


Incidence and seasonality of respiratory viruses causing acute respiratory infections in the Northern United Arab Emirates

Jae-Hyun Jeon^{1,2}  | Minje Han^{3,4} | Ho-Eun Chang^{3,5} | Sung-Soo Park^{6,7} |
Jae-Woong Lee^{6,7} | Young-Joon Ahn^{6,7} | Duck-Jin Hong^{3,4}

¹Department of Infectious Disease, Sheikh Khalifa Specialty Hospital, Ras Al Khaimah, UAE

²Department of Infectious Disease, Division of Internal Medicine, Veterans Health System Medical Center, Seoul, Republic of Korea

³Department of Laboratory Medicine, Sheikh Khalifa Specialty Hospital, Ras Al Khaimah, UAE

⁴Department of Laboratory Medicine, Seoul National University Hospital, Seoul, Republic of Korea

⁵Department of Laboratory Medicine, Seoul National University Bundang Hospital, Kyunggi-do, Republic of Korea

⁶Division of Intensive Care Medicine, Sheikh Khalifa Specialty Hospital, Ras Al Khaimah, UAE

⁷Division of Intensive Care Medicine, Seoul National University Hospital, Seoul, Republic of Korea

Correspondence

Duck-Jin Hong, MD, MS, Department of Laboratory Medicine, Division of Imaging and Laboratory, Sheikh Khalifa Specialty Hospital, Shohadaa Road, Ras Al Khaimah 6365, UAE.
Email: duckjin.hong@sksh.ae

Abstract

Background: The data on the seasonality of respiratory viruses helps to ensure the optimal vaccination period and to monitor the possible outbreaks of variant type.

Objectives: This study was designed to describe the molecular epidemiology and seasonality of acute respiratory infection (ARI)-related respiratory viruses in the United Arab Emirates (UAE).

Methods: Both upper and lower respiratory specimens were collected for the analysis from all the patients who visited the Sheikh Khalifa Specialty Hospital (SKSH) with ARI for over 2 years. The multiplex real-time reverse transcription polymerase chain reaction (rRT-PCR) test was used to detect respiratory viruses, which include human adenovirus, influenza virus (FLU) A and B, respiratory syncytial virus, parainfluenza viruses, human rhinovirus (HRV), human metapneumovirus, human enterovirus, human coronavirus, and human bocavirus.

Results: A total of 1,362 respiratory samples were collected from 733 (53.8%) male and 629 (46.2%) female patients with ARI who visited the SKSH between November 2015 and February 2018. The rRT-PCR test revealed an overall positivity rate of 37.2% (507/1362). The positive rate increased during winter; it was highest in December and lowest in September. FLU was the most frequently detected virus (273/1362 [20.0%]), followed by human rhinovirus (146/1362 [10.7%]). The FLU positivity rate showed two peaks, which occurred in August and December. The peak-to-low ratio for FLU was 2.26 (95% confidence interval: 1.52-3.35).

Conclusions: The pattern of FLU in the UAE parallels to that of temperate countries. The trend of the small peak of FLU in the summer suggests a possibility of semi-seasonal pattern in the UAE.

KEYWORDS

human influenza, molecular epidemiology, respiratory tract infections, seasons, United Arab Emirates (UAE)

1 | BACKGROUND

Acute respiratory infection (ARI) is responsible for a high global disease burden, and respiratory viruses are the most common causal

agents of ARIs.^{1,2} Influenza virus (FLU) causes considerable mortality and morbidity worldwide, even though FLU vaccines and antiviral agents are available. Moreover, clinically useful antiviral agents and vaccines do not exist for most of the other respiratory viruses.

Accordingly, understanding the epidemiology of respiratory viruses is important for promoting preparedness to tackle this public health threat.³⁻⁸

The epidemiology of ARI-related respiratory viruses in developed countries with temperate climates has been well studied.^{1,5,9} Contrary to the accumulating knowledge of ARIs in temperate regions, epidemiological research on acute respiratory viral illness in tropical and subtropical areas is limited, although the epidemiological diversity, according to local climate and latitude, has been well studied.^{8,10-12} The knowledge of the regional distribution of respiratory viruses is essential not only for local prevention and control of ARIs but also for global health decision-making.¹³ To our knowledge, limited information is available on the epidemiology and clinical characteristics of respiratory viral infections in the United Arab Emirates (UAE). Although a few studies in nearby countries with similar meteorology have described the epidemiology of ARIs, the reports cover a limited population group.¹⁴ Our study was designed to describe the molecular epidemiology of ARI-related respiratory viruses, including the seasonality of the viruses in the northern UAE for over 2 years.

2 | PATIENTS AND METHODS

2.1 | Clinical data and specimen collection

We collected both upper and lower respiratory specimens for the analysis from all the patients who visited the Sheikh Khalifa Specialty Hospital (SKSH) with acute respiratory illness between November 2015 and February 2018. Physicians were frequently encouraged throughout the year via SMS and e-mails to perform viral real-time reverse transcription polymerase chain reaction (rRT-PCR) tests to diagnose suspected acute ARI cases. An ARI was defined as the simultaneous occurrence of at least one respiratory symptom or sign (cough, purulent sputum, sore throat, nasal congestion, rhinorrhea, dyspnea, wheezing, or injected tonsils) and at least one of the following systemic symptoms: fever, chills, myalgia, or malaise. Enrolled cases were categorized into three age groups (pediatric: under 15 years of age; adult: 15 to 64 years of age; elderly: at least 65 years of age) and several variables were collected on clinical characteristics, including sex, age, and hospital admission status. If a patient was found to have the same virus two times separately within 3 weeks, then the infection was defined as a continuation of the previous episode of illness.

2.2 | Virus detection and identification

A Multiplex rRT-PCR Kit (Anyplex RV16, Seegene, Seoul, South Korea) was used to detect respiratory viruses. The rRT-PCR test targeted human adenovirus (HAdV), FLU A and B, respiratory syncytial virus (RSV), human parainfluenza viruses (HPIV) 1 to 4, human rhinovirus (HRV), human metapneumovirus (HMPV), human enterovirus (HEV), human coronavirus (HCoV)-229E, CoV-NL63, CoV-OC43, and human bocavirus (HBoV). Additional

rRT-PCR testing was performed to identify the subtypes of FLU A using a commercial kit (Allplex Respiratory Panel 1, Seegene, Seoul, South Korea) with the capability to differentiate FLU A virus subtypes A/H1N1, A/H3N2, and A/H1N1/pdm09, and RSV A and B viruses.

2.3 | Statistics

We used the Edwards harmonic technique method to measure the peak-to-low ratio.^{15,16} The Edwards technique is a geometrical model, which is an approach that fits a sine curve to a time series of frequencies by the use of ordinary regression methods. The peak-to-low ratio was interpreted as a measure of relative risk that compares the month with the highest incidence (peak) with the month with the lowest incidence (low or trough).¹⁵ The positivity rates for respiratory viruses during the discrete peak and low periods were compared using a direct method (χ^2 -test) to analyze statistical significance.¹⁷ We applied the Chi-squared (χ^2) test and Fisher's exact test to paired nominal data. Student *t* test was applied to analyze the means of continuous data. A two-sided alpha level of 0.05 defined statistical significance. All comparative statistical analyses were conducted using SPSS version 18.0 software (SPSS Inc, Chicago, IL).

2.4 | Ethical and regulatory oversight

Informed consent was waived as our study did not include any intervention that could change clinical decisions or the clinical courses of patients. The institutional review board of SKSH and Research Ethical Committee of Ministry of Health in Dubai granted ethical and regulatory approval. This study was performed in accordance with the ethical standards noted in the Declaration of Helsinki and its later amendments.

3 | RESULTS

In total, 1362 respiratory samples were taken from 733 (53.8%) male and 629 (46.2%) female patients. Of these patients, 1346 (98.8%) visited the emergency department and 16 (1.2%) visited the out-patient department. The numbers of cases in the pediatric, adult, and elderly groups were 198 (14.5%), 718 (52.7%), and 446 (32.8), respectively (Table 1). The median age was 5.0 years (95% confidence interval [CI]: 4.0-7.0), 40.0 years (95% CI: 38.0-41.0), and 77.0 years (95% CI: 75.0-78.0) for the pediatric, adult, and elderly groups. A nasopharyngeal swab was the most frequently used method for specimen collection (1316 specimens [96.6%]). A total of 46 specimens were taken by sputum collection and bronchoalveolar lavage. A total of 386 (28.5%) patients with ARI were admitted, regardless of whether the presence of any respiratory virus had been confirmed. The elderly group showed a higher overall admission rate than the other two groups (198/446 [44.4%] cases in the elderly group vs 190/916 [20.7%] cases in the other groups, $P < 0.01$).

TABLE 1 Baseline characteristics and incidence of detected viruses in patients with acute respiratory illness, categorized by age group

	Pediatric n = 198, N, %	Adult* n = 718, N, %	Elderly* n = 446, N, %	Total n = 1362, N, %
Sex, M:F*	108:90	365:353	260:186	733:629
Median age, years (95% CI)	5 (4.0-7.0)	40.0 (38.0-41.0)	77 (75.0-78.0)	49 (46.0-51.0)
Sampling site, upper airway (NPS)	198 (100)	700 (97.5)	418 (93.7)	1316 (96.6)
Lower airway (sputum)	0	18	28	46
Hospitalization with all-cause ARI*	27 (13.6)	163 (22.7)	198 (44.4)	388 (28.5)
Virus-positive cases*	102 (51.5)	291 (40.5)	114 (25.6)	507 (37.2)
Hospitalization in positive cases*	9 (8.8)	25 (8.6%)	35 (30.7%)	69 (13.6)
Positives rate by gender, M:F, %*	52.8:50.0	40.5:40.5	27.7:22.6	37.8: 36.6
The proportion of the detected viruses				
FLU	43 (42.2)	173 (59.5)	57 (50.0)	273 (53.9)
A/H1N1/pdm09	8	42	13	63
A/H3N2	13	72	20	105
A/H1N1/pdm09 + A/H3N2	0	6	2	8
B	21	43	15	79
HRV	29 (28.4)	83 (28.5)	34 (29.8)	146 (28.8)
HCoV	3 (2.9)	21 (7.2)	10 (8.8)	34 (6.7)*
RSV	14 (13.7)	6 (2.1)	8 (7.0)	28 (5.5)*
HMPV	6 (5.9)	8 (2.7)	4 (3.5)	18 (3.6)
HAdV	10 (9.8)	6 (2.1)	1 (0.9)	17 (3.4)
HPIV	4 (3.9)	5 (1.7)	2 (1.8)	11 (2.2)*
HEV	5 (4.9)	2 (0.7)	1 (0.9)	8 (1.6)
HBoV	0 (0.0)	2 (0.7)	0 (0.0)	2 (0.4)
Coinfection	15 (14.7)	21 (7.2)	4 (3.5)	40 (7.9)

Abbreviations: ARI, acute respiratory illness; BAL, bronchoalveolar lavage; CI, confidence interval; FLU, influenza virus; GW, general ward; HAdV, human adenovirus; HBoV, human bocavirus; HCoV, human coronavirus; HEV, human enterovirus; HMPV, human metapneumovirus; HPIV, human parainfluenza virus; HRV, human rhinovirus; ICU, intensive care unit; NPS, nasopharyngeal swab; RSV, respiratory syncytial virus.

* < 15.

† 15-64.

‡ ≥ 65 y old.

§ Statistically significant ($P < 0.05$).

¶ Statistically insignificant.

12 (cases) of HCoV-OC43, 11 of HCoV-229E, 8 of HCoV-NL63; 19 of RSV-A, 5 of RSA-B; 1, 5, 2, and 3 of HPIV-1,2,3, and 4, respectively.

The overall positivity rate for respiratory viruses was 37.2% (507/1362). There was no significant difference in the positivity rate between men and women (277/733 [37.8%] vs 230/629 [36.6%], respectively, $P = 0.65$). The positivity rate in the pediatric group (102/198 [51.5%]) was higher than that in the adult (291/718 [40.5%], $P = 0.007$) and elderly (114/446 [25.6%], $P < 0.01$) groups.

Among the virus-positive cases, the admission rate was significantly higher in the elderly group than in the other two age groups (35/114 [30.7%] positive cases vs 34/393 [8.7%] positive cases, $P < 0.01$). However, the admission rate did not differ significantly between virus-positive cases in the pediatric and adult groups (9/102 [8.8%] vs 25/291 [8.6%], $P = 0.94$).

The positivity rate for FLU was 20.0% (273/1362). FLU was the most commonly detected virus among all of the respiratory viruses (273/507 [53.8%] detected viruses; Table 1). The incidences of A/H3N2 and A/H1N1/pdm2009 FLU subtypes were 41.4% (113/273) and 26.0%

(71/273), whereas the incidence of FLU B was 28.9% (79/273). Subtyping was not performed in 18 cases of FLU A in November 2015. FLU was the most frequently detected respiratory virus in hospitalized virus-positive patients (31/69 [44.9%]). The admission rate of patients who had FLU infections was 11.4% (31/273). The admission rate of the A/H1N1/pdm09 sub-group was higher than that of the A/H3N2 sub-group (11/63 [17.5%] cases vs 7/105 [6.7%] cases, $P = 0.039$).

HRV was the second-most commonly detected virus (146/507 [28.8%] cases). The positivity rate for HRV did not differ between hospitalized and non-hospitalized patients (20/69 [29.0%] cases vs 126/438 [28.8%] cases, $P = 0.97$).

Nearly 8% (40/507 [7.9%]) of positive cases were coinfecting with two different viruses (Table 2). HRV and FLU were most frequently detected together in coinfection cases ($n = 9$). None of the patients were coinfecting with three or more viruses. The pediatric group showed the highest rate of coinfection (15/102 [14.7%]).

TABLE 2 Coinfection of respiratory viruses in patients with acute respiratory illness

Viruses		n	Viruses		n
FLU A +	HRV	7	HRV +	HCoV	3
	HCoV	3		HAdV	1
	RSV	1		RSV	3
FLU B +	HPIV	1		HEV	5
	HRV	2	HAdV +	HCoV	1
	HAdV	2		HPIV	1
	HMPV	2		RSV	1

Abbreviations: AdV, adenovirus; FLU, influenza virus; HCoV, Human coronavirus; HEV, human enterovirus; HRV, human rhinovirus; HMPV, human metapneumovirus; HPIV, human parainfluenza virus; RSV, respiratory syncytial virus.

Both the number of specimens and the positivity rate of all respiratory viruses increased in the winter season (Figure 1). The positivity rates were highest in December and lowest in September (lowest in 2016) and August (lowest in 2017) of each year. The FLU positivity rate showed two peaks, which occurred in August and December (Figure 2). A/H3N2 was the most common subtype of FLU and was detected throughout the year. The peak-to-low ratio of all respiratory viruses was 1.74 (95% CI: 1.33-2.27) and showed significant seasonality ($P < 0.01$; Table 3). The number of FLU and HRV cases was large enough to evaluate the associated seasonality. The peak-to-low ratio of FLU was 2.26 (95% CI: 1.52-3.35) and it had significant seasonality ($P < 0.01$). HRV was detected year-round and showed no significant seasonality. The peak-to-low ratio of HRV was 1.44 (95% CI: 1.00-2.34), which was insignificant ($P = 0.22$).

4 | DISCUSSION

ARI is highly prevalent and is responsible for a high burden of disease in many countries. Respiratory viral infection is the most common cause of ARI, and predicting the timing of peak respiratory virus activity is important for improving disease control.

In this study, the overall positivity rate of respiratory viruses and the incidence of each virus by age group were similar to those reported by previous studies describing the epidemiology of respiratory viruses.^{6,7,9,18} Several studies have reported that men are more susceptible to viral infection, and have more vigorous immune and behavioral responses.¹⁹⁻²¹ However, there was no difference in the positivity rate or the incidence of ARI by sex in our study. The higher positivity rate of respiratory viruses in the pediatric group was compatible with that reported in other studies.^{9,22}

Of the 1362 patients included in our study, 388 (28.5%) with ARI were admitted for further management. Our data showed a lower admission rate for virus-positive than virus-negative patients (13.6% vs 37.3%), implying a better prognosis for virus-related ARIs than that for ARIs of other etiologies, as noted in several previous studies.^{23,24} The higher admission rate in the elderly group is also in agreement with that reported by earlier studies.^{2,24,25}

FLU was the most common respiratory virus in all age groups, and the positivity rate was 20.0%, which is similar to previous data reported from studies in Oman.^{14,26} A/H3N2 was the most common subtype detected throughout the year. The high incidence of FLU and A/H3N2 may be related to the severe symptoms characteristic of these infections, which increase the likelihood of patients visiting the emergency department. Many studies have reported that ARI symptoms are more likely to be experienced by individuals infected with FLU than by those infected with other respiratory viruses. In addition, A/H3N2 infections are more severe than A/H1N1 or B infections.^{27,28} FLU vaccination could have influenced the incidence of FLU and its subtypes in the present study. However, regional information on FLU vaccination is not available in the UAE.

In this study, HRV was the second-most commonly detected respiratory in all age groups. This finding is in agreement with other studies.^{29,30} Good accessibility of patients with common cold to emergency department might explain the higher incidence of HRV in the UAE. However, the incidence of HRV could have been overestimated. Many patients tested positive for HRV at the emergency department, but actually had bacterial coinfections, and their more severe symptoms could have been attributable to the bacterial infections or combined comorbidities like asthma. RSV is known as the leading cause of ARI.^{1,9,31}

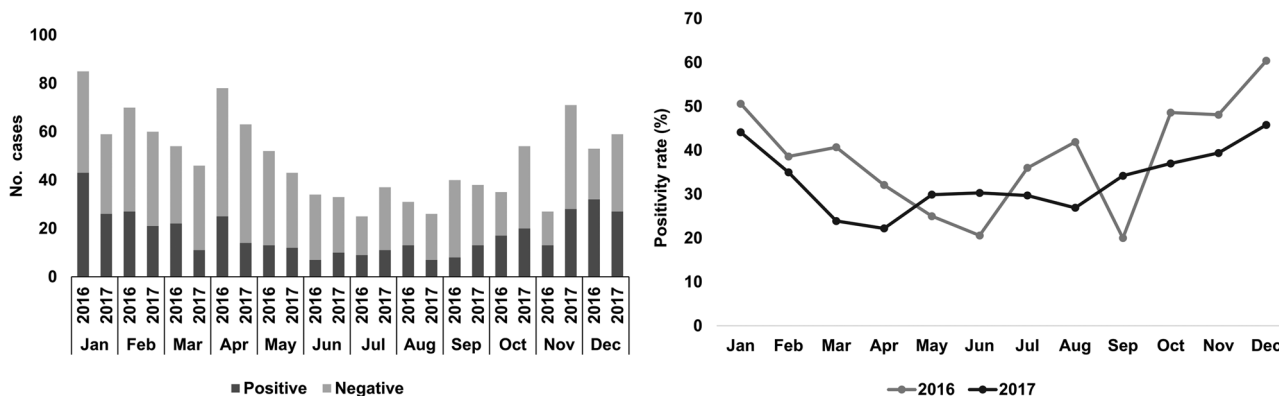


FIGURE 1 Monthly number and positivity rate of all respiratory viruses in 2016 and 2017, in patients with acute respiratory illness who visited the Sheikh Khalifa Specialty Hospital. Isolation rate and positivity rate of all respiratory viruses showed seasonal variation

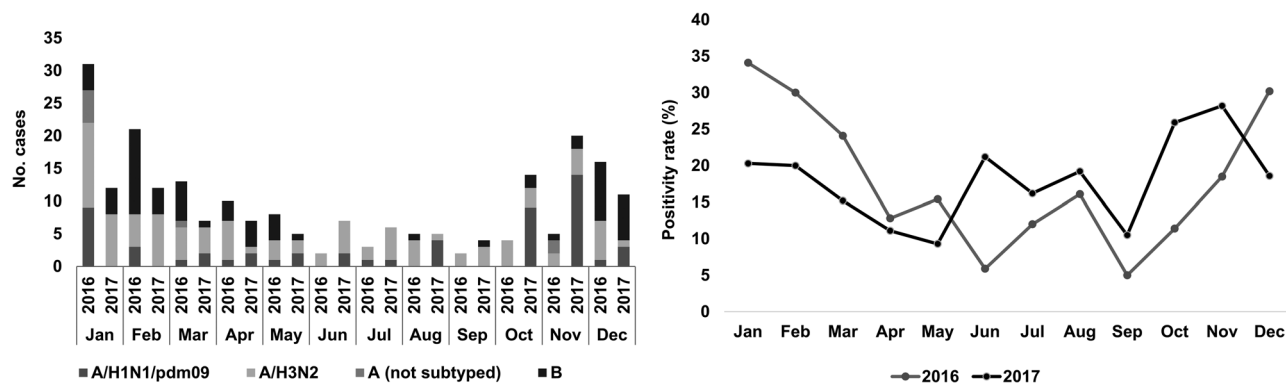


FIGURE 2 Monthly number and positivity rate of influenza viruses in 2016 and 2017, in patients with acute respiratory illness who visited the Sheikh Khalifa Specialty Hospital. Positivity rate showed two peaks in August and December. A/H3N2 was the most common FLU subtype and was detected throughout the year. FLU, influenza virus

TABLE 3 Seasonality analysis of acute respiratory infections performed using the geometrical model.

Viruses	Year	Peak/Low ratio (RR)	95% CI		P value*	Time of peak	Hemi-amplitude
			Lower	Upper			
All viruses	2016	1.94	1.29	2.92	<0.01	Dec 15	0.32
	2017	1.59	1.05	2.41	<0.01	Nov 29	0.23
	Overall	1.74	1.33	2.27	<0.01	Dec 8	0.27
FLU	2016	3.99	1.80	8.84	<0.01	Jan 24	0.60
	2017	1.57	1.00	2.74	0.01	Nov 15	0.22
	Overall	2.26	1.52	3.35	<0.01	Dec 24	0.39
HRV	2016	3.06	1.25	7.51	0.31	Sep 29	0.51
	2017	1.13	1.00	2.44	0.77	Feb 3	0.06
	Overall	1.44	1.00	2.34	0.22	Sep 27	0.22

Abbreviations: CI, confidence interval; FLU, influenza virus; HRV, human rhinovirus.
*by direct comparison of discrete time periods.

However, the incidence of RSV among positive cases in our study was lower than that reported in other publications.^{31,32} It is possible that the incidence of RSV was underestimated in the current study because comparatively small numbers of infants and young children were included. The hot and dry climate of the UAE could also be a possible explanation for the low incidence of RSV in this region. RSV is more common during the rainy season in tropical and subtropical areas, and is reported to have a low survival rate at high temperatures.^{32,33}

Small numbers of HCoV, HAdV, HMPV, HBoV, HEV, and HPIV cases were sporadically detected in our study. Reports suggest that because of the mildness of symptoms and the self-limiting nature of these infections, patients may not seek medical care, and this may lead to an underestimation of the incidence of infection.^{7,34} However, our data suggest that in the UAE, like in other temperate countries, a diverse set of respiratory viruses contribute to the ARI cases that compel patients to visit medical facilities, because of their severity. Because we have reported the incidence of such severe infections, we believe that the data in this study will be of value to medical institutions in the UAE.

Among the virus-positive cases in our study, the coinfection rate was 7.9% overall and 14.7% in the pediatric group. These are compatible with

the values mentioned in previous reports.⁹ However, several similarly designed studies showed higher rates of coinfection (from 13.2%-42.5%), particularly in young children.^{7,22,35} HRV was the most common virus to be found in cases of coinfection with other viruses in our study; this finding was in agreement with that reported in the literature.^{9,30} Coinfection with FLU and HRV was common in our study although other studies have reported a negative association between the two viruses.^{5,36} FLU and HRV may have been detected in coinfecting patients more frequently because the incidence of both viruses was higher than that of the other respiratory viruses in this study.

A characteristic semi-seasonality pattern on respiratory viral infection rates was observed in our study. FLU was the main contributing organism to the seasonal pattern; the subtypes A/H1N1/pdm09 and FLU B contributed predominantly to the winter peak. Low temperatures and low specific humidity during the winter season in the UAE may be the cause of the peak in the number of FLU cases in the winter.¹² In addition to the major peak in the winter, a small peak in August was also observed for FLU (semi-seasonal pattern), which parallels the patterns reported from temperate and tropical countries in the Northern Hemisphere.^{5,8,12} Most of the respiratory viral infections, including FLU, are more common

in the winter in temperate countries.⁸ However, FLU and RSV infections tend to show annual peaks in association with the rainy season in the tropical area.^{8,33,37} In subtropical areas, previous studies have observed that respiratory viruses, including FLU, peaked in the coldest months in temperate areas.^{38,39} The UAE is located in a subtropical area and does not have a rainy season. Thus, we expected a peak of FLU in the winter season, as is common in other subtropical areas.¹² However, FLU in the UAE showed a two-peaks semi-seasonal pattern, which has also been observed in some other regions located at similar latitudes (Taiwan and Nepal).⁸ The majority of the population of the UAE is exposed to a dry, air-conditioned environment for most of the day, especially during the summer season, because outside temperatures range from 39 to 45°C. Despite this relatively controlled environment, the summer peak of FLU in the UAE could be explained by prolonged effective contact rates, because of the increased indoor activity, and lowered relative humidity, which have been reported to be related to the incidence of viral illnesses.^{40,41} This finding implies the potential necessity for sustained FLU vaccination campaigns and repeated vaccinations to reduce the severity of FLU infections, especially for high-risk individuals.^{42,43} Nationwide data are needed to confirm the semi-seasonal pattern of FLU in the UAE.

Our study was subject to some limitations. First, this was a single center study with relatively small sample size; moreover, the decision of whether to collect a sample from the patient for viral testing was at the physician's discretion. Physicians in the emergency department may have preferred to perform a rapid influenza antigen test rather than to conduct a multiplex rRT-PCR test, which requires a longer time to produce results. Hence, the incidence of respiratory viruses may have been underestimated because of the low sensitivity of the rapid antigen test, and because viruses, other than the FLU, may not have been identified even if present in the samples.^{25,44} Second, our results may not be generalizable to the entire population of the UAE because most of the study specimens were taken from patients in the Northern Emirates. In addition, our study could have underestimated the degree of seasonality in the UAE because the seasonality of viral infections tends to be more apparent when analyses include mild cases that require minimal conservative care (for example, outpatient care in the primary clinic).⁴⁵

5 | CONCLUSION

To our knowledge, this is the first study to describe the rRT-PCR-based seasonal pattern of respiratory viruses related to ARI in the UAE. Moreover, the high sensitivity of the detection method enabled the collection of more reliable epidemiologic data. To date, very few studies have provided such data for the middle-eastern region. The seasonality of FLU was similar to that observed in temperate countries and was also consistent with a semi-seasonal pattern of incidence. This knowledge can serve as baseline data for more expansive future surveillance studies of respiratory viruses in the UAE and in the middle-eastern region.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

ORCID

Jae-Hyun Jeon  <http://orcid.org/0000-0002-1725-8468>

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