RESEARCH ARTICLE



Ambient air pollution, meteorology, and COVID-19 infection in Korea

¹Department of Cancer Biomedical Science, National Cancer Center Graduate School of Cancer Science and Policy, Goyang, Korea

²Institute of Research and Development, Duy Tan University, Danang, Vietnam

³Faculty of Pharmacy, Duy Tan University, Danang, Vietnam

⁴Department of Gastroenterology and Hepatology, Nghe An Oncology Hospital, Nghe An, Vietnam

Correspondence

Tho Thi Anh Tran, MD, MSc, Department of Gastroenterology and Hepatology, Nghe An Oncology Hospital, 460000 Nghe An, Vietnam. Email: trananhthohmu@gmail.com

Abstract

The outbreak of novel pneumonia coronavirus disease has become a public health concern worldwide. Here, for the first time, the association between Korean meteorological factors and air pollutants and the COVID-19 infection was investigated. Data of air pollutants, meteorological factors, and daily COVID-19 confirmed cases of seven metropolitan cities and nine provinces were obtained from 3 February 2020 to 5 May 2020 during the first wave of pandemic across Korea. We applied the generalized additive model to investigate the temporal relationship. There was a significantly nonlinear association between daily temperature and COVID-19 confirmed cases. Each 1°C increase in temperature was associated with 9% (lag 0-14; OR = 1.09; 95% CI = 1.03-1.15) increase of COVID-19 confirmed cases when the temperature was below 8°C. A 0.01 ppm increase in NO₂ (lag 0-7, lag 0.14, and lag 0-21) was significantly associated with increases of COVID-19 confirmed cases, with ORs (95% CIs) of 1.13 (1.02-1.25), 1.19 (1.09-1.30), and 1.30 (1.19-1.41), respectively. A 0.1 ppm increase in CO (lag 0-21) was associated with the increase in COVID-19 confirmed cases (OR = 1.10, 95% CI = 1.04-1.16). There was a positive association between per 0.001 ppm of SO₂ concentration (lag 0, lag 0-7, and lag 0-14) and COVID-19 confirmed cases, with ORs (95% CIs) of 1.13 (1.04-1.22), 1.20 (1.11-1.31), and 1.15 (1.07-1.25), respectively. There were significantly temporal associations between temperature, NO2, CO, and SO2 concentrations and daily COVID-19 confirmed cases in Korea.

KEYWORDS

air pollution, COVID-19, generalized additive model, Korea

1 | INTRODUCTION

The novel respiratory coronavirus disease was first reported in Wuhan city in the late of 2019 and rapidly spread to the rest of China within a short period by March 2020, the World Health Organization has officially declared the outbreak as a global pandemic as it has expanded globally. The number of infected cases accelerated worldwide at a rate not previously been seen in other respiratory pandemics. Though many intensive policies including case isolation, social distancing, widespread quarantine, and local/

national lockdowns have been applied in many countries to slow the spread of the virus, this infectious disease seems far from being under control.

It is essential to identify risk factors for a relatively high transmission rate of COVID-19. From the epidemiological triad perspective, the capacity of virus infection depends on whether the environment is an advantage for its survival and transmission, and it also depends on the host susceptibility.^{4,5} Air pollution with respect to meteorological factors may have effects on the trends of the respiratory viral outbreak by altering the immunity of the

host and the survival time of the virus.⁶ Consequently, ambient air pollution may play some roles in the propensity to COVID-19 infection. Recent emerging evidence has shown that long term exposure to ambient air pollution might increase COVID-19 mortality.⁷ In this study, we investigated the relationship between air pollutants, meteorological factors, and COVID-19 confirmed cases in Korea.

2 | MATERIALS AND METHODS

2.1 Data sources

2.1.1 | Setting

The study areas consist of seven metropolitan cities (Seoul, Incheon, Daejoen, Daegu, Gwangju, Ulsan, and Busan) and nine provinces (Gangwon, Gyeonggi, Chungbuk, Chungnam, Gyeongbuk, Gyeongnam, Jeollabuk, Jeollanam, and Jeju) in the geographic regions of 124.2° to 131.9° east longitude and 33.1° to 43.0° north latitude of South Korea. The shapefile map of Korea was obtained from the Korea Geographic Information System (GIS) Developer.⁸

2.1.2 | COVID-19 data

Confirmed new cases are daily reported by the Korea Centers for Disease Control and Prevention. Data at the city-province level have been available since 24 February 2020, which was after a few days from the confirmation of the "super case 31" on 18 February 2020. We select the cut-off date of 5 May 2020 because the social distancing rule of the country has been relaxed since May 06, 2020 with the re-opening of the business.

2.1.3 | Air pollution and meteorological data

Data on ambient air pollution and meteorology are provided by the Korea Environment Corporation 11 and Meteorological Agency. 12 We collected the daily measurement of particles with sizes $\leq 2.5~\mu m$ (PM $_{2.5}$), particles with sizes $\leq 10~\mu m$ (PM $_{10}$), ozone (O $_3$), nitrogen dioxide (NO $_2$), carbon monoxide (CO), and sulfur dioxide (SO $_2$) for each metropolitan city and province. It was reported that the highest mean of the incubation period was 7 days with the range up to 14 days in most of the cases 13,14 and even up to 21 days in some cases, 15 there might be a lagged association between the exposure and the outcome. In other words, previous days of air pollutant levels might have a greater influence on today's confirmed cases than today's air pollutant levels. Therefore, the data period for the ambient air pollution is selected from 3 February 2020 (as 21 days before the beginning date of confirmed new cases data) to 5 May 2020.

2.2 | Statistical analysis

2.2.1 | Descriptive analysis

Given the mean level of air pollutants and the total confirmed new cases for 17 cities and provinces, the Kriging predicting model which considers the autocorrelation was applied to produce the prediction of the surface. The general formula for the Kriging interpolation is as follows:

$$\hat{Z}(s_0) = \sum_{i=1}^{N} \lambda_i Z(s_i)$$

where $Z(s_i)$ is the established value at the i^{th} location, λ_i is the unknown weight for the measurement at the neighborhood data of the i^{th} location, and s_0 is the predicted location, and N is the number of measurements

2.2.2 | Temporal analysis

Meteorological factors and air pollutants in relation to confirmed new cases were examined by using a generalized additive model (GAM), which was known as the combination between linear and smooth functions with the fewest assumption. ^{17,18} The general formula for the GAM is as follows:

$$\ln (y_t) = \beta_0 + \beta_{1*} X_t + \sum_{k=1} \beta'_{k*} f(C_k) + \varepsilon_t, \varepsilon_t \sim N(0, \sigma^2)$$

where y_{it} indicates the total confirmed new cases (because the number of confirmed new cases can be -1 due to the change of the case from a city to another city, we added 2 to avoid the natural logarithm of 0), X_t indicates the mean level of the pollutant on day t, $f(C_k)$ represents the smooth function for meteorological factors including temperature, wind speed, humidity, and air pressure, and the linear function for the location and date.

Results were performed for the association between confirmed new cases on day 0 and meteorological factors and air pollutant levels on day 0 (lag 0), day –7 (lag 0-7), day –14 (lag 0-14), and day –21 (lag 0-21). Nonlinear associations between meteorological factors and confirmed new cases were firstly assessed in the GAM including temperature, wind speed, humidity, and air pressure, adjusting for location and date. Then the association between air pollutants was implemented in different models, including crude, partially adjusted (crude model + adjusted for location), mostly adjusted (partially adjusted model + adjusted for four meteorological factors), and fully adjusted (mostly adjusted model + adjusted for date).

All the statistical analyses were conducted in ArcGIS 10.4 software and using the "mgcv" package in R software (version 3.5.2). ¹⁹

 TABLE 1
 Summary statistics of confirmed new cases and air pollutants in Korea

	New cases	New cases PM _{2.5} , μg/m ³	PМ ₁₀ , µg/m ³	O ₃ , ppm	NO ₂ , ppm	CO, ppm	SO ₂ , ppm	Temperature, °C	Wind speed, m/s	Humidity (%)	Air pressure, hPa
Seoul	539	23.8 (10.8)	42.5 (14.5)	0.027 (0.010)	0.026 (0.011)	0.481 (0.123)	0.0031 (0.0006)	8.0 (5.7)	2.6 (0.8)	52.2 (14.1)	1008.6 (5.8)
Busan	113	17.6 (7.2)	33.9 (11.7)	0.036 (0.010)	0.016 (0.006)	0.377 (0.068)	0.377 (0.068) 0.0035 (0.0006)	10.6 (3.8)	3.5 (1.2)	56.6 (17.9)	1009.8 (5.5)
Daegu	9229	20.9 (8.5)	37.8 (13.0)	0.032 (0.010) 0.017 (0.008)		0.451 (0.127)	0.451 (0.127) 0.0028 (0.0007)	9.8 (5.0)	2.6 (1.1)	58.6 (16.8)	1012.1 (5.7)
Incheon	82	19.4 (9.2)	38.4 (12.9)	0.032 (0.010)	0.022 (0.011)	0.522 (0.115)	0.032 (0.010) 0.022 (0.011) 0.522 (0.115) 0.0039 (0.0007)	6.9 (4.8)	3.7 (1.4)	64.1 (13.7)	1012.9 (5.9)
Gwangju	20	17.9 (6.9)	34.0 (12.2)	0.035 (0.009)	0.015 (0.005)	0.432 (0.085)	0.035 (0.009) 0.015 (0.005) 0.432 (0.085) 0.0027 (0.0005)	9.3 (4.7)	1.6 (0.5)	59.7 (17.5)	1011.1 (5.5)
Daejeon	38	19.4 (7.4)	38.4 (12.8)	0.029 (0.010)	0.018 (0.007)		0.372 (0.098) 0.0024 (0.0005)	8.7 (5.3)	1.7 (0.6)	58.9 (14.9)	1011.2 (5.7)
Ulsan	40	17.3 (7.0)	33.8 (12.3)	0.036 (0.009)	0.018 (0.006)	0.485 (0.086)	0.485 (0.086) 0.0037 (0.0008)	10.0 (4.4)	2.3 (0.6)	58.6 (19.2)	1008.1 (5.6)
Sejong	45	22.2 (11.4)	44 (14.4)	0.032 (0.011)	0.019 (0.009)	0.448 (0.104)	0.448 (0.104) 0.0029 (0.0006)	8.0 (5.3)	1.6 (0.6)	55.3 (15.1)	1008.3 (5.7)
Gyeonggi	615	23.0 (9.6)	43.7 (14.3)	0.032 (0.009)	0.019 (0.008)	0.441 (0.089)	0.0031 (0.0005)	7.2 (5.5)	1.8 (0.8)	64.6 (13.7)	1012.0 (5.9)
Gangwon	44	22.0 (9.5)	38.3 (14.5)	0.035 (0.011)	0.013 (0.006)	0.457 (0.107)	0.457 (0.107) 0.0026 (0.0006)	6.8 (5.3)	2 (0.7)	58.9 (12.9)	992.4 (5.5)
Chungcheongbuk	40	24.3 (10.4)	42.0 (14.6)	0.033 (0.010)	0.015 (0.005)	0.441 (0.082)	0.441 (0.082) 0.0031 (0.0003)	7.2 (5.4)	1.9 (0.8)	58.1 (13.7)	998.5 (5.6)
Chungcheongnam	139	23.4 (10.3)	42.7 (14.3)	0.035 (0.008)	0.013 (0.004)	0.423 (0.068)	0.423 (0.068) 0.0032 (0.0004)	7.3 (5.0)	1.7 (0.8)	64.9 (12.6)	1013.0 (5.7)
Jeollabuk	13	18.2 (6.8)	35.6 (12.5)	0.038 (0.010)	0.013 (0.008)	0.426 (0.069)	0.038 (0.010) 0.013 (0.008) 0.426 (0.069) 0.0036 (0.0006)	8.3 (4.9)	2.4 (0.8)	59.9 (15.1)	1003.5 (5.7)
Jeollanam	14	16.4 (6.4)	31.7 (10.2)	0.037 (0.011)	0.012 (0.004)	0.405 (0.073)	0.037 (0.011) 0.012 (0.004) 0.405 (0.073) 0.0033 (0.0005)	9.5 (4.4)	1.9 (0.7)	59 (16.3)	1011.0 (5.5)
Gyeongsangbuk	1198	17.6 (8.9)	36.4 (14.4)	0.046 (0.008)	0.015 (0.005)	0.331 (0.092)	0.331 (0.092) 0.0012 (0.0004) 11.6 (3.5)	11.6 (3.5)	3.8 (1.4)	68 (13.6)	1014.6 (5.3)
Gyeongsangnam	105	23.8 (10.8)	42.5 (14.5)	0.027 (0.010)	0.026 (0.011)		0.481 (0.123) 0.0031 (0.0006)	8.0 (5.7)	2.6 (0.8)	52.2 (14.1)	1008.6 (5.8)
Jeju	6	17.6 (7.2)	33.9 (11.7)	0.036 (0.010)	0.016 (0.006)	0.377 (0.068)	0.377 (0.068) 0.0035 (0.0006)	10.6 (3.8)	3.5 (1.2)	56.6 (17.9)	1009.8 (5.5)
Korea	9610	20.1 (9.2)	37.9 (13.8)	0.034 (0.010)	0.016 (0.008)	0.431 (0.010)	0.431 (0.010) 0.0030 (0.0008)	8.6 (5.0)	2.4 (1.2)	60.6 (15.5)	1008.6 (8.0)
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Note: Data on air pollution and meteorology are presented as mean (standard deviation).

3 | RESULTS

3.1 | Descriptive analysis

Summary statistics for the total confirmed new cases, mean levels of air pollutants and meteorological factors are presented in Table 1. A total of 9610 cases were newly confirmed in Korea during 24 February 2020 and 5 May 2020, with the highest number of cases in Daegu (N=6556) and Gyeongsangbuk (N=1198) (Figures S1, S2). Daily levels of $PM_{2.5}$, PM_{10} , O_3 , NO_2 , CO, and SO_2 were $20.1\,\mu\text{g/m}^3$, $37.9\,\mu\text{g/m}^3$, $0.034\,\text{ppm}$, $0.016\,\text{ppm}$, $0.431\,\text{ppm}$, and $0.0030\,\text{ppm}$, respectively. Daily levels of temperature, wind speed, humidity, and air pressure were $8.6\,^{\circ}$ C, $2.4\,\text{m/s}$, 60.6%, and $1008.6\,\text{hPa}$, respectively.

The distribution of air pollutants across 16 metropolitan cities and provinces is shown in Figure 1 and is geographically predicted with Kriging interpolation in Figure 2. The concentrations of $PM_{2.5}$, PM_{10} , and NO_2 were generally higher in Seoul and Gyeonggi, whereas those of CO and SO_2 were mostly higher in Incheon and Ulsan than remaining areas. The concentration of O_3 was observed to be higher in Jeju than in other areas.

The correlation between air pollutants and meteorological factors are presented in Table 2. In general, concentrations of air pollutants were positively correlated with others, whereas the concentration of O_3 was negatively correlated with concentrations

of PM_{2.5}, NO₂, CO, and SO₂ (P < .001). Additionally, temperature and humidity were significantly associated with all the air pollutants except PM₁₀. Wind speed was negatively associated with PM_{2.5} and positively associated with NO₂. Air pressure was negatively associated with PM_{2.5}, PM₁₀, CO, and SO₂, but positively associated with O₃.

3.2 | Meteorological factors and COVID-19 confirmed cases

Figure 3 presents the exposure-response for the mean value of temperature, wind speed, humidity, and air pressure in relation to log-transformed of COVID-19 confirmed cases. There was significantly nonlinear relationship between daily temperature and COVID-19 confirmed cases (P < .001 for lag 0, lag 0-7, and lag 0-14, and P = .008 for lag 0-21). Additionally, daily humidity was significantly nonlinear associated with COVID-19 confirmed cases (P = .01 for lag 0 and P = .008 for lag 0-14).

Based on results from the GAM, the cut-off temperature of 8°C was selected to perform the linear association between temperature and COVID-19 confirmed cases in the subgroup of above and below thresholds (Table S1). In particular, an 1°C increase in temperature was associated with 12% (lag 0; OR = 1.12; 95% CI = 1.06-1.18), 13%

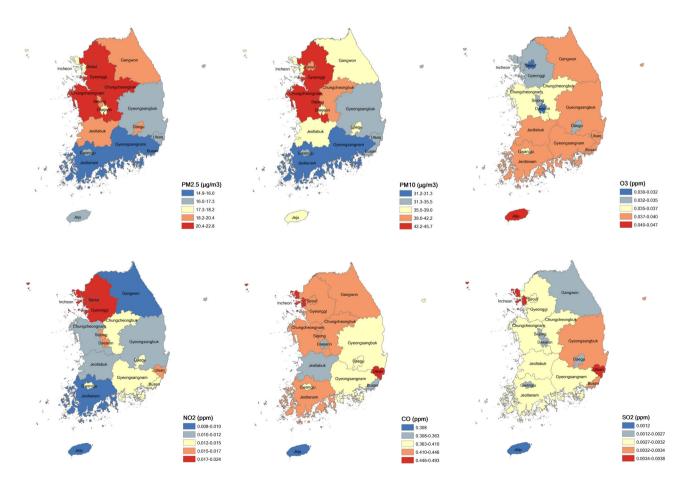


FIGURE 1 Regional distribution of air pollutants in Korea during 3 February 2020 and 5 May 2020

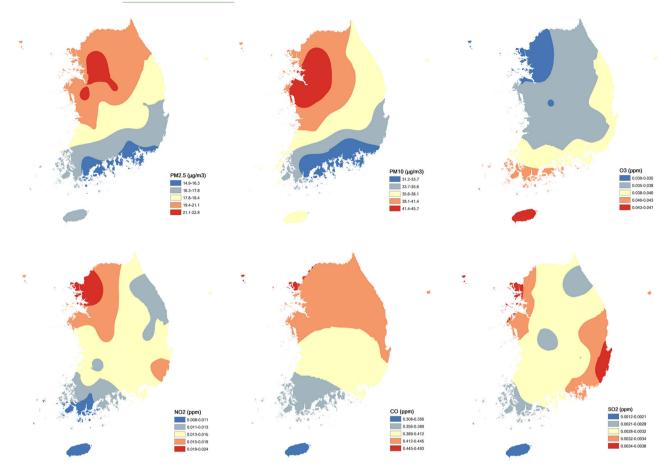


FIGURE 2 Kriging interpolation for air pollutant concentrations in Korea during 3 February 2020 and 5 May 2020

(lag 0-7; OR = 1.13; 95% CI= 1.07-1.20), and 9% (lag 0-14; OR = 1.09; 95% CI = 1.03-1.15) increases of confirmed cases when the temperature was below 8°C. Similar association between temperature and confirmed cases when the temperature was above 8°C, but for lag 0 only (OR = 1.10; 95% CI = 1.02-1.18). Additionally, the cut-off humidity of 60% for lag 0% and 50% and 70% for lag 0 to 14 were adapted but the effect of 10% increase in humidity was not significant (data not shown).

3.3 | Air pollutants and COVID-19 confirmed cases

Figure 4 and Table S2 summarize the temporal association between air pollutants and COVID-19 confirmed cases in different adjusted models and lag settings. Findings from the fully adjusted model showed that 0.01 ppm increase in NO $_2$ (lag 0-7, lag 0-14, and lag 0-21) was significantly associated with increases of COVID-19 confirmed cases, with ORs (95% CIs) of 1.13 (1.02-1.25), 1.19 (1.09-1.30), and 1.30 (1.19-1.41), respectively. Besides, 0.1 ppm increase in CO (lag 0-21) was associated with the increase in COVID-19 confirmed cases (OR = 1.10; 95% CI = 1.04-1.16). Furthermore, we observed the positive association between per 0.001 ppm of SO $_2$ concentration (lag 0, lag 0-7, and lag 0-14) and COVID-19 confirmed

cases, with ORs (95% CIs) of 1.13 (1.04-1.22), 1.20 (1.11-1.31), and 1.15 (1.07-1.25), respectively.

4 | DISCUSSION

Given that COVID-19 is a respiratory disease that could rapidly spread to the community and the SARS-CoV-2 might remain in aerosols for hours, this study examined the association between concentrations of air pollutants and the number of COVID-19 confirmed cases in Korea. We applied the Kriging interpolation to elucidate the regional distribution of PM_{2.5}, PM₁₀, NO₂, CO, and SO₂ concentrations across 17 metropolitan cities and provinces. We found that daily mean temperature was significantly nonlinear associated with COVID-19 confirmed cases. Additionally, we observed the temporally positive association between NO₂, CO, and SO₂ concentrations and daily confirmed new cases in Korea. This evidence may support the important role of air quality in the prevention of COVID-19.

Recent data from 122 cities in China also reported the significantly nonlinear association between temperature and daily confirmed new cases. In particular, Xie et Zhu found that each 1° C increase of temperature was related to 4.86% (95% CI = 3.21-6.51)

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	PМ _{2.5} , µg/m³	PM_{10} , $\mu g/m^3$	O ₃ , ppm	NO ₂ , ppm	CO, ppm	SO ₂ , ppm	Temperature, °C	Temperature, °C Wind speed, m/s Humidity (%)	Humidity (%)	Air pressure, hPa
PM _{2.5} , µg/m³	:									
$PM_{10},\mu g/m^3$	0.71 (<0.001)	÷								
O_3 , ppm	-0.18 (<0.001) 0.16 (<0.001)	0.16 (<0.001)	:							
NO_2 , ppm	0.51 (<0.001)	0.26 (<0.001)	0.26 (<0.001) -0.56 (<0.001)	:						
CO, ppm	0.65 (<0.001)	0.31 (<0.001)	0.31 (<0.001) -0.49 (<0.001)	0.63 (<0.001)	:					
SO ₂ , ppm	0.29 (<0.001)	0.23 (<0.001)	0.23 (<0.001) -0.18 (<0.001)	0.36 (<0.001) 0.45 (<0.001)	0.45 (<0.001)	:				
Temperature, °C	0.11 (<0.001)	-0.05 (0.05)	-0.34 (<0.001)	0.26 (<0.001)	0.25 (<0.001)	0.07 (0.004)	:			
Wind speed, m/s -0.06 (0.03)	-0.06 (0.03)	-0.01 (0.82)	0.02 (0.46)	0.07 (0.01)	0.04 (0.11)	-0.04 (0.16)	0.03 (0.26)	:		
Humidity (%)	-0.15 (<0.001) -0.04 (0.05)	-0.04 (0.05)	0.18 (<0.001)	-0.14 (<0.001)	-0.14 (<0.001) -0.17 (<0.001) -0.06 (0.02)		0.12 (<0.001)	-0.18 (<0.001)	:	
Air pressure, hPa	-0.08 (0.002)	-0.06 (0.02)	0.20 (<0.001)	-0.04 (0.15)	-0.15 (<0.001)	-0.15 (<0.001) -0.14 (<0.001) -0.35 (<0.001)	-0.35 (<0.001)	-0.01 (0.76)	-0.10 (<0.001)	:

increase of daily confirmed cases when the temperature was below 3°C. However, in the current study, threshold was obtained at 8°C, with a 9% increase of COVID-19 confirmed cases when the temperature was below 8°C. Nevertheless, previous studies consistently found the relationship between temperature and the transmission of other coronavirus-related outbreaks.

Ambient air pollution has been suggested to be associated with respiratory viral infection. 20 A previous study reported a pooled estimate of 3% (95% CI = 6%-13%) increases the mortality from non-malignant respiratory disease per $10\,\mu\text{g/m}^3$ increase of PM $_{2.5}$ concentration. 21 Air pollutants can affect the respiratory tract by enhancing apoptosis, microRNA abnormal expression, and FOXP3 loci hypermethylation at the cellular level. 22 At the molecular level, exposure to air pollutants can cause neutrophil infiltration, monocyte differentiation, and increase Th17 cells, which may combine with viral infection in the severity of diseases. 22

Regarding the association between short-term exposure to air pollutants and COVID-19 infection, Zhu et al 17 recently reported the evidence from China. In this study, $10\,\mu\text{g/m}^3$ increases of O_3 and NO_2 (lag 0-14) were associated with 4.76% (95% CI=1.99-7.52) and 6.94% (95% CI = 2.38-11.51) increases of daily confirmed cases, respectively. 17 However, significant associations between PM $_{2.5}$ and PM $_{10}$ concentrations and daily confirmed cases were not observed in our data of Korea. We additionally found the positive association between CO concentration and daily confirmed cases at lag 0 to 21. Such kind of consistent and inconsistent findings may come from the general air quality of each country and the activity of the factory during the outbreak.

In the current study, the odds of COVID-19 cases appear to fall for SO_2 and increase for CO and NO_2 across lag times of 7 days to 21 days prior confirmed cases (Figure 4), which may suggest the weaker effect of SO_2 and the stronger effect of CO and NO_2 at longer lag times. However, the possible explanation has still been unclear.

Considering the collinearity issue, the daily mean level of air pollutants was log-transformed to improve normal distribution and their simultaneous effects of all the six pollutants were further investigated in a principal component analysis (PCA) by using the "factoextra" package.²³ The PCA identified two principal components, which cumulative explained variances were approximately 70% across the lag effects (Figure S3). The component 1 was characterized by the level of six air pollutants, whereas the component 2 was mostly characterized by PM_{2.5}, PM₁₀, O₃, and NO₂ concentrations only (Table S3). The PCA-derived components for air pollutant concentrations were nonlinear associated with COVID-19 infection (Figure S4). The joint effect of air pollutants on confirmed cases was therefore suggested to be different at the cut-off PCA score of zero (Figure S4).

According to the authors' knowledge, this is the first study that provides evidence for the association between meteorological factors and air pollutants and COVID-19 infection during the first wave of the outbreak in Korea. We performed different adjusted models to obtain the findings. This study additionally considered the lag effect to examine the prevalence of confirmed new cases after 7, 14, and 21 days of short-term exposure with air pollutants.

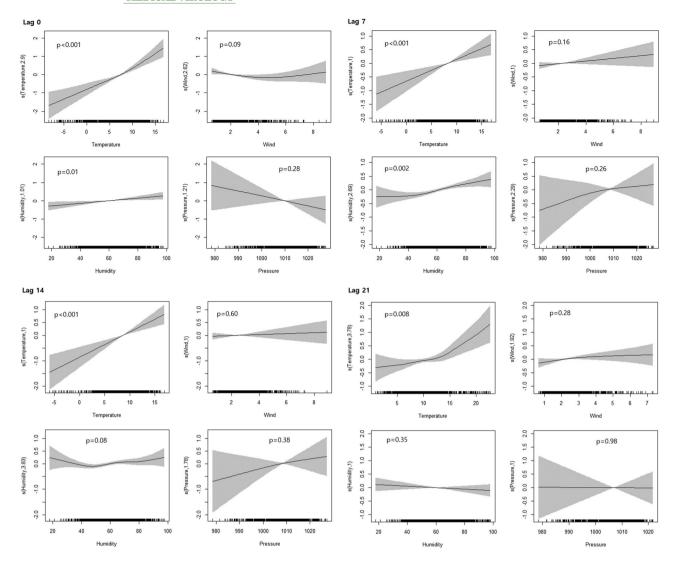


FIGURE 3 Effects of temperature, wind speed, humidity, and air pressure on COVID-19 confirmed cases in Korea The x axis represents the mean level of each meteorological variable (0, 7, 14, and 21-day moving). The y axis represents the smoother to the fitted values. *P*-value indicates the significant level of the smooth terms

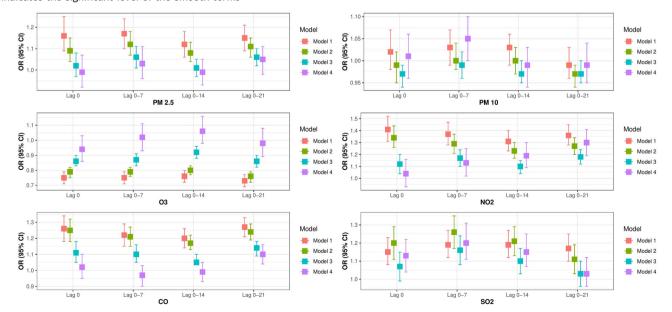


FIGURE 4 Temporal relationship between ambient air pollution and COVID-19 confirmed cases in Korea Model 1: univariate; Model 2: model 1 + adjusted for location; Model 3: model 2 + smooth function of temperature, wind speed, humidity, and air pressure; Model 4: model 3 + adjusted for date

Despite strengths and novelty, this study remains some limitations. First, since data on the concentration of air pollutants and the level of meteorological factors were obtained at city-province level, such the regional distribution of air pollutants at the district level might be more informative. However, due to the up-to-date research question and the personal information issue of confirmed cases, we were not able to assess the more detailed information at this time. Second, COVID-19 transmission was affected by air quality only. Several factors such as immunology, mask-wearing, and hand-washing habits, people gathering as well as the management policy of the government such as social distancing may jointly affect the daily COVID-19 confirmed cases. Those kinds of factors were not been included in our analyses.

In conclusion, this study found the significant temporal association between NO_2 , CO, and SO_2 concentrations and daily COVID-19 confirmed cases in Korea. Further studies considering other social factors and national implementations are needed to confirm the findings and develop the appropriate control program to minimize the transmission of the novel disease.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Conceptualization, methodology, writing-original draft preparation, and writing-review and editing: TTAT and TH; data curation: TH.

DATA AVAILABILITY STATEMENT

Data are available on request to the authors.

ORCID

Tung Hoang (b) http://orcid.org/0000-0001-6653-3406
Tho Thi Anh Tran (b) http://orcid.org/0000-0002-4712-257X

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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