Journal of Digital Convergence
Vol. 18. No. 12, pp. 425-434, 2020

ISSN 2713-6434 / eISSN 2713-6442
https://doi.org/10.14400/JDC.2020.18.12.425

Molecular epidemiologic trends of norovirus and rotavirus infection and relation with climate factors: Cheonan, Korea, 2010-2019

Eun Ju Oh[1], Jang Mook Kim[2], and Jae Kyung Kim[3*]
[1]Ph. D., Student, Department of Medical Laser Cooperative Curriculum, Dankook University Graduate School of Medicine, Chungnam, Republic of Korea
[2]Professor, Department of Health Administration, Dankook University College of Health Sciences, Chungnam, Republic of Korea
[3]Professor, Department of Biomedical Laboratory Science, Dankook University College of Health Sciences, Chungnam, Republic of Korea

노로바이러스 및 로타바이러스 감염의 역학 및 기후요인과의 관계: 천안시, 2010-2019

오은주[1], 김장묵[2], 김재경[3*]
[1]단국대학교 의과대학 의학레이저협동과정 대학원 박사과정 학생
[2]단국대학교 보건복지대학 보건행정학과 교수, [3]단국대학교 보건복지대학 임상병리학과 교수

Abstract Background: Viral infection outbreaks are emerging public health concerns. They often exhibit seasonal patterns that could be predicted by the application of big data and bioinformatic analyses. Purpose: The purpose of this study was to identify trends in diarrhea-causing viruses such as rotavirus (Gr.A), norovirus G-I, and norovirus G-II in Cheonan, Korea. The identified related factors of diarrhea-causing viruses may be used to predict their trend and prevent their infections. Method: A retrospective analysis of 4,009 fecal samples from June 2010 to December 2019 was carried out at Dankook University Hospital in Cheonan. Reverse transcription-PCR (RT-PCR) was employed to identify virus strains. Information about seasonal patterns of infection was extracted and compared with local weather data. Results: Out of the 4,009 fecal samples tested using multiplex RT-PCR (mRT-PCR), 985 were positive for infection with Gr.A, G-I, and G-II. Out of these 985 cases, 95.3% (n = 939) were under 10 years of age. Gr.A, G-I, and G-II showed high infection rates in patients under 10 years of age. Student's t-test showed a significant correlation between the detection rate of Gr.A and the relative humidity. The detection rate of G-II significantly correlated with wind-chill temperature. Conclusion: Climate factors differentially modulate rotavirus and norovirus infection patterns. These observations provide novel insights into the seasonal impact on the pathogenesis of Gr.A, G-I, and G-II.

Key Words : diarrhea-causing virus, climate, rotavirus, norovirus G-I, norovirus G-II infection, temperature

요 약 바이러스감염으로 인한 설사는 전 세계적으로 공중 보건의 주요 문제이며 사망률의 큰 부분을 차지하고 있지만 기후데이터를 이용하여 분석한 연구는 많지 않다. 따라서 본 연구는 설사를 유발하는 바이러스인 Rotavirus Gr.A, Norovirus G-I & GII의 감염과 기후와의 인과관계를 분석하여 조기진단과 치료를 용이하게 하고 계절성 질환을 더욱 관리하고 예방하는데 기여하고자 하였다. 2010년 6월부터 2019년 12월까지 단국대학교 병원에서 시행한 대변 시료 4,009개의 설사바이러스 6종의 멀티플렉스 역전사 PCR(mRT-PCR)검사결과와 다양한 기후 요인 중 체감온도, 상대습도, 일조율과의 상관관계를 후향적으로 분석하였다. 4,009 개의 대변 샘플 중 985 개는 Rotavirus Gr.A, Norovirus G-I & GII 감염에 대해 양성이었다. 이 985 건 중 95.3 % (n = 939)는 10 세 미만으로 Rotavirus Gr.A, Norovirus G-I & GII는 10 세 미만 환자에서 높은 감염률을 보였다. 우리는 기상 빅데이터와 연령, 시기별 감염분석 등에 기초하여 Rotavirus Gr.A의 감염이 상대 습도에 따라 유의한 상관 관계가 있음을 확인하였고 Norovirus G-II의 감염은 체감 온도와 유의한 상관 관계가 있음을 확인하였다. 본 연구는 기후요인에 따른 Rotavirus Gr.A, Norovirus G-I & GII 감염의 분포에 대한 이해도를 향상시킴으로써 바이러스성 설사질환과 관련된 보건정책의 설정이나 계절적 영향에 대한 새로운 통찰력을 제공하는데 유용한 자료가 될 것으로 기대한다.

주제어 : 설사바이러스, 기후, 로타바이러스, 노로바이러스, 온도

*Acknowledgments-This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (NRF-2019R1I1A3A01059633).
*Corresponding Author : Jae Kyung Kim(nerowolf2@dankook.ac.kr)
Received October 25, 2020　　Revised November 19, 2020
Accepted December 20, 2020　　Published December 28, 2020

1. Introduction

Acute gastritis is the most common type of infection that affects both children and adults[1]. It exhibits various clinical symptoms such as vomiting, diarrhea, fever, and decreased diet, and some may require hospitalization[6]. The number of deaths from diarrhea viral gastroenteritis is steadily decreasing in developed countries due to improvements in hygiene standards and lifestyles worldwide, but the incidence and mortality rates in developing countries are still high[7]. Diarrhea caused by gastrointestinal infection accounts for a large proportion of mortality worldwide [5] and is a major public health problem [4]. In children under 5 years of age, severe diarrhea requires hospitalization, resulting in loss of productivity and economic loss due to hospitalization and outpatient visits for treatment [3, 8].

Pathogens that cause viral gastroenteritis with diarrhea include astrovirus (AstV), enteric adenovirus (EAdV), group A rotavirus (RotV [Gr.A]), and norovirus (NoV) [6, 7, 10]. Although there are differences that occur over time, group A rotavirus (RotV [Gr.A]) and norovirus (NoV) account for most of the occurrences [6]. Rotavirus (RotV) is the most common and major pathogen worldwide that causes severe diarrhea in infants under 5 years of age [8]. Rotavirus belongs to the *Reoviridae* and is classified into 10 groups of A-J, depending on the antigen that makes up the surface. It is also an important cause of diarrhea in the elderly [11]. Norovirus belongs to the family *Caliciviridae* [12] and include six gene groups GI-GVI based on the partial sequence of genomic RNA [9]. The genogroup of norovirus that causes human infection has three types (GI, GII, GIV), and GII accounts for a large proportion of infection by noroviruses. GII is highly likely to mutate, resulting in major genotype changes every 23 years, which is known to be associated with the epidemic [6]. Among norovirus GIIs, genotype GII.4 is the most common genotype of norovirus enteritis [6]. Currently, norovirus disease is a major cause of acute gastritis across all age groups[12, 13] and the elderly aged 65 years or older have the highest risk of norovirus-related death, while children under 5 had the highest risk of norovirus-related medical visits [12]. Except for RotV, there is no vaccine for diarrhea-causing viruses (DV), and the prevention of infection is challenging [10].

High effects of rotavirus vaccines against rotavirus infection (vaccine efficacy, 8598%) were identified in the United States, Latin America, and European countries. The rotavirus vaccine has reduced hospitalization rates and severe infections caused by rotavirus [14]. However, basic research on vaccines for other DV are needed and the scale of vaccination needs to be expanded. Since efforts for generating vaccines are ongoing and a vaccine is still underway, the current best clinical practice to avoid disease outbreak is early and accurate monitoring of infection.

The incidence of gastrointestinal infection is seasonal, and is associated with environmental variables, especially temperature and humidity[5]. For example, humidity in the surrounding environment can affect the survival of the virus, influencing its infection propagation [15-18]. Although it is not entirely clear how environmental factors correlate with DV, preventive medical studies are currently being conducted in many countries to determine the prevalence of diarrhea-causing viruses and their relationship to climatic factors.

Laboratory monitoring of gastroenteritis accompanied by diarrhea has been conducted in preference to other diseases, and is now in place in many countries [4, 5, 19]. Although there have been many investigations into the molecular mechanics of climate factors and diarrhea-causing viruses, they have been limited to short-term studies. We examined the relationship between molecular biological mechanics and climatic factors in RotV, Nor-GI, and Nor-GII over a longer period of time from June 2010 to December 2019. The purpose of this study was to identify trends in diarrhea-causing viruses such as rotavirus (Gr.A), norovirus G-I, and norovirus G-II in Cheonan, Korea. The identified related factors of diarrhea-causing viruses may be used to predict their trend and prevent their infections.

2. Materials and methods

This was a retrospective study in which 4,009 stool specimens from June 2010 to December 2019, were tested in the Department of Laboratory Medicine, Dankook University Hospital, Cheonan, using multiplex reverse transcription PCR (mRT-PCR) targeting three species of diarrhea viruses (rotavirus [Gr.A], norovirus G-I, norovirus G-II). The samples were subjected to nucleic acid extraction within 24 h. The nomenclature and taxonomy of these viruses were selected according to the criteria of the International Committee on Taxonomy of Viruses. Data on the age and sex of the study participants were retrieved from patient records. We were unable to collect information on the incubation period of the viruses because of the retrospective nature of the study and because the time of hospital visit after the onset of the disease was different for each patient. This study was approved by the Institutional Review Board of Dankook University, Republic of Korea (approval number 2019-12-007). This study was conducted in accordance with the Declaration of Helsinki.

2.1 Real-time multiplex reverse transcription -PCR (mRT-PCR) analysis

Stool specimens were diluted with 1 mL of distilled water, and 200 μl of the diluted solution was extracted using a Minelute RNA Spin Kit (Qiagen, Germany). The extracted nucleic acid was used to synthesize cDNA with RevertAid First Strand cDNA Synthesis Kit (Fermentas, Canada) according to the manufacturer's protocol. cDNA was used for mRT-PCR. The mRT-PCR for the three viruses was performed using the Seeplex Diarrhea-V ACE detection kit (Seegene, Korea) according to the manufacturer's instructions with a PTC-200 PCR system (MJ Research USA). The following target genes for DV were used: VP4 for rotavirus (Gr.A); ORF2 for norovirus-GI/GII. The internal mRT-PCR control was the Cesa3 gene of *Arabidopsi thaliana.* Distilled water was used as negative control. mRT-PCR for the three viruses was performed using Seeplex A Diarrhea-V ACE detection kit with dual specificity oligonucleotides (Seegene) and the three pathogens were detected in a single test tube.

The mRT-PCR products were electrophoresed on a 2% agarose gel with ethidium bromide for 30 min at 100-150 V. The agarose gel was rinsed with distilled water, amplification was assessed by visualizing the gel on a UV trans-illuminator, and the results were analyzed after an image was acquired. Table 1.

Table 1. Target genes for diarrhea-causing viruses.

Target viruses	Target region	Gene size (bp)
Arabidopsis (Internal control)	Cesa3	1,000
Group A Rotavirus (Gr.A)	VP4	541
Norovirus G-I (G-I)	ORF2	304
Norovirus G-II (G-II)	ORF2	214

2.2 Climatic variables

Meteorological data of the Cheonan region were collected from June 1, 2010 to December 31, 2019, and those from the National Institute of Environmental Research (including the ASOS data for the Cheonan region) were also collected for the same period. The National Institute of Environmental Research, a research institute under the Ministry of Environment in South Korea, oversees domestic environment-related research and education. The Cheonan region of Chungcheongnam-do, Korea has an area of 636.3 km^2 and a typical temperate climate due to its location at 36.47N and 127.13E. The variables examined in the study were the month, date, year, daily temperature, wind-chill temperature, average monthly temperature, relative humidity, precipitation, atmospheric pressure, age, and sex of the patients. The ASOS is a manual weather-measurement system used by the Korean Meteorological Agency, which is dedicated to observing weather factors; therefore, weather information obtained from the ASOS is recognized by the Korean Meteorological Agency. The Wind-chill temperature was calculated using the following formula provided by the Korean Meteorological administration:

Wind-chill temperature = 13.12 + 0.6215 T − 11.37V0.16 + 0.3965V0.16 T,

where T is the air temperature (C) and V is the wind speed (km/h), measured 10 m above the ground.

2.3 Statistical analysis

SAS software, version 9.4 (SAS Institute Inc., Cary, NC, USA) was used to perform descriptive statistical analysis, frequency analysis, Student's t-test, and binomial logistic-regression analysis to investigate the relationship of meteorological data and particulate matter concentrations with Gr.A, G-I, and G-II infection rates. Continuous data were presented as the mean, whereas categorical data were presented as the frequency, percentage, and interquartile range (IQR), where appropriate. For all analyses, a two-tailed p-value <0.05 indicated a statistically significant difference.

3. Results

3.1 Overall statistics

In this study, the fecal samples of 4,009 patients who visited Dankook University Hospital for diarrhea between June 2010 and December 2019 were tested. Of the total 4,009 patients, 2,294 were men (57.22%) and 1,715 were women (42.78%). Of the 4,009 samples taken during the study, 985 (24.57%) tested positive for Gr.A, G-I, and G-II. The detection rates for Gr.A, G-I, and G-II were 24.0% (n = 551/2,294) for males and 37.7% (n = 434/1,715) for females. The detection rate of Gr.A was 10.0% (n = 229/2,294) for males and 11.1% (n = 190/1,715) for females. The detection rate of G-I was 0.5% (n = 11/2,294) for males and 0.3%(n = 5/1,715) for females. The detection rate of G-II was 13.6% (n = 311/2,294) for males and 13.9% (n=229/1,715) for females (Table 2). G-II was the most frequently detected virus with 27.49% (n = 550/4,009) followed by Gr.A with 21.06% (n = 419/4,009).

3.2 Statistics by age

Gr.A had the highest detection rate of 97.6% (n = 409/419) in patients under the age of ten, and the second-highest detection rate of 1.4% (n = 6/419) in patients between ages 10-20 (Table 2). G-I had the highest detection rate of 87.5% (n = 14/16) in patients under the age of ten, and the second-highest detection rate was 12.5% (n = 2/16) for patients between 10 − 20 years of age (Table 2). G-II had the highest detection rate of 93.8% (n = 516/550) in patients under ten years of age, and the second-highest detection rate was 4.2% (n = 23/550) in patients between 10 − 20 years of age (Table 2). Distinct infection patterns were observed in different age groups.

3.3 Statistics by year

During the study period (2010-2019), the overall detection rate of Gr.A, G-I, and G-II was the lowest at 12.82% (n = 66/515) in 2019 and the highest at 35.1% (n = 126/359) in 2011. Gr.A had detection rates of 8.9%, 7.1% and 9.4% in 2011,

Table 2. Age/Sex demographics of the patient

	Rotavirus (Gr.A)		Norovirus G-I		Norovirus G-II	
Age	N	%	N	%	N	%
<10	409	97.6	14	87.5	516	93.8
10~19	6	1.4	2	12.5	23	4.2
20~29	1	0.2	0	0	1	0.2
30~39	0	0	0	0	2	0.4
40~49	1	0.2	0	0	2	0.4
50~59	0	0	0	0	1	0.2
60~69	1	0.2	0	0	3	0.5
70~80	1	0.2	0	0	1	0.2
80~89	0	0	0	0	1	0.2
90~	0	0	0	0	0	0
Sex						
Male	229	54.7	5	68.8	239	56.5
Female	190	45.3	11	31.2	311	43.5

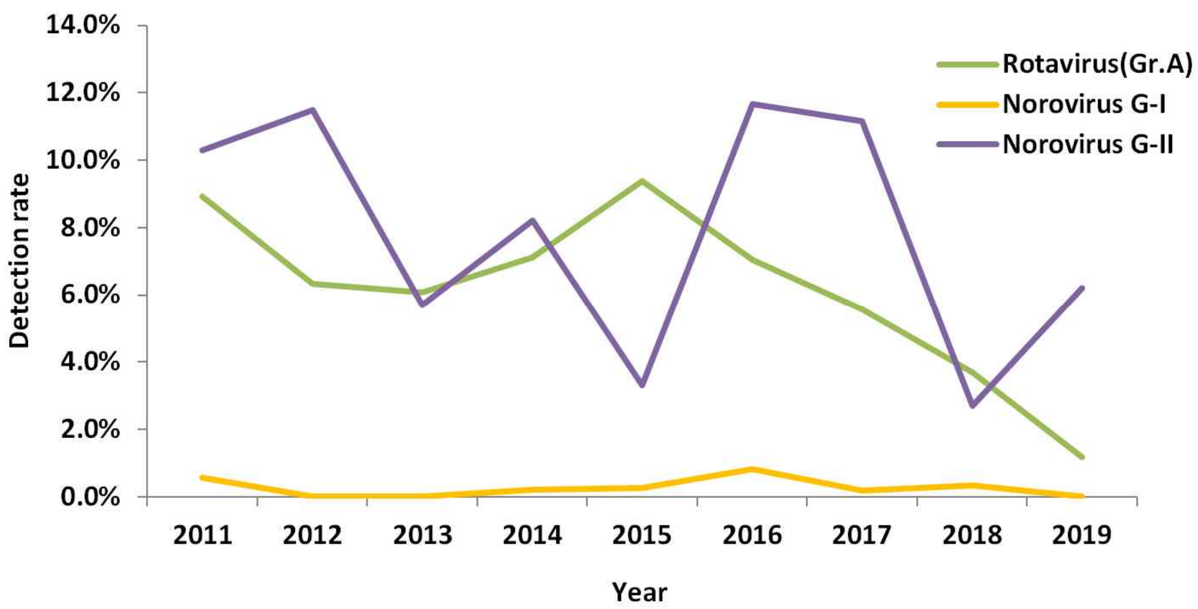

Fig. 1. The Detection rate of rotavirus (Gr.A) and noroviruses G-I and G-II at Dankook University Hospital, Cheonan, Korea, 2010-2019, aggregated by year.

2014 and 2015 respectively. G-II had detection rates of 11.5%, 11.7% and 11.1% in 2012, 2016, and 2017 respectively. G-I had detection rates of 0.7%, 0.6% and 0.8% in 2010, 2011, and 2016 respectively (Fig. 1). Infections exhibited seasonal variations, with peaks in winter.

3.4 Statistics by month

The detection rate of Gr.A was the highest at 23.4% (n = 75/320) in March and the lowest at 2.7% (n = 8/297) in September. G-I had the highest detection rate of 0.9% (n = 3/316) in February and the lowest at 0.0% (n = 0/405, 0/316, 0/370) in May-July. G-II had the highest detection rate of 28.2% (n = 115/408) in December, the lowest detection rate of 4.1% (n = 13/316) in June and 4.1% (n = 11/267) in October (Fig. 2).

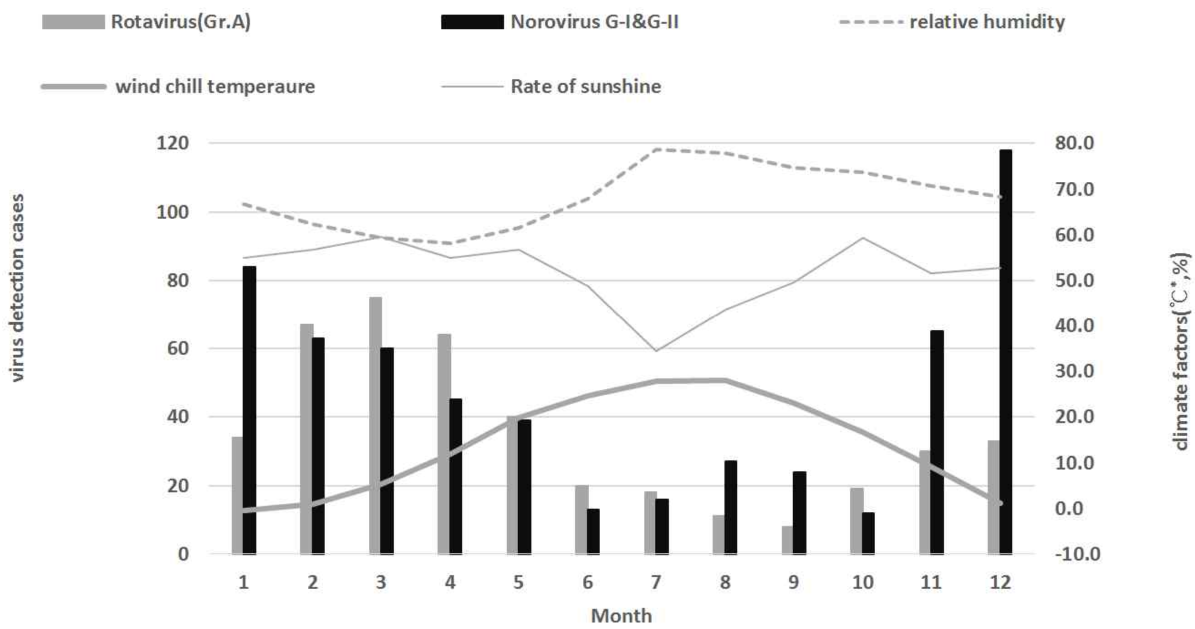

Fig. 2. Correlation between climatic factors and rotavirus (Gr.A) and norovirus G-I and G-II detection cases in 2010-2019, aggregated by month. * wind-chill temperature

Table 3. Comparison of monthly mean meteorological factors and viral diarrhea infection

Pathogen	Meteorological factors	95% CI		P-value
		Lower	Upper	
Rotavirus (Gr.A)	Wind chill Temperature (℃)	-0.156	-0.03	0.004**
	Relative Humidity (%)	-0.27	-0.08	<0.001***
	Rate of sunshine	-0.077	0.063	0.85
Norovirus G-I	Wind chill Temperature (℃)	-0.015	0.001	0.044*
	Relative Humidity (%)	-0.014	0.009	0.645
	Rate of sunshine	-0.009	0.008	0.867
Norovirus G-II	Wind chill Temperature (℃)	-0.32	-0.147	<0.001***
	Relative Humidity (%)	-0.247	0.015	0.083
	Rate of sunshine	-0.128	0.066	0.524

*p<0.05, **p <0.01, ***p<0.001

3.5 Analysis by climatic factors

During the study, the detection rate of Gr.A was the highest at a wind chill temperature of 5.3℃ and relative humidity of 59.3% and the detection rate was the lowest at a wind -chill temperature of 23.0℃ and relative humidity of 74.6% (Fig. 2).

The detection rates of G-I and G-II were the highest at a wind chill temperature of 1.1℃ and relative humidity of 68.3%, and the lowest at a chill temperature of 16.6℃ and relative humidity of 73.6%. In addition, Gr.A, G-I, and G-II infections showed increased detection rates in winter and spring (Fig. 2). Student's t-test analysis showed that the detection rate of Gr.A and relative humidity ($p<0.001$) were significantly correlated (Table 3). The detection rate of G-II was significantly correlated with the wind-chill temperature ($p < 0.001$) (Table 3). However, there was no significant correlation between the detection rate of norovirus G-I and relative humidity, atmospheric pressure, rate of sunshine or wind-chill temperature (Table 3). High infection rates were associated with lower temperatures.

4. Discussion

In this study, the detection rates of Gr.A, G-I, G-II were not gender-specific, but were highest in population under the age of 10. Out of the three viruses, Gr.A, G-I, and G-II, the highest detection rate was observed with of G-II, followed by Gr.A and G-I, which was the same as other studies that analyzed norovirus detection rates in temperate climates [9].

Gr.A had the highest detection rate in 2015, but tended to decline over the years, whereas G-I and G-II had the highest detection rate in 2016 and did not show a trend of decline that was different from that of Gr.A. The results show that since the introduction of the rotavirus vaccine in 2007, the rate of rotavirus infection decreased drastically after 2010.

Gr.A was found to develop in winter and spring, from January to April, especially in March, in a large number of cases. Some studies have shown that Gr.A infection occurred in spring, fall, and winter but did not occur in summer [20]; however, the prevalence of rotavirus-related gastritis typically occurs in winter and early spring in temperate climate countries, consistent with previous studies that showed occurrence in January and March, including a Japanese study that the main period of rotavirus as February and March [2, 6,7, 21]. Although the detection rate of G-I in seasonal distributions remained unchanged and there was no significant change in annual trends, G-II was detected from November to April, showing a trend that was prevalent from winter to early spring. Overall, G-I and G-II were observed to be common in winter. Norovirus-related diseases occur throughout the year, but the norovirus activity, which is the main cause of acute diarrhea, generally occurs from January to March, with the most common winter [12, 19] followed by fall, spring, and continuous high levels of norovirus detection until early summer in June [2, 22]. However, a German study found that norovirus outbreaks occurred from November to October of the year. Similar to studies that have shown that norovirus outbreaks are high in winter and spring in temperate regions and peak year-round in December [13, 20, 23, 24], our results showed a rise from November and marked a significant high in December. In the Northern Hemisphere, norovirus is generally shown to be active in cold winter months [12]; however, in Korea, it occurs almost continuously in spring or summer (March or June) as well as in winter [24]. The detection rates of Gr.A, G-I, and G-II during the study period particularly correlated with temperature changes. The detection rates of the viruses were high even at low relative humidity, and relative humidity was shown to have a negative effect on the detection rates of Gr.A. Sensory temperature was shown to have a negative effect on the detection rate of norovirus G-II. Korea is geographically located in the temperate climate zone of the mid-latitude and has four distinct seasons. Under this climate, past rate of norovirus food poisoning has been nearly half as high in winter as in summer. [24, 25]. This may reflect the important effect of temperature and humidity on the activity of the virus.

Several climate factors, including temperature, humidity and rainfall are related to the occurrence of rotavirus and norovirus. Rotavirus infections are more common in cold and dry seasons, and precipitation can increase norovirus transmission, indicating an influence of temperature and relative humidity on these two viruses [4]. In Europe, gastritis due to rotavirus reaches its peak in late winter [4]. Norovirus activity is generally negatively correlated with the mean temperature [19, 26]. Noroviruses last longer at a temperature range of 15-20℃ than at other temperatures [9] and humidity is also an important environmental factor that affects the survival and transmission of norovirus. The correlation between humidity and norovirus occurrence was statistically confirmed, and most previous studies concluded that low relative humidity is associated with norovirus epidemics [9]. The results of the Korea Centers for Disease Control and Prevention report correlate the detection rate of the causative pathogens causing acute diarrhea with climate change, traffic, overseas travel, and dining out indicating that the pattern of acute diarrhea tends to occur throughout the year, especially as the living environment improves due to the improvement of the standard of living, including the increased use of air conditioners and boilers etc. [24, 25]. The cold and relatively dry conditions of our country in winter may help the activity and spread of norovirus [24].

Studies show that among the pathogens that cause acute diarrhea, viral pathogens are detected intensively in the cold and humid winter months, with some changes in the general pattern [22]. Viral pathogens infections have shown a strong negative correlation between higher temperatures and higher relative humidity, but just before 2017 the general infection pattern of viral pathogens during the cold and humid winter season became weaker [22]. Data from California in the United States reported an association of noroviruses with high humidity environments, and in Germany, noroviruses are constantly detected throughout the year [2, 9]. In Africa, although a high prevalence rate is observed at certain times of the year, rotavirus infections are detected throughout the year.

In general, cool and dry weather conditions lead to a high incidence of rotavirus, while the association between temperature and norovirus infection has not been concluded [28]. At low temperatures, the pathogen is more stable and persists longer on hands, feces, and contaminated objects, promoting transmission. In addition, people living in subtropical or tropical regions are more sensitive to cold weather. During this period, people tend to stay close to each other and spend more time indoors. Therefore, vulnerable people are more likely to interact with infected people and contaminated surfaces, air, food, and water [28].

This study has some limitations. First, conducting surveys for ten years in a single city can be considered relatively short term. Therefore, our results may be biased in terms infections. Based on changes in seasons, sex, and age, we were able to identify differences in positive rates in Gr.A, G−I, and G−II infections. In addition, the rate of rotavirus infection has declined since 2010 in Korea since the introduction of the rotavirus vaccine in 2007; however, unlike that of rotavirus, the rate of infection with norovirus without vaccine has relatively increased [6, 21] of viral dynamics. Second, because sample data were treated anonymously and the patients' residences were not specified, some of the tested samples may have been provided by patients who did not reside in the study area. Thus, due to differences in geographical location among patients, there may be differences in seasonal distributions of Gr.A, G−I, and G−II observed in this study. Although most previous studies have shown that virus outbreaks are related to low temperatures and low humidity, these findings may not apply to all countries and regions [9]. It is important to identify the regional impact of environmental factors on viral epidemics due to regional and climatic differences, and to investigate these variables in a wide range of climatic conditions, including long−term bacterial and viral pathogen detection and changes in correlation with climatic factors [9, 22]. Finally, the results reflect a trend established after the introduction of the rotavirus vaccine in Korea in 2007 [21]; however, rotavirus vaccination status was not verified in the 4,009 patients with rotavirus that were included in the study.

Despite these limitations, our research provides some insights into changes in positive rates of Gr.A, G-I, and G-II

Therefore, our results will be very important for assessing and formalizing the potential effects of vaccines as progress continues in the field of norovirus vaccine development [12], and we expect our findings to help with effective prevention strategies against acute diarrhea viral infection, including vaccine development. Since the occurrence of acute diarrhea is expected to increase in the future due to social and environmental changes such as climate change, it is necessary to focus more on the accumulation of long-term analysis data on viral pathogen detection and changes in correlation with climatic factors. Studies on viral infection prevention and management measures to cope with climate and environmental changes [2, 22] in different geographical regions, such as climate factors, age, and gender, and other variables are needed [5].

REFERENCES

[1] Y. Kang, S. Park, H. Koh & S. Kim. (2018). Correlation between the occurrence of acute gastroenteritis in children and regional temperature at a tertiary hospital emergency department in Korea. *Pediatric Emergency Medicine Journal, 5*(*1*), 19-24. DOI: 10.22470/pemj.2018.00192

[2] J. I. Song, M. J. Park, Y. M. Lee, C. D. Kim, H. K. Lee, S. S. Kim & J. H. Lee. (2017). Comparison of clinical features between noroviral and rotaviral gastroenteritis, *Soonchunhyang Medical Science*, *23*(*1*), 29-33. DOI: 10.15746/sms.17.006

[3] J. O. Park, J. S. Jeon, & J. K. Kim. (2019). Epidemiologic Trends of Diarrhea-causing Virus Infection Analyzed by Multiplex Reverse Transcription PCR in Cheonan, Korea, 2010-2018, *Microbiology and Biotechnology Letters, 47(2)*, 317-322.

[4] N. Ouedraogo, S. M. Ngangas, I. J. Bonkoungou, A. B. Tiendrebeogo, K. A. Traore, I. Sanou, A. S. Traore & N. Barro. (2017). Temporal distribution of gastroenteritis viruses in Ouagadougou, Burkina Faso: seasonality of rotavirus. *BMC Public Health*, *17*, 274. DOI: 10.1186/s12889-017-4161-7

[5] M. Ghazani, G. FitzGerald, W. Hu, G. Toloo and Z. Xu. (2018). Temperature Variability and Gastrointestinal Infections: A Review of Impacts and Future Perspectives. *International Journal of Environmental Research and Public Health*. 15(4),766. DOI: 10.3390/ijerph15040766

[6] Y. S. Kim & J. Y. Chung. (2020). Molecular detection and epidemiology of etiologic agents among children with acute gastroenteritis at a secondary hospital from 2015 to 2018, *Pediatric Infection Vaccine*. *7*(*2*):e13. DOI: 10.14776/piv.2020.27.e13

[7] J. K. Kim & J. W. Kim. (2014). Molecular epidemiologic trends of diarrhea-causing virus infection from clinical specimens in Cheonan, Korea, in 20102012, *Journal of Clinical Laboratory Analysis* 28, 47-51.

[8] S. H. Lee & S. J. Yang (2017). Factors associated with rotavirus vaccination behavior among mothers of infants: using the Health Belief Model, *Journal of Korean Public Health Nursing*, 31(1), 34-46.

[9] S. S. Chenar & Z. Deng. (2017). Environmental indicators for human norovirus Outbreaks, *International Journal of Environmental Health Research*, *27* (*1*), 40-51. DOI: 10.1080/09603123.2016.1257705

[10] J. O. Park, J. S. Jeon & J. K. Kim. (2019). Epidemiologic Trends of diarrhea-causing virus infection analyzed by multiplex reverse transcription PCR in Cheonan, Korea, 2010-2018, *Microbiology Biotechnology Letters*, *47*(*2*), 317-322. DOI: 10.4014/mbl.1811.11007

[11] GBD 2016 Diarrhoeal disease collaborators. (2017). Estimates of global, regional, and national morbidity, mortality, and aetiologies of diarrhoeal diseases: a systematic analysis for the Global Burden of Disease Study 2015, *Lancet Infectious Diseases*, *17*, 909-948. DOI: 10.1016/S1473-3099(17)30276-1.

[12] A. J. Hall, B. A. Lopman, D. C. Payne, M. M. Patel, P. A. Gastaaduy, J. Vinj & U. S. Parashar. (2013). Norovirus disease in the United States, *Emerging Infectious Diseases 19* (*8*), 1198-2105. DOI: 10.3201/eid1908.130465

[13] K. M. Guarines, R. P. G Mendes, J. J. F. de Magalhes, L. Pena. (2019). Norovirus-associated gastroenteritis, Pernambuco, Northeast Brazil, 2014-2017, *Journal of Medical Virology*, *92*(8), 1093-1101. DOI: 10.1002/jmv.25631

[14] J. M. Yoon, T. H. Han, S. W. Yoon, Y. J. Kim & S. H. Oh. (2018). Changes in the occurrence of rotavirus gastroenteritis before and after the introduction of rotavirus vaccine among hospitalized pediatric patients and estimates of rotavirus vaccine effectiveness, *Pediatric Infection Vaccine*, *25*, 26-34. DOI:10.14776/piv.2018.25.1.26

[15] Y. G. Karim, M. K. Ijaz, S. A. Sattar, C. M. Johnson-Lussenburg. (1985). Effect of relative humidity on the airborne survival of rhinovirus-14, *Canadian Journal of Microbiology, 31*, 1058-1061. DOI: 10.1139/m85-199

[16] W. S. Miller & M. S. Artenstein. (1967). Aerosol stability of three acute respiratory disease viruses. *Proceedings of the Society for Experimental Biology and Medicine,125*, 222-227.
DOI: 10.3181/00379727-125-32054.

[17] C. B. Hall. (2007). The spread of influenza and other respiratory viruses: complexities and conjectures. *Clinical Infectious Diseases 45*, 353-359.
DOI: 10.1086/519433

[18] S. K. Kim, H. Sung, & M. N. Kim. (2018). Kinetic studies and infection control of respiratory viruses, Korean *Journal of Healthcare-Associated Infection Control and Prevention, 23*(*1*):17.
DOI: 10.14192/kjhaicp.2018.23.1.1

[19] C. S. Yen, Y. C. Huang, C. J. Chen, S. S. Shie, S. L. Yang, C. G. Huang, K. C. Tsao, C. H. Chiu, Y. C. Hsieh, C. Y. Kuo, K. Y. Huang, & T. Y. Lin. (2020). Detection of norovirus and rotavirus among inpatients with acute gastroenteritis in a medical center in northern Taiwan, 2013-2018, *Journal of Microbiology, Immunology and Infection, S1684-1182*(*20*), 301-572.
DOI: 10.1016/j.jmii.2020.06.016

[20] K. Lee, D. S. Kim, & M. S. Chong. (2018). Multiplex PCR based epidemiological study for the causes of acute diarrheal disease in adults living in Jeju island, *Annals of Clinical Microbiology, 21*(*1*).
DOI: 10.5145/ACM.2018.21.1.1

[21] M. R. Choi & Y. S. Kwon. (2016). The comparison of benign convulsion with noroviral and rotaviral gastroenteritis, *Journal of the Korean Child Neurology Society 24*(*3*), 95-101.

[22] B. S. Goh, K. Y. Kim, S. W. Kim, & W. K. Lee. (2019). Correlation change between the detection rate of pathogens causing acute diarrheal disease and climatic elements in Daegu, *Journal of Health Information & Statistics 44*(*1*), 32-40.
DOI: 10.21032/jhis.2019.44.1.32

[23] K. Muhsen, E. Kassem, U. Rubenstein, S. Goren, M. Ephros, L. M. Shulman & D. Cohen. (2019). No evidence of an increase in the incidence of norovirus gastroenteritis hospitalizations in young children after the introduction of universal rotavirus immunization in Israel, *Human Vaccines & Immunotherapeutics, 15*(*6*), 1284-1293.
DOI: 10.1080/21645515.2019.1599522

[24] J. G. Kim & J. S. Kim. (2019). Characteristics of norovirus food poisoning outbreaks in Korea over the past ten years and the relation with climate factors, *Journal of Environment and Health Science. 45*(*6*), 622-629.
DOI: 10.5668/JEHS.2019.45.6.622

[25] Y. S. Kim, K. H. Park, H. S. Hyang, C. Changsun, & G. J. Bahk. (2014). Correlations between climatic conditions and foodborne disease, *Food Research International, 68*, 24-30.
DOI: 10.1016/j.foodres.2014.03.023

[26] I. Samandoulgou, R. Hammami, R. M. Rayas, I. Fliss, & J. Jean. (2015). Stability of secondary and tertiary structures of virus-like particles representing noroviruses: effects of pH, ionic strength, and temperature and implications for adhesion to surfaces. *Applied Environmental Microbiology. 81*, 7680-7686.
DOI: 10.1128/AEM.01278-15

[27] G. S. Seo & S. C. Choi. (2010). Diarrhea (Based on acute infectious diarrhea) *The Korean Journal of Medicine*: *78*, 49-53.

[28] P. Wang, B. W. Goggins, & Y. Y. Chan. (2018). A time-series study of the association of rainfall, relative humidity and ambient temperature with hospitalizations for rotavirus and norovirus infection among children in Hong Kong, *Science of the Total Environment 643*, 414-422.
DOI: 10.1016/j.scitotenv.2018.06.189.

오 은 주(Eun Ju Oh) [정회원]

· 2006년 2월 : 충남대학교, 보건학석사
· 2020년 3월 ~ 현재 : 단국대학교 의과대학 박사과정
· 관심분야 : 진단검사의학, 감염, 면역, 환경
· E-Mail : evejoh@naver.com

김 장 묵(Kim, Jang Mook) [정회원]

· 1996년 12월 : Cleveland State University, MBA
· 2011년 8월 : 연세대학교, 보건학 박사
· 2015년 9월 ~ 현재 : 단국대학교 보건행정학과 교수
· 관심분야 : 보건정책, 병원경영, 융합보건과학
· E-Mail : jangmook@dankook.ac.kr

김 재 경(Jae Kyung Kim) [정회원]

· 1993년 2월 : 단국대학교 대학원 석사
· 2008년 8월 : 단국대학교 대학원 박사
· 2015년 9월 ~ 현재 : 단국대학교 임상병리학과 교수
· 관심분야 : 진단검사의학, 감염, 면역, 환경
· E-Mail : nerowolf2@dankook.ac.kr