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REVIEW ARTICLE

Global Seasonality of Human Coronaviruses: A Systematic Review

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In the context of the coronavirus disease 2019 pandemic, we aimed to systematically address the global seasonal patterns of human coronavirus (HCoV) infections. We identified relevant articles from MEDLINE, EMBASE, and CINAHL Plus as of May 11, 2020. The main outcomes were the peak months of HCoV infections each year and the months during which more than 5% of positive respiratory specimen tests were attributable to HCoV. Of 707 articles reviewed, 22 met the inclusion criteria. The annual percentage of HCoV infections reached a peak in February globally. We found a higher HCoV positivity rate among studies that tested only children (median: 5.9%, range: 0.9%–18.4%), compared with other studies of adults alone (median: 5.2%, range: 3.3%–7.1%) or the entire population (median: 1.9%, range: 0.2%–8.1%). We found the largest global peak of HCoV during the winter season, with the highest rate of positivity among children.

Keywords. climate; coronavirus; epidemic; seasonality; weather.

Periodic surge in disease incidence corresponding to seasons is characteristic of many infectious diseases [1]. Although the mechanisms underlying seasonal occurrence remain poorly understood, recognition of periodic oscillation is of public health importance in the view of resource allocation and setting.

Human coronaviruses (HCoVs) are common causes of acute respiratory infections, leading to a wide range of disease severity. The 2 emergent zoonotic HCoV infections, namely, severe acute respiratory syndrome coronavirus 1 (SARS-CoV-1) and Middle East respiratory syndrome coronavirus (MERS-CoV), have not established sustained community transmission in the past. However, the zoonotic SARS-CoV-2 continues its rampant spread across the globe, causing more than 6 million cases of coronavirus disease 2019 (COVID-19) and 390 000 deaths, as of June 7, 2020 [2].

Predicting the fate of SARS-CoV-2 remains a challenge because of its unique virulence, transmissibility, and genetic adaptation. To develop timely and effective countermeasures to combat COVID-19, information about the periodicity of the common endemic HCoV subtypes (HCoV-OC43, -HKU1, -229E, and -NL63) may be useful to inform public health strategies considering that SARS-CoV-2 may become an endemic seasonal virus. The aim of this report is to systematically collate and evaluate the existing evidence describing seasonal patterns in the incidence of nonzoonotic HCoV globally.

METHODS

This study was performed in accordance with PRISMA guidelines [3]. Our research question was formulated in accordance with PICO (P = population, I = intervention, C = comparison, and O = outcome): how does the incidence of coronavirus (O) among adults and children (P) vary by season (I)? We searched MEDLINE (beginning in 1946), EMBASE (beginning in 1947), and CINAHL Plus (beginning in 1937) to find relevant articles through May 11, 2020 without language restrictions. We used the following Medical Subject Heading terms in exploring MEDLINE: coronavirus AND (season OR climate OR weather). Each term was modified to an appropriate thesaurus term suitable for other databases. In all databases, we used narrower terms of each broad thesaurus term by activating the "explode" function. We also manually screened references of relevant articles to find additional articles.

Inclusion criteria were as follows: a prospective or retrospective study that included HCoV-OC43, -HKU1, -229E, or -NL63; ≥1 consecutive year study period; and clearly reported proportions of coronavirus infections of study populations in each month or season. Studies that used multiple-year data were retrieved as presented. We excluded studies on SARS-CoV-1 or -2 and MERS-CoV because occurrences of these viruses were observed in

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situations carefully controlled with special isolation precautions unlike for other HCoVs. Because the purpose of this study was to evaluate seasonality of HCoV infections, we excluded studies that lacked information about the proportion of HCoV infections per month or season. We also excluded studies that reported the number of HCoV cases but not the number of specimens.

Two investigators (S.P. and Y.J.C.) independently performed study selection. Articles written in other languages than English were translated using the Google Translator (https://translate.google.com/) before reviewing full texts. We quantified the interrater agreement for study selection using the Cohen's kappa coefficient. Two investigators (S.P. and Y.L.) extracted the data from study articles using a uniform method. From eligible studies, we collated the following information: author, year, country, study design, study population, subtypes of virus, participants' age, observation period, sample size, positive proportion of HCoV tests, months with ≥5% positive HCoV tests, and peak months, or month of year when the incidences are at their highest, of HCoV infections. Information on peak months and months with ≥5% positive tests were aggregated from consecutive annual data. If the data collection period was <12 months, data were combined with those collected during the previous or following year. For example, if a study collected data from May to December 2005 and from January to December 2006, data were combined into a single observation over 20 months for measurement.

Two investigators (S.P. and Y.L.) assessed the risk of study bias using a modified Hoy's tool [4]. We used 9 items to evaluate validity of each study. Items with high risk of bias (answered as "no") were assigned a score of 1; and items with low risk of bias (answered as "yes") were assigned a score of zero. External validity was assessed by 4 items: study's target population was similar to the national population; study's sampling frame was similar to the target population; study used random selection to collect participants; and study minimized nonresponse bias by obtaining response rate ≥75%. Internal validity was assessed by 5 items: study directly collected data from individual participants or specimens; study used an acceptable case definition; diagnostic tool had validity and reliability; study used the same mode of data collection for all participants; and study reported numerators and denominators of the variables of interest. We classified studies as being at low (0–1), moderate (2–4), or high (5–9) risk of bias.

Patient Consent Statement

This systematic review is exempt from ethics approval and patient consent from the Hallym University Institutional Review Committee because the study collected and synthesized data from aggregated, anonymized data in the public domain.

RESULTS

Our search identified 758 articles and conference abstracts (Figure 1). Fifty-two duplicates were removed. After screening titles and abstracts, we excluded 606 studies that did not meet eligibility criteria for this systematic review. We then reviewed full text of 101 articles and excluded another 79 studies that were ineligible. We ultimately included 22 studies with 979 400 specimens from 12 countries in the systematic review. Interrater agreement for study selection was good (Cohen's kappa = 0.917, 97.1% agreement).

The included studies were published between 2005 and 2020 (Table 1) [5–26]. More than half of the studies (14 of 22) were performed in Asia [6–19]. Only 1 study followed participants longitudinally and collected specimens from them periodically [25]. Two studies collected respiratory specimens from cohorts [23, 25]. Two studies used surveillance samples [21, 26]. Sixteen studies reported HCoV infection by screening all 4 subtypes of virus [5, 7, 9–11, 13, 14, 16–22, 24, 25]. The range of proportions of positive specimens was 0.2%–18.4% (median: 4.45%) (Table 2). We classified 1, 21, and 0 studies as having low, moderate, and high risk of bias, respectively (Supplementary Table 1).

Figure 2 depicts the proportions of HCoV infections peaked in the winter season (February, 22.4%; January, 16.3%; and December, 14.3%). A small number of studies reported peaks during summer months (June, 4.1%; July, 4.1%; and August, 2.0%) [5, 6, 13, 14, 17]. Around 38.8% of observation periods

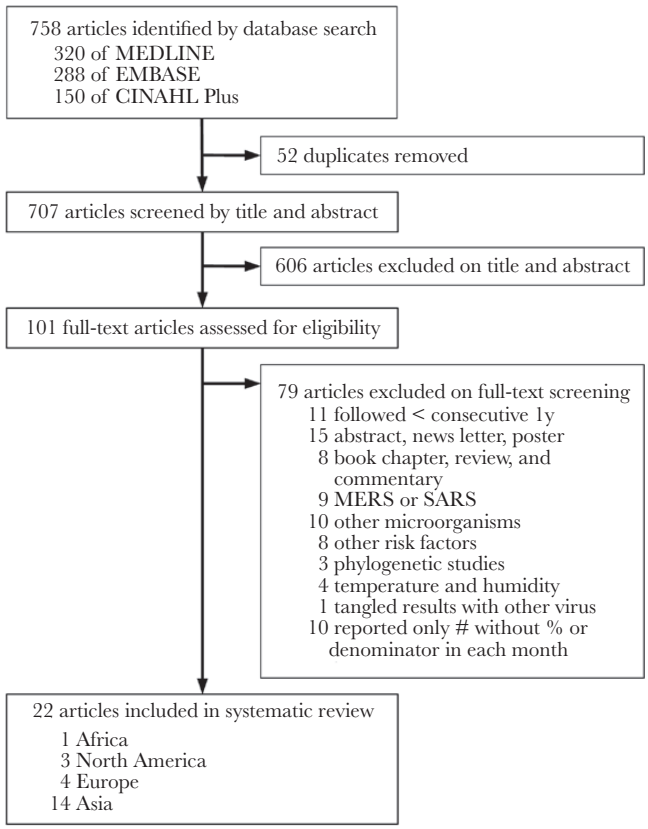

Figure 1. Study selection. MERS, Middle East respiratory syndrome; SARS, severe acute respiratory syndrome.

Table 1. Studies Included in the Systematic Review

Study, year	Country	Population	HCoV subtype	Age
Africa				
Brini Khalifa et al [5], 2019	Tunisia	ARI patients	O/H/N/E	0–12 months
North America				
Dominguez et al [24], 2009	USA	ARI patients	O/H/N/E	Children
Killerby et al [26], 2018	USA	Surveillance samples	O/N/E	0–96 years
Galanti et al [25], 2019	USA	Healthy individuals	O/H/N/E	0–63 years
Europe				
van der Zalm et al [23], 2009	Netherlands	Healthy individuals	O/N/E	Birth–1 year
Gaunt et al [21], 2010	UK	Surveillance samples	O/H/N/E	Children, adults
Jevsnik et al [22], 2016	Slovenia	ARI patients	O/H/N/E	Children, adults
De Conto et al [20], 2019	Italy	ARI patients	O/H/N/E	2 days–14 years
Asia				
Ren et al [13], 2019	China	ARI patients	O/H/N/E	14–97 years
Xin et al [15], 2012	China	ARI patients	N	29 days–15.9 years
Feng et al [9], 2014	China	ARI patients	O/H/N/E	Children, adults
Zeng et al [17], 2018	China	ARI patients	O/H/N/E	Children
Zhang et al [18], 2018	China	ARI patients	O/H/N/E	1 days–103 years
Zhao et al [19], 2019	China	ARI patients	O/H/N/E	1 months–14 years
Chiu et al [8], 2005	Hong Kong	ARI patients	O/N/E	Children, adults
Yip et al [16], 2016	Hong Kong	ARI patients	O/H/N/E	22 days–95 years
Matoba et al [12], 2015	Japan	ARI patients	O/N/E	Unclear
Al-Khannaq et al [6], 2016	Malaysia	ARI patients	N/E	Adults
Toh et al [14], 2019	Malaysia	ARI patients	O/H/N/E	Children, adults
Al-Romaihi et al [7], 2020	Qatar	ARI patients	O/H/N/E	0–14 years
Kim et al [10], 2016	South Korea	ARI patients (COPD)	O/H/N/E	Adults
Ko et al [11], 2017	South Korea	ARI patients	O/H/N/E	0–91 years

Abbreviation: ARI, acute respiratory infection; COPD, chronic obstructive pulmonary disease; E, human coronavirus (HCoV)-229E; H, HCoV-HKU1; N, HCoV-NL63; O, HCoV-OC43; UK, United Kingdom; USA, United States of America.

showed that more than 5% of specimens tested positive for HCoVs in February and March [5, 7, 8, 10–12, 16, 17, 19–26]. Around 10 to 22% of observation periods showed that more than 5% of specimens had positive test results during fall (September, 10.2%; October, 12.2%; and November, 22.4%) [5–8, 10, 12, 17, 19, 20, 23, 25]. Some research that studied children only showed higher HCoV positivity rate (median: 5.9%, range: 0.9%–18.4%) [5, 7, 15, 17, 19, 20, 23, 24] than the studies of adults alone (median: 5.2%, range: 3.3%–7.1%) [6, 10] or the general populations (median: 1.9%, range: 0.2%–8.1%) [8, 9, 11, 13, 14, 16, 18, 21, 22, 25, 26].

DISCUSSION

This review describes the incidence and proportion of common nonzoonotic HCoV among various populations, providing a snapshot of the global seasonality of this virus. We found a consistent winter peak of HCoV incidence in the northern hemisphere, with modest decline in the summer months. Various factors may contribute to the seasonal occurrence of HCoV, as in other respiratory viruses. Human factors, such as behaviors and activities that are closely associated with proximity of humans to one another, may contribute in seasonal cycles in virus transmission [27]. Environmental factors such as humidity have been noted with improving duration of viral survival in the environment, and thus they may increase the chance of indirect transmission of viruses [28]. However, these descriptions carry an important caveat of societal changes over the past centuries with industrial revolutions that relocated outdoor agricultural workplaces into indoor factories and offices, while moving human lifestyle away from nature and outdoor climate [29]. In the context of urbanization, a consistent thermal comfort zone could be maintained indoors, causing even further disconnection from daily and seasonal outdoor climate fluctuations. Nonetheless, it is important to address the current questions related to seasonality of HCoV in light of the COVID-19 pandemic. The apparent seasonality of HCoV across the globe suggests that this phenomenon might be mined to produce improved understanding of transmission of COVID-19 and improve public health intervention.

The observed seasonal variation of HCoV rates may have resulted from a dynamic interaction of factors as in other respiratory viruses [30]. The typical winter peak seasonality of respiratory viruses is highly dependent on geographic location and climate. In northern and southern hemisphere temperate regions, an annual seasonal pattern is predictably limited to

Table 2. Positive Proportion of Human Coronavirus (HCoV) Tests, Months with ≥5% Positive HCoV Tests, and Peak Months of HCoV Infections in Included Studies

Study	Observation Period	n[a]	Positive, %	Positive ≥5%	Peak Month
Africa					
Brini Khalifa et al [5]	September 2013–December 2014	515	18.4	All year round	April–June
North America					
Dominguez et al [24]	December 2004–November 2005	1683	5.0	January–May	January
Killerby et al [26]	July 2014–December 2015	854 575	0.2	January–March, December	February
Galanti et al [25]	October 2016–April 2018	4215 (214)	4.5	January–March, May, July, November–December	May
Europe					
van der Zalm et al [23]	October 2003–September 2006	668 (305)	7.6	January–April, August, November–December	December
Gaunt et al [21]	July 2006–December 2007	11 661 (7383)	2.3	February, March	February
	January 2008–June 2009			None	February
Jevsnik et al [22]	October 2009–December 2010	718, 156	8.1, 1.9	February–April, December	February
	January–October 2011			January–April	February
De Conto et al [20]	October 2012–December 2013	2892 (2575)	9.1	November, January–March	February
	January–December 2014			January–June, August, December	March
	January–September 2015			January, March	January
Asia					
Ren et al [13]	May 2005–December 2006	4335	0.7	None	October
	January–December 2007	2214	0.5	June	June
	January 2008–April 2009	1847	1.9	None	April
Xin et al [15]	April 2006–March 2008	878	0.9	None	September
Feng et al [9]	January–December 2009	28 369	1.4	None	March
	January–December 2010			None	February
	January–December 2011			None	November
	January 2012–September 2013			None	September
Zeng et al [17]	July 2009–December 2010	11 399	4.3	June, August–October, December	October
	January–December 2011			February, April, June, October–November	April
	January–December 2012			January, March–August	April
	January–December 2013			May–September	July
	January–December 2014			January	January
	January 2015–June 2016			September, June	September
Zhang et al [18]	July 2010–June 2015	13 048	2.3	None	February
Zhao et al [19]	May 2008–March 2014	700	10.7	All year round	Spring (March–May)
Chiu et al [8]	August 2001–August 2002	581	4.4	February, July, November–December	November
Yip et al [16]	September 2008–December 2009	8275	0.9	None	December
	January–December 2010			None	December
	January–December 2011			None	May = September
	January–December 2012			None	January = November
	January 2013–August 2014			February	February
Matoba et al [12]	January–December 2010	4342	7.6	January–March, October–November	January
	January–December 2011			January–March, July–August	January
	January–December 2012			January–April, June, November–December	December
	January–December 2013			January–March	January
Al-Khannaq et al [6]	March 2012–February 2013	2060	3.3	July–August, October	July
Toh et al [14]	June 2017–May 2018	599	1.0	None	August–September = October–November = November–December = December–January
Al-Romaihi et al [7]	January–December 2012	1846	8.3	None	February
	January–December 2013	2081	6.0	None	February
	January–December 2014	2901	5.9	None	May

Table 2. Continued

Study	Observation Period	n[a]	Positive, %	Positive ≥5%	Peak Month
	January–December 2015	4614	5.1	None	January
	January–December 2016	5314	5.0	None	December
	January–December 2017	14 190	5.6	March, November–December	December
Kim et al [10]	January 2010–December 2012	477	7.1	January–April, June, November–December	April
Ko et al [11]	January–December 2013	3467	O/H: 4.1, N/E: 1.7	Unclear	Unclear
	January–December 2014			December	December
	January–December 2015			February	February

[a]If the number of participants and specimen were different, the number of participants is shown in the parenthesis.

a few months during winter [31]. It has been suggested that differences in host susceptibility, environmental factors, and population behavior are potential determinants for seasonal incidence of respiratory virus infections [32]. Other authors have found that low temperatures during winter prolong the stability of viruses in fomites [33]. Nevertheless, none of these associations have been proven to be causal for incidences. Regardless of the cause, identifying the seasonal pattern of HCoV is important when planning strategies to mitigate the spread of SARS-CoV-2. Our finding indicates that the seasonality of HCoV peaks during winter in the northern hemisphere across the globe, as with other respiratory viruses [34].

Most studies included in this review reported the percentage of HCoV detection in patients presenting with acute respiratory infections. As expected, considerable variation was found in the percentage of HCoV infections reported by the included studies. In Norway, among children hospitalized with respiratory tract infection, HCoV was responsible for 9.1% of all infections [35]. Among 1404 children in Mexico with community-acquired pneumonia from 2010 to 2013, HCoV accounted for 7.2% of infections [36]. Among 219 respiratory specimens from patients admitted to pediatric hematology and oncology department in Turkey, HCoV accounted for 14.8% of all respiratory viruses [37]. Several factors such as case definition, study setting, population structure, and differences in the host and pathogen across the globe may have contributed to the observed variability and should be considered when interpreting the study result. Another notable finding was that HCoV positivity rates in studies that exclusively tested children were higher than in studies of the general population, which is consistent with findings from other respiratory viruses [34]. It is in line with a recent cohort study from Michigan that showed the highest infection frequency of HCoV in children <5 years (18 per 100 person-years), with little variation in older age groups (range, 7 to 11 per 100 person-years) [38]. These findings may not be generalizable to SARS-CoV-2 given the unclear virologic properties of SARS-CoV-2; however, like other respiratory viruses, HCoV infects people of all ages, both in adults and children.

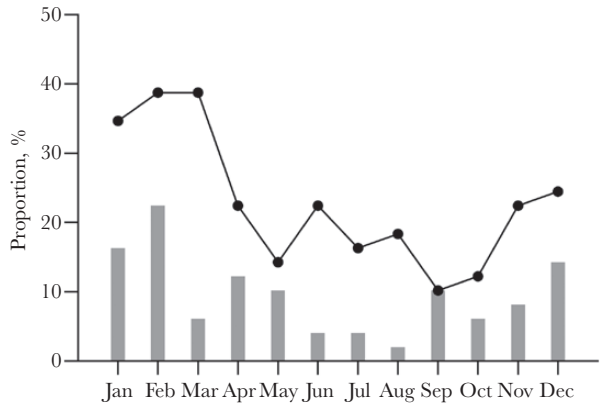

Figure 2. Monthly distribution of human coronavirus (HCoV) infection worldwide. The bar indicates the proportion of the peaks in HCoV infection per observation period. The line indicates the proportion of studies that reported more than 5% of specimens that tested positive for HCoV.

Our review has potential limitations. First, by comparing proportions of individuals who tested positive for HCoV, rather than the total number of HCoV cases, the observed seasonal patterns may have been driven by periodic changes in other respiratory pathogens. Moreover, we did not distinguish between temporal trends of the annual and seasonal occurrences in studies that presented aggregated data on given seasons [7]. However, we found similar results when we compared differences in the total number of HCoV cases. Second, we did not directly assess factors that may lead to higher numbers of HCoV cases. Seasonality may or may not have a direct causal relationship with HCoV transmissibility, but if it does, it can be challenging to detect such an association because epidemiological data represent case events, not transmission events. Several studies have investigated the role of geospatial factors (ie, latitude) and societal factors (ie, population density) on the seasonal occurrence of respiratory viruses [29]. Our findings may not be generalizable because the only available published data were mostly from countries in the northern hemisphere. Yet, given the wide range of variations in environments within the studied areas (ie, the United States, China), these factors were not included in our analysis. Finally, previous studies have

shown the difference in seasonality between alpha-coronavirus (ie, HCoV-229E) and beta-coronavirus (ie, HCoV-OC43); therefore, our finding may not be directly extrapolated as a general characteristic of SARS-CoV-2 [39, 40]. Nonetheless, the lack of population immunity against SARS-CoV-2 in the setting of social distancing makes the temporal trend of COVID-19 largely unpredictable. Although it would be challenging to estimate the seasonality of SARS-CoV-2 at this time, it is plausible that if there are overlapping virus-specific characteristics with other HCoVs, our finding may add a piece of information in regard to public health preparedness.

CONCLUSIONS

This systematic review reveals that common HCoVs tend to spread during the winter months across the globe, with higher positivity rate in children compared with adults. If the virologic properties of SARS-CoV-2 on seasonality of transmission is similar to general HCoV, it may be possible to estimate the months most likely to be at higher risk of spread of COVID-19, allowing for public health preparedness and response efforts.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases online*. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Acknowledgments

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Potential conflicts of interest. All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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Supplementary Table 1. Risk of bias scores of included studies

Study	ex1	ex2	ex3	ex4	in1	in2	in3	in4	in5	Total
Africa										
Brini Khalifa et al [5]	1	1	1	0	0	0	0	0	0	3
North America										
Dominguez et al [24]	1	1	1	0	0	0	0	0	0	3
Killerby et al [26]	0	0	0	1	0	0	0	0	0	1
Galanti et al [25]	1	1	1	0	0	0	0	0	0	3
Europe										
van der Zalm et al [23]	1	1	1	0	0	0	0	1	0	4
Gaunt et al [21]	1	1	0	0	0	0	0	1	0	3
Jevsnik et al [22]	1	1	1	0	0	0	0	1	0	4
De Conto et al [20]	1	1	1	0	0	0	0	1	0	4
Asia										
Ren et al [13]	1	1	1	0	0	0	0	0	0	3
Xin et al [15]	1	1	1	0	0	0	0	0	0	3
Feng et al [9]	1	1	1	0	0	0	0	0	0	3
Zeng et al [17]	1	1	1	0	0	0	0	0	0	3
Zhang et al [18]	1	1	1	0	0	0	0	0	0	3
Zhao et al [19]	1	1	1	0	0	0	0	0	0	3
Chiu et al [8]	1	1	1	0	0	0	0	0	0	3
Yip et al [16]	1	1	1	0	0	0	0	0	0	3
Matoba et al [12]	1	1	1	0	0	0	0	0	0	3
Al-Khannaq et al [6]	1	1	1	0	0	0	0	0	0	3
Toh et al [14]	1	1	1	0	0	0	0	0	0	3
Al-Romaihi et al [7]	1	1	1	0	0	0	0	0	0	3
Kim et al [10]	1	1	1	0	0	0	0	0	0	3
Ko et al [11]	1	1	1	0	0	0	0	0	0	3

External validity: ex1 - study’s target population was similar to the national population, ex2 - study’s sampling frame was similar to the target population, ex3 - study used random selection to collect participants, and ex4 - study minimized non-response bias by obtaining response rate ≥75%; internal validity: in1 - study directly collected data from individual participants or specimens, in2 - study used an acceptable case definition, in3 - diagnostic tool had validity and reliability, in4 - study used the same mode of data collection for all participants, and in5 - study reported numerators and denominators of the variables of interest.