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RESEARCH ARTICLE

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Usefulness of national respiratory virus surveillance data for clinicians who manage adult patients

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The Korean Centers for Disease Control and Prevention (KCDC) provides weekly respiratory virus (RV) surveillance reports on its website (the KCDC data). Clinicians in clinical settings wherein the use of PCR for RVs is not a routine laboratory test for adult patients with acute respiratory illness (ARI) may question the clinical utility of such a national RV surveillance dataset in predicting RV outbreaks among their adult patients. We compared the KCDC data to the RV PCR data of adult patients who visited a tertiary care center. During a period of 108 weeks, a total of 6955 (5598 pediatric and 1257 adult) patients underwent RV PCR tests for ARI; most of these tests were administered while the patients were admitted (n = 6,920; 99.5%). From the KCDC website, we collected the RV PCR test results of 22 540 patients. Three graphs of weekly positivity rates were made for adults, children, and the KCDC data per each RV, and these graphs were then compared with one another. Whereas RV outbreaks were coincident between the KCDC and the adult graph with respect to influenza virus, respiratory syncytial virus, human metapneumovirus, and human coronavirus, the same was not true for human bocavirus, parainfluenza virus, rhinovirus, and adenovirus. However, a negative predictive value of the KCDC data in the prediction of the occurrence of an outbreak in the adult graph was high for the respective eight RVs (85-100%). A national RV surveillance dataset may be useful in identifying RV outbreaks in adult patients with severe ARI.

KEYWORDS
adult, respiratory tract infections, sentinel surveillance, viruses

1 | INTRODUCTION

Polymerase chain reaction (PCR) tests for common respiratory viruses (RVs) are rarely included as a part of routine diagnostic tests performed in the majority of adult patients with acute respiratory illnesses (ARIs) other than the influenza virus (IFV) because the clinical significance of these RVs has been stressed more so in pediatric patients and effective antiviral treatments remain underdeveloped.[1,2] However, considering that recent studies have shown their serious adverse impacts in adults,[3–5] it may be necessary for clinicians who manage adult patients with ARI caused by one of these RVs to suspect the cause early; identify it quickly; and prevent it from spreading within the community or hospital through education, vaccination, or other methods of infection control. In current clinical practice, without the routine performance of RV PCR tests for adult patients with ARI, a national or regional laboratory RV surveillance database may be a useful adjunct to that end. The use of such datasets in clinical practice is already well-accepted for IFV, which causes massive outbreaks in both children and adults throughout the community, leading to serious symptoms in some.[6]

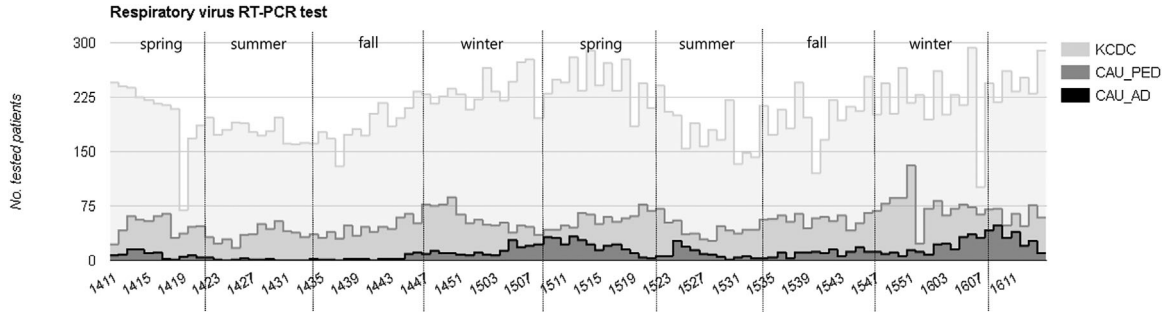

FIGURE 1 The number of patients who underwent a respiratory virus multiplex PCR test between the 8th week of 2014 and the 14th week of 2016 (KCDC, the Korea Influenza and Respiratory Surveillance System data by the Korean Centers for Disease Control and Prevention; CAU-PED, the dataset of pediatric patients from the study hospital; CAU-AD, the dataset of adult patients from the study hospital). Each week is designated by a four-digit number (eg, 1411 indicates the 11th week of 2014)

Based on a national surveillance influenza dataset, the Korean Centers for Disease Control and Prevention (KCDC) sends warning messages about ongoing outbreaks of IFV through various media every winter and clinicians carefully respond to the signs, particularly since the 2009 influenza pandemic. However, regarding other RVs, whether the clinical use of such datasets in adult hospitalized patients with ARI is plausible remains unclear. Thus, we compared the national RV surveillance data of the KCDC (the KCDC data) to RV PCR data from adult patients who visited a tertiary care center for ARI and evaluated the usefulness of national RV surveillance data in clinical practice.

2 | PATIENTS AND METHODS

This study was performed at Chung-Ang University Hospital, an 850-bed tertiary care teaching hospital in Seoul, Republic of Korea. We identified all patients who received an RV PCR test between March 11, 2014 and March 31, 2016 and collected data regarding patient demographics and RV PCR tests (dates, results, and test performance location). For both the adult group (≥16 years old) and the pediatric group, the number of positive test results and the positivity rate were recorded weekly for each of the eight RVs: IFV, rhinovirus (RHV), respiratory syncytial virus (RSV), human metapneumovirus (hMPV), adenovirus (ADV), human coronavirus (hCoV), human bocavirus (hBoV), and parainfluenza virus (PIV).

The Korea Influenza and Respiratory Surveillance System is the only public source of laboratory-based epidemiological data showing community outbreaks of IFV and the other seven RVs in South Korea. The system was organized by the KCDC nearly two decades ago.[7] After several revisions, the system now includes 200 sentinel sites throughout the country, including data on primary care clinics for pediatrics (n = 100), internal medicine (n = 71), and family medicine (n = 29). Each sentinel site provides weekly reports of the number of patients who present with influenza-like illnesses (ILIs) among those evaluated at KCDC sentinel sites. Of these, 36 also provide respiratory specimens from patients with ARI (laboratory sentinel site). The KCDC posts the data, including the rate of ILI prevalence among examined patients and the prevalence for the eight RVs among the tested specimens, on its website every week.[8] Relevant KCDC data were retrieved from the KCDC website during the present study's period.

For each RV, we developed three graphs of weekly positivity rates representing the adult rates, the pediatric rates, and the KCDC rates. Although this study focused on adult patients, the pediatric data of the study hospital were also included because the KCDC data included those from all age groups and the pediatric data were thought to be helpful in addressing some differences between the KCDC data and the adult data. We compared the KCDC graph to the adult graph in three ways. First, we compared them based on the timing of outbreaks and seasonal peaks for each RV. Second, we examined whether the occurrence of an outbreak in the KCDC graph in a given week could predict that in the adult graph in the same week. An outbreak of any RV was regarded to occur at a given week if the detection rate of the RV was >3% during that week. The detection rate of 3% was selected because most of the RV outbreaks in our data began just after the weekly detection rate went up over the value. The predictability of the KCDC data for the occurrence of an outbreak in the adult data was presented as a positive predictive value (PPV), a negative predictive value (NPV), sensitivity (SN), and specificity (SP). Third, a statistical correlation between the KCDC graph and the adult/pediatric graph was assessed using Pearson's correlation coefficients with 95% confidence intervals using Fisher transformation.

For coding purposes, we labeled each week with a four-digit number, with the first two digits denoting the year and the last two denoting the week (eg, 1411 indicates the 11th week of 2014). Using this method, each season of the study period was defined as follows: spring (from 1408 to 1422, from 1510 to 1522, and from 1610 to 1614), summer (from 1423 to 1435, and from 1523 to 1535), fall (from 1436 to 1448, and from 1536 to 1548), and winter (from 1449 to 1509, and from 1549 to 1609).

3 | RESULTS

During the 108-week study period (from the 8th week of 2014 to the 14th week of 2016), a total of 6955 patients underwent RV

PCR tests for ARI at the study hospital, with nearly all (n = 6920, or 99.5%) undergoing tests during admission. Of the 6955 study patients, 81.9% (5698) and 18.1% (1257) were pediatric and adult patients, respectively. The mean age of the pediatric patients was 4.1 years [standard deviation (SD): 2.7] and the mean age of the adult patients was 63.7 years (SD: 19.7). Males comprised a small majority of both groups: 3199 pediatric patients (56.1%) and 640 adult patients (50.9%). RVs were detected in more than two-thirds of the pediatric patients (3927/5698, or 68.9%) and in more than one-fourth of the adults (332/1257, or 26.4%), respectively. In the KCDC data, 22 540 patients underwent RV PCR tests during the study period.

Figure 1 shows histograms of the frequency of RV PCR tests in weekly units during the study period for each dataset. In all three graphs, tests were most frequently performed between winter and spring. In contrast with the KCDC data, the number of tests performed increased gradually over time among both adult and pediatric patients.

Figures 2 show graphs of weekly RV positivity rates, with three graphs present for each RV, respectively, and Table 1 summarizes the characteristic features presented in Figure 2. IFV was the virus most commonly detected in the adult patients, followed by RHV, RSV, and hMPV. RHV was the virus most commonly detected in the pediatric patients, followed by RSV, ADV, and PIV. RHV was the most common virus in the KCDC data, followed by IFV, PIV, and ADV. Of the three dataset, the mean weekly positivity rate was highest among pediatric patients for most of the RVs, with the exception of IFV, which was highest in the KCDC data (Table 1). Regarding IFV, RSV, hMPV, and hCoV, the outbreaks represented in the three graphs were consistent with one another. However, in the graphs representing outbreak trends for RHV and ADV, the temporal trends were not as consistent across the datasets as they were for the other RVs (Figure 2). The numbers of hBoV-positive and PIV-positive tests were very small among adult patients (Table 1) and positive cases occurred only sporadically (Figure 2). Thus, for these two RVs, comparison among the three graphs was difficult.

Table 2 presents the relationship between the KCDC graph and the adult or pediatric graph as well as the predictabilities of the KCDC data for the occurrence of an outbreak in the adult or pediatric data. A statistically significant correlation between the KCDC data and adult data was observed with respect to IFV, RSV, hMPV, and hCoV. For all eight RVs, the relationship between the KCDC data and the pediatric data was observed to be statistically significant. Predictabilities of the KCDC data for the occurrence of an outbreak in the adult data were the best for IFV. NPVs of the KCDC data for the occurrence of an outbreak in the adult data were generally high regarding the eight RVs (85-100%), whereas PPVs were high for such in the pediatric data (72.3-100%).

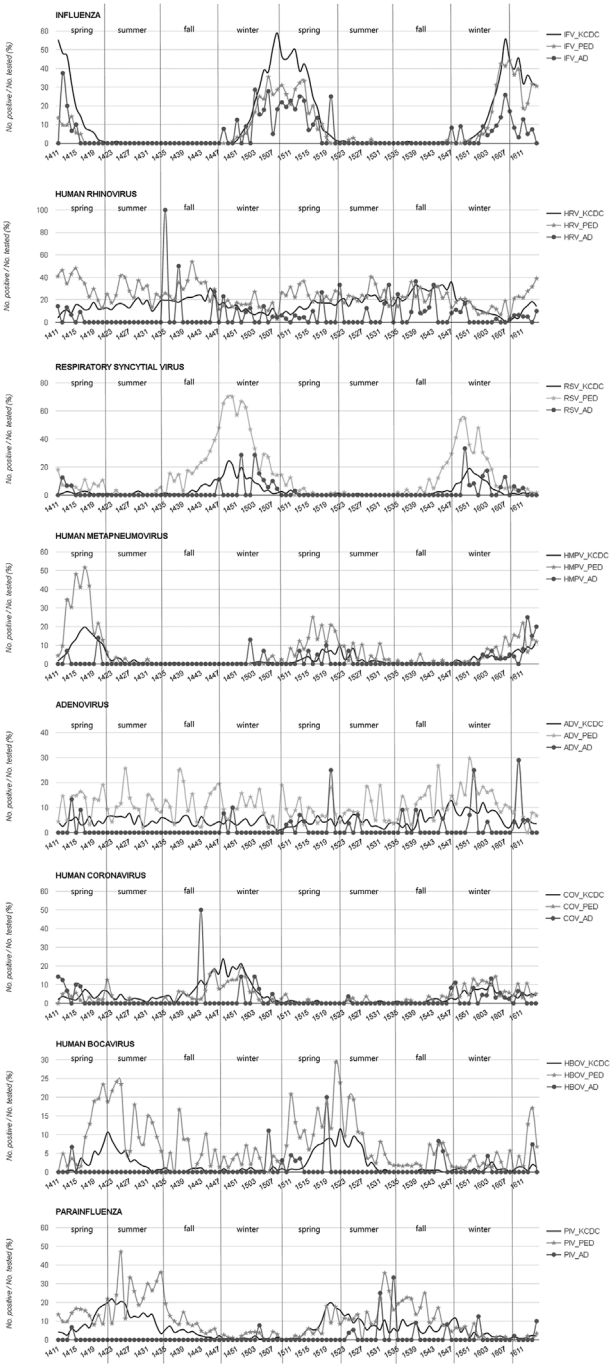

FIGURE 2 Twenty-four epidemic curves of weekly positivity rates of respiratory virus according to multiplex PCR tests with three curves for each respiratory virus between the 8th week of 2014 and the 14th week of 2016 (KCDC, the Korea Influenza and Respiratory Surveillance System data by the Korean Centers for Disease Control and Prevention; CAU-PED, the dataset of pediatric patients from the study hospital; CAU-AD, the dataset of adult patients from the study hospital). Each week is designated by a four-digit number (eg, 1411 indicates the 11th week of 2014)

4 | DISCUSSION

Outbreaks of IFV, RSV, hMPV, and hCoV among the adult patients who underwent an RV PCR test for ARI at a tertiary care center in this study coincided with outbreaks observed in the KCDC data. For these four RVs, statistically significant correlations were also found between the KCDC data and the adult data. Our study results strongly support the clinical use of the national laboratory surveillance data during the outbreak of IFV, regarding that the correlation

TABLE 1 Characteristic features of the epidemic curves shown in Figure 2

Respiratory virus	Number of the positive RV PCR[a] test results (mean value of WPRs[b])			Outbreak seasons	Seasonal peak	Timing of outbreaks among the three curves	Comparison of mean WPR[b] values among the three curves
	CAU-AD[c]	CAU-PED[d]	KCDC[e]				
Influenza virus	115 (5.0%)	482 (7.9%)	3135 (12.3%)	Winter to spring	Late winter	Coincident	KCDC>CAU-PED>CAU-AD
Rhinovirus	67 (6.3%)	1334 (24.2%)	3569 (16.2%)	Year-round	Unremarkable	Unable to compare	CAU-PED>KCDC>CAU-AD
Respiratory syncytial virus	41 (2.4%)	922 (13.7%)	825 (3.4%)	Late fall to winter	Early winter	Coincident	CAU-PED>KCDC>CAU-AD
Human metapneumovirus	36 (1.7%)	399 (6.6%)	670 (2.9%)	Winter to early summer	Late spring	Coincident	CAU-PED>KCDC>CAU-AD
Adenovirus	35 (1.8%)	659 (11.2%)	1111 (4.9%)	Year-round	Unremarkable	Unable to compare	CAU-PED>KCDC>CAU-AD
Human coronavirus	27 (2.1%)	244 (3.8%)	1002 (4.3%)	Fall to winter	Early winter	Coincident	KCDC ≈ CAU-PED>CAU-AD
Human bocavirus	14 (0.7%)	387 (7.3%)	446 (2.0%)	Year-round (CAU-PED[d])/ spring to summer (KCDC[e])	Late spring	Unable to compare	CAU-PED>KCDC>CAU-AD
Parainfluenza virus	11 (1.1%)	512 (10.3%)	1345 (6.3%)	Spring to early winter	Late spring or summer	Unable to compare	CAU-PED>KCDC>CAU-AD

CAU-AD, the dataset of adult patients from the study hospital; CAU-PED, the dataset of pediatric patients from the study hospital; KCDC, the Korea Influenza and Respiratory Surveillance System data by the Korean Centers for Disease Control and Prevention; RV, respiratory virus.

[a]Respiratory virus multiplex reverse transcriptase PCR,

[b]Weekly positivity rate,

[c]Data from adult study patients,

[d]Data from pediatric study patients,

[e]Data from the Korea Influenza and Respiratory Surveillance System by the Korean Centers for Disease Control and Prevention.

coefficient between the KCDC data and adult/pediatric data was the highest and the predictabilities were the best for IFV as compared with that for the other RVs. However, our data also show that such clinical consideration of the national data may be plausible during outbreaks of RSV, hMPV, and hCoV. Given that the numbers of hBoV-positive and PIV-positive RV PCR tests were so small in adult patients, if RV PCR tests would be more frequently performed for adults outside of the flu season (see the outbreak seasons of these two RVs in Table 1), a similar correlation would likely be observed for these two RVs. Furthermore, we should pay attention to the fact that the NPVs of the KCDC data for the occurrence of an outbreak in the adult data were high regarding all eight RVs. In other words, for each of the eight RVs, an occurrence of no outbreak in the KCDC data may be predictive of an occurrence of no outbreak of the respective RV among adult hospitalized patients. If one of these RVs was frequently detected in a hospital or any locale in a manner not consistent with its prevalence in the KCDC data, we might suspect that hospital or local RV outbreaks were ongoing separate from community outbreaks. All of these findings suggest that the KCDC data may be a helpful adjunct in uncovering outbreaks of RVs in adult hospitalized patients with ARI, especially in those clinical practices that currently do not perform RV PCR tests in ARI patients routinely.

Importantly, prior to the clinical utilization of the national data, we should call to mention some characteristic features of the data. For example, the KCDC data include all age groups. Regarding the fact that RV PCR tests are usually more frequently performed in children than in adults and more frequently have positive results among children than among adults, it is well-understood that the values of the weekly positive rates in the KCDC data are mostly positioned between higher rates from the pediatric data and lower ones from the adult data (Table 1). In other words, the pediatric graph may be an inflated form of the KCDC graph, whereas the adult graph may represent a deflated form of the KCDC graph. This may be responsible for the fact that, with regard to the predictability of the KCDC data for the occurrence of an outbreak in the other two datasets, PPVs were high for the pediatric data and NPVs were high for the adult data, generally for all 8 RVs. Considering that RVs have some differences in their impacts on adults and children, we suggest that the KCDC data should be classified according to age group.

This study has two important limitations. First, it did not provide important characteristics of the study patients such as types or severity of their illnesses, except for age and sex. Second, the KCDC data were compared to data from only one tertiary care center in Seoul.

TABLE 2 Relationship between the KCDC data and adult or pediatric data of the study hospital (presented by Pearson's correlation coefficients with 95% confidence intervals) and predictability of the KCDC data for the occurrence of an outbreak in the adult or pediatric data (presented by PPV, NPV, SN, and SP)

		Relationship	Predictabilities			
Type of respiratory virus	Group	Correlation coefficient (95% CI)	PPV	NPV	SN	SP
Influenza virus	Adults	0.74 (0.61 to 0.87)*	73.3% (33/45)	93.7% (59/63)	89.2% (33/37)	83.1% (59/71)
	Children	0.89 (0.81 to 0.98)*	88.9% (40/45)	98.4% (62/63)	97.6% (40/41)	92.5% (62/67)
Rhinovirus	Adults	0.19 (−0.004 to 0.37)	39.6% (42/106)	100% (2/2)	100% (42/42)	3.0% (2/66)
	Children	0.25 (0.06 to 0.43)*	99.1% (105/106)	0 (0/2)	98.1% (105/107)	0 (0/1)
Respiratory syncytial virus	Adults	0.41 (0.24 to 0.59)*	35.7% (10/28)	85.0% (68/80)	45.5% (10/22)	79.1% (68/86)
	Children	0.91 (0.83 to 0.99)*	100% (28/28)	51.3% (41/80)	41.8% (28/67)	100% (41/41)
Human metapneumovirus	Adults	0.33 (0.14 to 0.51)*	45.5% (15/33)	92.0% (69/75)	71.4% (15/21)	79.3% (69/87)
	Children	0.84 (0.74 to 0.95)*	93.9% (31/33)	81.3% (61/75)	68.9% (31/45)	96.8% (61/63)
Adenovirus	Adults	0.02 (−0.22 to 0.17)	18.8% (16/85)	78.3% (18/23)	76.2% (16/21)	20.7% (18/87)
	Children	0.25 (0.06 to 0.44)*	96.5% (82/85)	8.7% (2/23)	79.6% (82/103)	40.0% (2/5)
Human coronavirus	Adults	0.22 (0.03-0.41)*	27.7% (13/47)	85.2% (52/61)	59.1% (13/22)	60.5% (52/86)
	Children	0.75 (0.62 to 0.87)*	72.3% (34/47)	77.0% (47/61)	70.8% (34/48)	78.3% (47/60)
Human bocavirus	Adults	0.07 (−0.12 to 0.27)	4.3% (1/23)	88.2% (75/85)	9.1% (1/11)	77.3% (75/97)
	Children	0.69 (0.55 to 0.83)*	95.7% (22/23)	44.7% (38/85)	31.9% (22/69)	97.4% (38/39)
Parainfluenza virus	Adults	0.05 (−0.24 to 0.15)	10.1% (7/69)	92.3% (36/39)	70.0% (7/10)	36.7% (36/98)
	Children	0.55 (0.39 to 0.71)*	97.1% (67/69)	69.2% (27/39)	84.8% (67/79)	93.1% (27/29)

CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value; SN, sensitivity; SP, specificity.
*P-value <0.05.

Comparisons of the KCDC data with data from other centers in various geographic regions may yield different results.

In conclusion, national RV surveillance data may provide clinicians who manage adult patients with ARI with some assistance in predicting an RV outbreak among their patients.

CONFLICTS OF INTEREST

None to report.

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