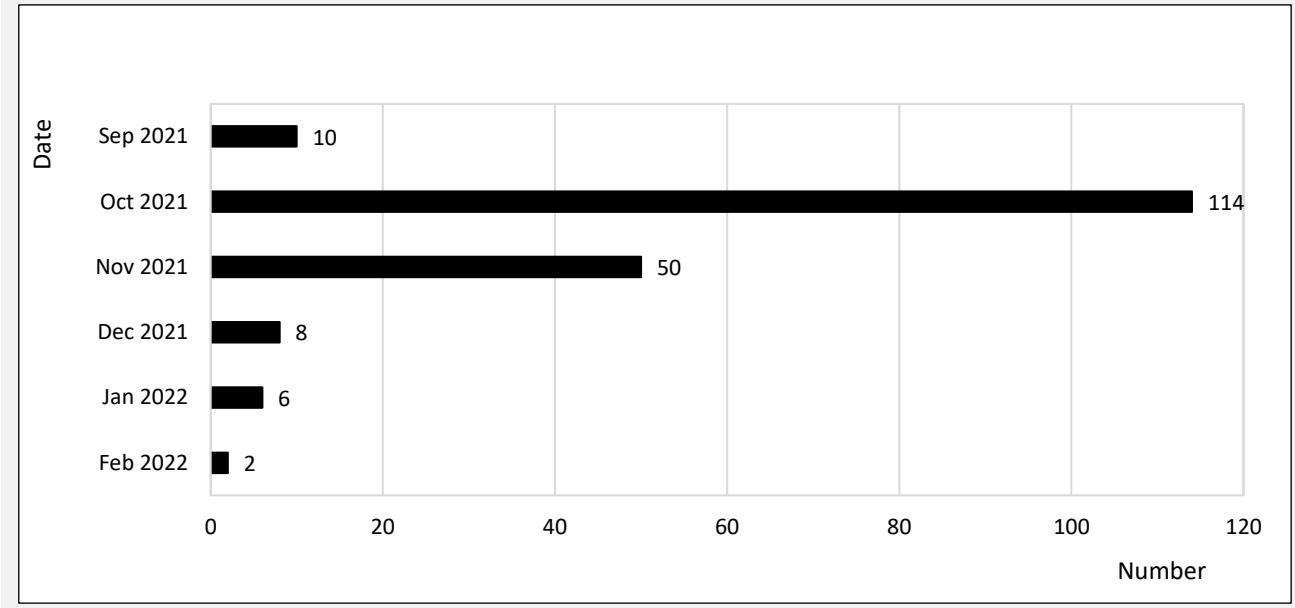

Figure 1. The incidence of parainfluenza virus from September 2021 to February 2022.

est percentage, followed by group 4 (21.1%) (Table 2). The incidence of PIV showed no statistical difference by gender in any group.

Percentage of parainfluenza virus positive cases

From September 2021 to February 2022, the positive rate of respiratory pathogens was 68.3% (423/619). PIV accounted for 44.9% (190/423) of cases with respiratory pathogens for these six months. In particular, in October 2021 it reached the highest proportion at 90.5% (114/126). Particularly, among the positive cases for respiratory pathogens from September to November 2021, PIV steadily accounted for high percentages of 52.6% to 90.5%. The PIV outbreak occurred in the autumn of 2021, and it was continuously detected until winter (Table 3). The number of cases in which PIV3 was positive was 185, 4 in PIV4, and one in which PIV3 and PIV4 were simultaneously positive.

Distribution of co-infections accompanied with parainfluenza viral infection

In the PIV positive cases, the overall rate of more than two respiratory pathogens was 32.6% (62/190). The most common type of co-infection was PIV3 with Rhino/Entero (67.7%), followed by PIV3 with adenovirus (8.1%) and PIV3 with Rhino/Entero and adenovirus (8.1%) (Table 4).

DISCUSSION

The positive rate of respiratory pathogens was highest in group 4 (65.3%), followed by group 3 (62.8%) (Table 1). On the other hand, the positive rate of PIV was highest in group 3 (58.4%), followed by group 4 (21.1%) (Table 2). This is consistent with the fact that PIV is known to account for the majority of the viral croup in children aged 6 months to 6 years [21].

PIV accounted for only 2.2 - 6.75% of the pathogens causing acute respiratory infections before the COVID-19 pandemic [3,4,6-8,10]. However, it was reported that detected PIV was as low as 0.0 - 3.57% during the COVID-19 pandemic [6-8,11,12,22], although there were differences according to the period and region. Conversely, it was also reported that the PIV detection rate increased by 15.5% due to viral competition during the COVID-19 pandemic [13]. In this study, PIV accounted for more than 50% of the positive cases for respiratory pathogens from September to November 2021 and even 90.5% (114/126) in October (Table 3).

PIV has been known to show distinct seasonal patterns and longer duration of epidemic when compared with Flu or RSV [2,6]. It showed type-specific seasonal distribution patterns, and PIV3 was most prevalent in spring and summer and PIV4 in autumn [5,21]. In the authors' previous studies [3,6], PIV3 was prevalent in spring and summer and PIV4 in autumn before the COVID-19 pandemic, which was consistent with several other reports [2,11,21,23]. But in this study, PIV3 was not detected at all from March 2020 to August 2021, when COVID-19 was prevalent. However, during the recent COVID-19 pandemic, the outbreak of PIV became unexpectedly prevalent in autumn and continued until winter (Table 3). Hodjat et al. reported that some seasonal respiratory viruses might emerge out of normal season for such pathogens [20]. In addition, there is a study that reported a distribution outside the typical seasonality of PIV in 2020 during the COVID-19 pandemic [11]. In this study, it was very unusual that PIV was not detected at all for a year and a half during the COVID-19 pandemic, but suddenly became prevalent in autumn out of the seasonality known before.

The co-infections mostly identified with PIV were in Rhino/Entero and adenovirus (Table 4). The most common pattern was PIV3 with Rhino/Entero (67.7%), followed by PIV3 with adenovirus (8.1%) and PIV3 with Rhino/Entero and adenovirus (8.1%). Therefore, the high co-infection rate in these pathogens is considered to be partially attributed to their high incidence like in our previous study [3]. This co-infection can be confirmed due to the capability of multiplex PCR method detecting multiple pathogens at the same time with high sensitivity. Four out of five cases (80.0%) where PIV4 was detected showed co-infection patterns, and this was consistent with the authors' previous study findings where the highest co-infection rate was with PIV4 [3]. Previously, the prediction for the epidemic of respiratory viruses showed good accuracy. It was reported that the prediction for Flu showed better predictability in temperate regions. Temperature and humidity are well known to be associated with the seasonality of Flu and RSV [2]. Seasonality of respiratory viruses could have been very important clinical information for clinicians to care for patients, but it is clear that the COVID-19 pandemic is making it difficult to predict the seasonality of these viruses. Furthermore, human factors like lifestyle changes due to COVID-19 pandemic also contributed significantly to the distribution patterns of respiratory pathogens. There was also a report that warned on the possibility of reemergence of other epidemic diseases in children due to the lockdown during the COVID-19 pandemic [24]. In conclusion, human behaveioral factors like changes in daily lifestyle and quarantine measures according to the COVID-19 pandemic can act as a very influential factor in the distribution of respiratory viruses. The need to prepare for this is emphasized as various changes in the distribution of respiratory viruses may occur when COVID-19 restrictions are relaxed in the future [11,15].

This study showed the incidence of PIV according to the age groups and changed seasonal trend of PIV. This information might be considered to be helpful to clinicians in managing their patients by coping with the changing trends of this viral infection.

CONCLUSION

The COVID-19 pandemic has brought many changes in our daily lives. This study confirmed that the seasonal distribution of PIV was clearly different from before the COVID-19 pandemic. This phenomenon is fully expected to affect the incidence or distribution of other respiratory pathogens and previously known viral epidemiology. Therefore, clinicians should pay attention to these changes in terms of public health.

Ethical Approval:

This study was exempted by the Institutional Review Board of Kyungpook National University Chilgok Hospital, Daegu, Korea (IRB File No.: 2022-02-030).

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Declaration of Interest:
None.

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