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Impact of climate and ambient air pollution on the epidemic growth during COVID-19 outbreak in Japan

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ABSTRACT

Coronavirus disease 2019 (COVID-19) rapidly spread worldwide in the first quarter of 2020 and resulted in a global crisis. Investigation of the potential association of the spread of the COVID-19 infection with climate or ambient air pollution could lead to the development of preventive strategies for disease control. To examine this association, we conducted a longitudinal cohort study of 28 geographical areas of Japan with documented outbreaks of COVID-19. We analyzed data obtained from March 13 to April 6, 2020, before the Japanese government declared a state of emergency. The results revealed that the epidemic growth of COVID-19 was significantly associated with increase in daily temperature or sunshine hours. This suggests that an increase in person-to-person contact due to increased outing activities on a warm and/or sunny day might promote the transmission of COVID-19. Our results also suggested that short-term exposure to suspended particles might influence respiratory infections caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Further research by well-designed or well-controlled study models is required to ascertain this effect. Our findings suggest that weather has an indirect role in the transmission of COVID-19 and that daily adequate preventive behavior decreases the transmission.

1. Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a new pandemic infectious disease. It was first identified in December 2019 in a cluster of viral pneumonia cases linked to a wet market in Wuhan, the capital of Hubei Province, China (Zhu et al., 2020a). COVID-19 had rapidly spread from Wuhan to many other countries in the world through global travel by March 2020 (Chen et al., 2020; Lu et al., 2020; Phan et al., 2020; Xu et al., 2020a). The World Health Organization (WHO) declared COVID-19 as a global pandemic on March 11, 2020 (WHO, 2020a).

SARS-CoV-2 is mainly transmitted human-to-human through close contact, respiratory droplets, fomites, and contaminated surfaces. Its transmission is similar to that of other respiratory viruses such as influenza or human coronavirus (Cheng et al., 2020; Lai et al., 2020; Sungnak et al., 2020; WHO, 2020b). Airborne transmission may occur via airborne particles smaller than 5 μm in diameter. Some outbreak reports related to indoor crowded spaces have suggested the possibility of airborne transmission, combined with droplet transmission such as during choir practice, in restaurants, or in fitness classes (Wiersinga et al., 2020; WHO, 2020b). A recent experimental study using transgenic mice expressing human angiotensin-converting enzyme 2 (hACE2) indicated that SARS-CoV-2 can be experimentally transmitted among hACE2 mice by close contact, through respiratory droplets, but is hardly transmitted through exposure to the airborne particles (Bao et al., 2020). A recent study also indicated that the role of airborne particles as a carrier for the virus diffusion is not evident (Bontempi, 2020a).

Many similar infectious diseases displayed seasonal patterns in their incidence (Fares, 2013; Fisman, 2017; Pascual and Dobson, 2005). Infections with severe acute respiratory syndrome coronavirus (SARS-CoV), influenza virus, human rhinovirus, and respiratory syncytial virus were directly associated to ambient air temperature and humidity

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(Barreca et al., 2012; Casanova et al., 2010; Chan et al., 2011; Ikäheimo et al., 2016; Jaakkola et al., 2014; Paynter, 2015; Tan et al., 2005). The association of respiratory viral infection with ambient air pollution has also been reported (Ciencewicki and Jaspers, 2007; Croft et al., 2019). Therefore, environmental factors such as climate and ambient air pollution may play an important role in the progression and spread of the disease.

Many studies have shown the influence of environmental factors including temperature, humidity, and/or ambient air pollution on the spread of COVID-19. Most studies reported a positive association of the spread with air pollution (Fattorini and Regoli, 2020; Li et al., 2020a; Xu et al., 2020b; Zhu et al., 2020b). Studies suggested an optimum range of 5°C–15 °C in temperature for its transmission (Gunthe et al., 2020; Sajadi et al., 2020). However, the association with climate conditions has not been consistent and is controversial. A positive association with an increase in ambient air temperature has been suggested (Bashir et al., 2020; Li et al., 2020a; Menebo, 2020; Tosepu et al., 2020; Xie and Zhu, 2020). Conversely, several studies suggest a negative association (Liu et al., 2020a; Méndez-Arriaga, 2020; Prata et al., 2020; Qi et al., 2020; Ujiie et al., 2020; Wu et al., 2020). Some studies have shown an association with an increase in humidity (Baker et al., 2020), whereas others have suggested an association with lower air humidity (Ahmadi et al., 2020; Liu et al., 2020a; Wu et al., 2020). Furthermore, some studies showed no association with temperature (Jüni et al., 2020; Yao et al., 2020) or humidity (Gunthe et al., 2020; Tosepu et al., 2020).

Climatic conditions and ambient air pollution vary across the world. Thus, the influence of environmental factors on the spread of the disease needs to be studied in each country. In addition, studies postulating that the date of infection (i.e., exposure to SARS-CoV-2) corresponded to the observation date of environmental factors are scarce. An average time interval between transmission and reporting of confirmed COVID-19 cases was suggested to be 14 days (Dong et al., 2020; Jüni et al., 2020; Lauer et al., 2020). Thus, Jüni et al. analyzed the epidemic growth of the disease concerning the stipulated incubation period (14 days) with reference to the environmental factors to ascertain the strength of the association (Jüni et al., 2020). However, further matching between the date of infection and the observation date of the environmental factors is important to examine the associations. The objective of this study was to evaluate the effect of climate and/or air pollution on the spread of COVID-19. Our study sought to estimate the date of infection and to determine the influence of environmental factors on spread of the disease.

2. Methods

2.1. Study design and areas

A longitudinal cohort study involving different geographical areas of Japan with documented outbreaks of COVID-19 was designed to determine the association between the epidemic growth and the environmental factors within the same epidemic period. The number of cases dramatically increased from mid-March in Japan. This prompted the Japanese government to release the first emergency declaration in seven main epidemic areas (Saitama, Chiba, Tokyo, Kanagawa, Osaka, Hyogo, and Fukuoka) on April 7, 2020. Then, the second emergency declaration was imposed nationwide on April 16 (Fig. S1). Japanese government asked people to avoid unnecessary outings, avoid crowded areas, practice social distancing, wear masks, and change their behavior (Tashiro and Shaw, 2020). Conscious behavioral changes were strongly observed after those declarations, and the number of COVID-19 cases decreased consequently (Fig. S1). The trend of the number of cases after the emergency declaration does not indicate the epidemic growth of the disease. In addition, if the data after emergency declaration is included in our analysis, the results could include bias that was influenced by the change of people's behavior due to the intervention by the government. Thus, to examine the association of the epidemic growth with the environmental factors, we determined the analysis period from March 13 to April 6, 2020 before the emergency declaration. Weather and air pollution levels are changed in a short term. The number of confirmed cases has been daily reported. However, the differences of operating speed in testing practices of COVID-19 infection affect count of the number of confirmed cases in a day. The time window of five days is short enough that no substantial changes in testing strategy are expected so that the confirmed cases in each region represent a constant level of the true actual cases (Jüni et al., 2020). Thus, we divided the analysis period into five periods (with 5-day slots): March 13–17, March 18–22, March 23–27, March 28–April 1, and April 2–6. This was done to evaluate the association in a longitudinal manner.

2.2. Data collection

2.2.1. Case of COVID-19

We collected data during the COVID-19 outbreak in Japan (May 22, 2020), as a comma-separated values file from the online dashboard provided by the J.A.G JAPAN Corporation (J.A.G JAPAN, 2020). The J.A.G JAPAN Corporation has collected data on a daily basis and provided these data as the license of NonCommercial 4.0 International (CC BY-NC 4.0). These data include necessary information about all COVID-19 cases reported by the Ministry of Health, Labour and Welfare (MHLW) and the local governments of Japan. All this information has been submitted together with sex, age groups, identified date [when COVID-19 was identified as positive by the SARS-CoV-2 reverse transcription polymerase chain reaction (RT-PCR) test], and the date of onset of symptoms. In addition, residential area, occupation, history of traveling abroad, data sources from the MHLW and local governments, and so forth have been also recorded. The COVID-19 cases infected in Japan were included in this study. The COVID-19 cases in the Diamond Princess cruise ship docked at Yokohama were excluded. The incubation period for COVID-19 was reported at approximately 5 days from virus exposure to symptoms onset (Guan et al., 2020; Lauer et al., 2020; Li et al., 2020b). Thus, cases returning from foreign country that entered to Japan within 5 days before onset of the disease, cases identified as positive by the RT-PCR test at the airport quarantine depot, and cases living in a foreign country were excluded from our study.

We identified the date of onset of the symptoms in each case from collected data. The median of the time interval between the date of onset and the date identified as positive by the RT-PCT test was 6 days from January to April 12. The mean value was approximately 6.5 days. Thus, in the absence of a date of onset of symptoms, we estimated the date of onset by subtracting 6 days from the date identified as a positive. Furthermore, we estimated the date of infection from the date of onset. As described above, the incubation period for COVID-19 was approximately 5 days. Thus, we deduced the date of infection by subtracting 5 days from the date of onset.

We counted the number of cases daily from their date of infection in terms of municipality, including Tokyo. We included all areas with at least cumulative 50 cases in this study since the beginning of the epidemic (set on January 15, 2020; Fig. S1) as of April 7, 2020. Areas affected by large localized cluster occurrence were excluded from the study.

2.2.2. Demographics

We obtained demographic data from the surveyed areas. This includes population, percentage of inhabitants aged ≥65 years, total land surface area (km^2), inhabitable area (km^2), taxable income, tax debtor, life expectancy at birth (MIAC, 2019), and health expenditure (Cabinet Office, 2020). We calculated the urban density (using population and inhabitable area) and taxable income per person (using taxable income and tax debtor).

2.2.3. Environmental data

The daily meteorological data were obtained from Japan

Meteorological Agency (JMA, 2020). This includes mean, minimum, and maximum ambient air temperature; precipitation; sunshine hours; wind speed; vapor pressure; relative humidity; and minimum relative humidity. The mean absolute humidity was calculated by vapor pressure and saturated water vapor pressure at its corresponding temperature. If the vapor pressure was not available, the absolute humidity was determined from relative humidity and its corresponding temperature (Shaman and Kohn, 2009).

Data of hourly ambient air pollutants were collected from the Atmospheric Environmental Regional Observation System (AEROS) provided by the Ministry of the Environment (MOE, 2020). These pollutants include nitrogen monoxide (NO), nitrogen dioxide (NO_2), photochemical oxidant (Ox), suspended particle matter (SPM), and fine particulate matter ($PM_{2.5}$). The daily mean data for each pollutant were calculated based on the hourly data. In the absence of these data from the Japan Meteorological Agency, data were obtained from the AEROS stations. The 5-day mean data during March 13–17, March 18–22, March 23–27, March 28–April 1, and April 2–6 were used for statistical analyses.

2.3. Index for the epidemic growth

Rate ratios (RR) were calculated as the cumulative count of confirmed cases in an area since the beginning of the epidemic as of March 13, March 18, March 23, March 28, and April 2 divided by the cumulative count of confirmed cases since the beginning of the epidemic as of March 17, March 22, March 27, April 1, and April 6, respectively. The observational period was 5 days across all areas. A rate ratio of two indicates that the number of cases doubled within 5 days.

2.4. Statistical analyses

We used weighted random-effects regression analysis with accommodation of correlated longitudinal data to determine the association between the logarithm of the rate ratio of COVID-19 and the exposure variables (Jüni et al., 2020), including regional climate and air pollution. Associations were expressed as ratios of rate ratios (RRRs) per 1 °C increase in temperature; 1 mm increase in precipitation; 1 h increase in sunshine hours; 1 m/s increase in mean wind speed; 5% increase in relative humidity; 1 g/kg (dry air) increase in absolute humidity; 1 ppm increase in NO, NO_2, and Ox; and 1 μg/m^3 increase in SPM and $PM_{2.5}$. The sites of analyses were geographical areas with five longitudinal periods. The logarithm of the RR of COVID-19 (dependent variable) and exposure variables (independent variables) were well defined at the level of geographical areas with five longitudinal periods. RRR values one of >1 indicate that an increase in a continuous exposure variable is associated with an increase in the epidemic growth.

We determined the association of epidemic growth with exposure variables using univariate and multivariable analyses for 28 geographical areas, divided to five periods from March 13 to April 6, 2020 with a longitudinal manner. In the multivariable analyses, we examined the association of epidemic growth with exposure variables on the regional climate or air pollutants, adjusting for male inhabitants, inhabitants aged ≥65 years, urban density, taxable income, health expenditure, and life expectancy at birth as the possible specified covariates. After correlations (using Pearson's test) among exposure variables were examined, further multivariable models were examined to determine the robustness of the associations with exposure variables. We used $p < 0.05$ to indicate statistical significance. All data analyses were performed using SPSS statistical software, version 26 (IBM Corp, Armonk, NY, USA).

3. Results

3.1. Characteristics of surveyed areas

We included 28 geographical areas and enrolled 6529 cases in our analyses after reviewing the inclusion and exclusion criteria (Fig. 1). These areas were urban in nature, with a population of >200,000 (Table S1). The baseline characteristics of the surveyed areas are displayed in Table 1. The median case count per 1 million inhabitants for the 28 geographical areas during entire study period was 132.5 [interquartile rage (IQR) 67.3–171.1]. The median RR representing epidemic growth was 1.63 (IQR, 1.18–2.06) during March 13–17, 1.97 (IQR, 1.54–3.00) during March 18–22, 1.83 (IQR, 1.62–2.34) during March 23–27, 1.61 (IQR, 1.31–1.78) during March 28–April 1, and 1.32 (IQR, 1.24–1.41) during April 2–6, respectively. The highest RR value was observed during March 18–22, followed by March 23–27. The median percentage of the inhabitants aged ≥65 years was 24.0% (IQR 22.9–25.9) and the median life expectancy at birth (i.e., lifetime) was 84 years (IQR, 84.1–84.6). Those indicate a high rate of elderly people in Japan.

The environmental exposure data are shown in Table 2. In the entire surveyed period, the median values of mean temperature and mean daily maximum temperature were 11.6 °C (IQR, 9.3–12.8) and 16.0 °C (IQR, 13.4–17.9), respectively, indicating typical early spring in Japan. The median values of precipitation and sunshine hours were 2.2 mm (IQR, 0.0–6.1) and 7.1 h (IQR, 5.6–8.2), respectively, indicating moderately containing a fine day. The median values of mean NO, NO_2, Ox, SPM, and $PM_{2.5}$ were 1.7 ppb (IQR, 1.1–2.6), 12.2 ppb (IQR, 8.4–14.8), 34.6 ppb (IQR, 31.8–38.7), 11.4 μg/m^3 (IQR, 9.3–14.1), 9.5 μg/m^3 (IQR, 7.2–11.2), respectively. The maximum values of mean daily maximum NO, NO_2, Ox, SPM, and $PM_{2.5}$ were 7.8 ppb (converted to 9.6 μg/m^3), 28.0 ppb (converted to 52.6 μg/m^3), 51.5 ppb (converted to 103.0 μg/m^3), 22.9 μg/m^3, and 19.9 μg/m^3. The ambient environmental quality standards within short time exposure to NO_2, Ox, SPM, and $PM_{2.5}$ in Japan were 40–60 ppb for 24 h, 60 ppb for 1 h, 200 μg/m^3 for 1 h, and 35 μg/m^3 for 24 h, respectively (Kawamoto et al., 2011). SPM is defined as airborne particles with a diameter ≤10 μm. SPM is particulates collected through an instrument which completely (100%) excludes particulate matter with aerodynamic diameter > 10 μm. PM_{10} is defined as airborne particles that pass through a size regulator inlet with a 50% efficiency cut off at 10 μm aerodynamic diameter. If the nomenclature of PM is used, SPM would be called PM_7 (Wakamatsu, 2011). The main Ox component in photochemical air pollution is ozone (O_3; up to 90%) (Stokinger and Coffin, 1968). Ambient ozone is a marker for hazardous Ox types in air (WHO, 2006). The WHO air quality guidelines of shot time exposure for NO_2, O_3, PM_{10}, and $PM_{2.5}$ were 200 μg/m^3 for 1 h, 100 μg/m^3 for 8 h, 50 μg/m^3 for 24 h, 25 μg/m^3 for 24 h (WHO, 2006). Overall, the results of air pollutants had not exceeded the ambient environmental quality standards and the WHO air quality guidelines overall.

3.2. Exposure variables

Univariate analyses of variables showed significant positive association between the epidemic growth and sunshine hours and mean wind speed. In addition, there was a significant negative association with NO_2 (Table 3). No significant association was found with mean temperature, mean daily minimum temperature, mean daily maximum temperature, precipitation, mean relative humidity, mean daily minimum relative humidity, and air pollutants (NO, Ox, SPM, or $PM_{2.5}$). Fig. S2 shows bubble plots of the RR of COVID-19 on these variables. However, after adjusting for demographic variables with multivariable regression analyses, the associations became insignificant except for the association with the sunshine hours. Conversely, the associations with overall mean temperature [RRR, 1.04; 95% confidence interval (CI), 1.01–1.08], mean daily minimum temperature (RRR, 1.03; 95% CI, 1.00–1.06), mean daily maximum temperature (RRR, 1.04; 95% CI, 1.01–1.08), and SPM (RRR, 1.03; 95% CI, 1.00–1.05) became positively significant (Table 3).

NO_2 is a product of combustion processes such as vehicle exhaust and is found in the atmosphere generally in close association with other

Fig. 1. Geographic patterns of COVID-19 confirmed case counts (per 1,000,000 inhabitants) in 28 geographical areas of Japan from March 13 to April 6, 2020.

primary pollutants, including suspended particles. It is a precursor of ozone, and it coexists alongside other photochemical oxidants (WHO, 2006). Correlations among exposure variables showed that NO_2 was highly correlated with Ox ($r = -0.449$, $p < 0.001$), SPM ($r = -0.497$, $p < 0.001$), and $PM_{2.5}$ ($r = -0.532$, $p < 0.001$; Table S2). In the presence of sunlight, emissions of volatile organic compounds and nitrogen oxide (NOx) lead to the production of high concentrations of secondary particulate matter (Jiang et al., 2016; Kroll and Seinfeld, 2008). The correlation between mean temperature and sunshine hours was very low ($r = 0.108$, $p = 0.253$; Table S1). Based on these findings, we further examined to determine the strength of the associations with individual exposure variables (Table 4). For Model 1, we used mean temperature

Table 1
Status of epidemic growth during COVID-19 outbreak and demographic characteristics in analyzed geographical areas ($n = 28$).

Variable	Median	IQR
No. of cases		
March 13–17	4	1–7
March 18–22	9	7–20
March 23–27	20	13–32
March 28–April 1	23	15–35
April 2–6	26	17–36
Entire period	80	61–120
Case count (per 1,000,000 inhabitants)		
March 13–17	7.58	1.00–8.35
March 18–22	17.54	9.59–17.96
March 23–27	29.63	18.17–39.98
March 28–April 1	41.85	18.25–54.05
April 2–6	35.94	20.28–43.36
Entire period	132.54	67.33–171.07
Rate ratio		
March 13–17	1.63	1.18–2.06
March 18–22	1.97	1.54–3.00
March 23–27	1.83	1.62–2.34
March 28–April 1	1.61	1.31–1.78
April 2–6	1.32	1.24–1.41
Population (1,000,000 inhabitants)	0.90	0.48–1.49
Male inhabitant (%)	48.6	47.9–49.7
Inhabitants aged ≥65 years (%)	24.0	22.9–25.9
Urban density (1000 inhabitants/km^2)	6.3	4.4–8.2
Taxable income (1,000,000 JPY/inhabitant)	3.5	3.4–3.8
Health expenditure (1,000,000 JPY/inhabitant)	0.19	0.18–0.20
Life expectancy at birth (year)	84.3	84.1–84.6

Abbreviations: IQR, interquartile rage; JPY, Japanese Yen.

and sunshine hours, while adjusting for demographic variables. In addition, we used mean temperature and NO_2 (Model 2) and mean temperature and SPM (Model 3), while adjusting for demographic variables. Model 1 showed a significant positive association with mean temperature (RRR, 1.05; 95% CI, 1.01–1.08) and sunshine hours (RRR, 1.02; 95% CI, 1.00–1.04). Model 2 (RRR, 1.04; 95% CI, 1.01–1.08) and Model 3 (RRR, 1.03; 95% CI, 1.00–1.07) showed a significant positive association with mean temperature. No association was found with NO_2 and SPM in Model 2 and Model 3.

4. Discussion

In this longitudinal cohort study of 28 geographical areas with 6529 confirmed COVID-19 cases, the epidemic growth of COVID-19 during the follow-up period from March 13 to April 6, 2020, indicating typical early spring in Japan, was not significantly associated with precipitation, wind speed, relative humidity, absolute humidity, NO, NO_2, Ox, and $PM_{2.5}$. However, we found significant associations with mean temperature, mean daily minimum temperature, and mean daily maximum temperature. We also found a significant association with sunshine hours.

One assumption for these results is elucidated by the relationship between climatic conditions and human activities or behaviors. A study in Tokyo reported that the use of parks positively increased in an ambient temperature of 7°C–27 °C. This was due to increased exercise, playing, getting fresh air, or associations within the community (Thorsson et al., 2007). A Swedish study showed that the total attendance in the park increased especially during warm weather (−3.6 °C–20.1 °C). The participants also assessed the current weather conditions as being good for outdoor activity with clear skies, high air temperatures, and low wind speeds (Eliasson et al., 2007). A Canadian study conducted from November 2007 to May 2008 also showed that a 5 °C increase in ambient temperature was associated with a 14% increase in pedestrians. A shift from snowy to dry conditions was associated with a 23% increase in pedestrians, and a 5% increase in a sunlit area was associated with a 2% increase in pedestrians (de Montigny et al., 2012). The COVID-19 virus is primarily transmitted among people through respiratory droplets and contact routes (Burke et al., 2020; Chan et al., 2020; Huang et al., 2020; Li et al., 2020b; Liu et al., 2020b). High rates of secondary infection have been reported among household members and those in close contact with COVID-19 cases during travel (who are likely to get within 1–2 m) (Bi et al., 2020; Li et al., 2020c). The WHO has adapted a 1-m social distancing policy, based primarily on the assumption that SARS-CoV-2 is transmitted in large isolated droplets within this range (WHO, 2020b). A recent experimental study indicated that ultraviolet light from the sunlight inactivated SARS-CoV-2 (Bianco et al., 2020). However, our results suggest that an increased person-to-person contact due to increased outing activities on warm and/or sunny days will promote the transmission of the virus.

Our study revealed a significant association of the epidemic growth of COVID-19 with SPM in the multivariable analysis, after adjusting for demographic variables. This association disappeared after the mean temperature was entered in the model (Model 3). However, ambient air concentration of SPM was highly correlated with mean temperature ($r = 0.419$, $p < 0.001$). Thus, there is an underlying association of the epidemic growth of COVID-19 with SPM.

Coarse particles represented by SPM and PM_{10} include those inhalable particles having a high probability of deposition in the nasopharyngeal region of the human respiratory tract. The fine fraction of PM_{10} is cut off from the coarse fraction at 2.5 μm in an aerodynamic diameter (called $PM_{2.5}$) and has a high probability of deposition in the tracheobronchial and alveolar regions of the human respiratory tract (Oberdörster et al., 2005; USEPA, 2019). Epidemiological findings showed a relationship between short-term exposure to coarse particles and respiratory infection (USEPA, 2019). The SARS-CoV-2 infection

Table 2
Ambient environmental exposure levels in analyzed geographical areas ($n = 28$).

Variable	March 13–17	March 18–22	March 23–27	March 28–April 1	April 2–6
Mean temperature (°C)	8.1 (6.8–8.8)	13.6 (12.6–14.6)	11.6 (10.6–12.5)	10.3 (9.5–12.0)	12.0 (11.4–13.0)
Mean daily minimum temperature (°C)	3.4 (1.9–4.5)	7.6 (5.7–9.3)	6.8 (4.6–8.2)	6.3 (5.6–9.2)	7.0 (5.8–8.2)
Mean daily maximum temperature (°C)	13.1 (11.8–13.9)	19.3 (17.9–20.3)	16.4 (15.6–17.6)	13.9 (13.0–15.7)	17.3 (16.1–18.1)
Precipitation (mm)	3.4 (2.2–5.2)	0.2 (0.0–1.0)	2.0 (0.0–4.3)	11.0 (9.0–16.2)	0.0 (0.0–0.4)
Sunshine hours (h)	6.4 (5.8–7.1)	8.3 (7.6–9.4)	7.5 (7.0–7.9)	1.0 (0.4–2.3)	9.2 (7.2–9.6)
Mean wind speed (m/s)	3.0 (2.2–3.6)	3.0 (2.3–3.9)	3.0 (2.1–3.5)	2.8 (2.1–3.7)	3.4 (2.5–3.9)
Mean relative humidity (%)	62.2 (58.3–64.2)	55.4 (51.6–60.2)	54.7 (50.7–60.5)	79.2 (75.3–83.4)	54.0 (50.8–57.9)
Mean daily minimum relative humidity (%)	38.0 (35.2–42.7)	33.1 (28.9–39.4)	33.0 (28.8–38.4)	65.9 (59.5–69.0)	31.3 (29.2–35.0)
Mean absolute humidity (g/kg, DA)	4.1 (3.9–4.3)	5.3 (5.0–5.5)	4.7 (4.3–5.3)	6.4 (6.1–6.8)	4.6 (4.3–4.9)
NO (ppb)	2.1 (1.4–2.6)	2.0 (1.1–3.0)	2.8 (1.9–3.5)	1.3 (1.0–1.7)	1.3 (0.8–1.7)
NO_2 (ppb)	12.9 (8.7–14.3)	14.3 (9.1–18.6)	14.4 (12.9–17.4)	10.2 (8.0–12.8)	9.7 (7.2–11.0)
Ox (ppb)	32.5 (30.1–34.6)	36.9 (34.2–40.0)	34.1 (32.8–35.5)	30.7 (25.9–33.0)	40.7 (38.5–42.2)
SPM (μg/m^3)	9.6 (8.9–10.7)	15.2 (13.6–16.8)	12.5 (11.2–15.6)	10.1 (7.2–12.4)	11.1 (9.7–12.5)
$PM_{2.5}$ (μg/m^3)	7.8 (6.5–9.6)	11.7 (10.5–13.9)	10.6 (8.2–12.9)	6.9 (6.0–7.9)	9.8 (8.3–11.2)

Values are expressed as median (interquartile rage). Abbreviations: DA, dry air; Ox, photochemical oxidant; NO, nitrogen monoxide; NO_2, nitrogen dioxide; $PM_{2.5}$, fine particulate matter; SPM, suspended particulate matter.

Table 3
Correlation between epidemic growth of COVID-19 and ambient environmental factors.

Variable	Ratio unit	Univariate		Multivariable	
		RRR (95% CI)	*p* value	Adjusted RRR (95% CI)	*p* value
Mean temperature	1 °C	1.03 (1.00–1.06)	0.056	1.04 (1.01–1.08)	0.018*
Mean daily minimum temperature	1 °C	1.02 (1.00–1.04)	0.053	1.03 (1.00–1.06)	0.037*
Mean daily maximum temperature	1 °C	1.04 (1.00–1.08)	0.060	1.04 (1.01–1.08)	0.020*
Precipitation	1 mm	0.99 (0.98–1.00)	0.091	0.99 (0.98–1.00)	0.060
Sunshine hours	1 h	1.03 (1.00–1.05)	0.035*	1.03 (1.01–1.05)	0.011*
Mean wind speed	1 m/s	1.13 (1.04–1.23)	0.005**	1.06 (0.96–1.16)	0.238
Mean relative humidity	5%	0.98 (0.95–1.02)	0.344	0.97 (0.94–1.01)	0.105
Mean daily minimum relative humidity	5%	0.98 (0.95–1.01)	0.220	0.98 (0.96–1.00)	0.058
Mean absolute humidity	1 g/kg, DA	1.03 (0.98–1.09)	0.259	1.04 (0.98–1.11)	0.159
NO	1 ppb	0.96 (0.90–1.02)	0.200	1.04 (0.97–1.10)	0.278
NO_2	1 ppb	0.98 (0.97–1.00)	0.033*	1.01 (0.99–1.02)	0.540
Ox	1 ppb	1.02 (1.00–1.04)	0.082	1.01 (0.99–1.03)	0.402
SPM	1 μg/m^3	1.01 (0.98–1.05)	0.356	1.03 (1.00–1.05)	0.026*
$PM_{2.5}$	1 μg/m^3	1.01 (0.98–1.04)	0.698	1.03 (1.00–1.06)	0.083

Values are expressed as ratios of rate ratios (95% CIs) and 2-sided *p* values. Significant at * $p < 0.05$, ** $p < 0.01$. Multivariable analysis is adjusted for male inhabitant, inhabitants aged ≥65 years, urban density, taxable income, health expenditure, and life expectancy at birth; Abbreviations: DA, dry air; CI, confidence interval; RRR, ratio of rate ratio; NO, nitrogen monoxide; NO_2, nitrogen dioxide; Ox, photochemical oxidant; SPM, suspended particulate matter; $PM_{2.5}$, fine particulate matter.

primarily targets the respiratory tract. Angiotensin-converting enzyme 2 (ACE2) is the cellular receptor for SARS-CoV-2. This virus engages the ACE2 as the entry receptor. The spike glycoprotein of the virus mediates viral entry via binding with the human ACE2 (Hoffmann et al., 2020; Yan et al., 2020). Recent COVID-19 study reports that ACE2 expression is highest in the nose and that it decreases following a gradient along the lower respiratory tract, from proximal (high) to distal (low) pulmonary epithelial cultures (Hou et al., 2020). The findings highlight the susceptibility of the nasal pathways to SARS-CoV-2 with subsequent aspiration-mediated virus seeding to the lung in its pathogenesis. Several studies indicate that chronic exposure to air pollutants delays/complicates the recovery of COVID-19 cases and leads to more severe and lethal forms of the disease. However, studies on the role of respiratory viruses in the pathogenesis of respiratory infections are still scarce (Domingo and Rovira, 2020; Domingo et al., 2020). Our results suggest that suspended particles may influence a respiratory infection by SARS-CoV-2. Ambient air concentrations of SPM were low in our study. Although one Chinese study suggested positive associations of short-term exposure to $PM_{2.5}$, PM_{10}, carbon monoxide, NO_2, and O_3 with COVID-19 confirmed cases (Zhu et al., 2020b), further research is recommended for verification, especially in areas having higher air concentration of coarse particles or by a well-controlled animal study or an *in vitro* study.

For evaluating the effects of climate and/or air pollution on the spread of COVID-19 infection (i.e., epidemic growth), we analyzed those data before emergency declaration that would not be influenced by the change of people's behavior due to the intervention by government. This is a strength of our study. However, our study had some limitations. First, we estimated the date of infection from the date of onset and the reported mean incubation period of COVID-19. When the date of onset was not available, we estimated the date of onset from the date when COVID-19 was identified as positive by the RT-PCR test. Thus, actual dates of infection could not be estimated. However, the identified or reported cases (not estimated dates of infection) and their approximate concordant measurement time points have often been used in a nationwide or global epidemiological study on the associations of the COVID-19 infection with the climate or air pollutants. Our study on the basis of the estimated date of infection could strength the evidence of the associations. Second, we analyzed only 28 geographical areas with 6529 cases on the municipality basis. This sample size of the surveyed area was not large enough. However, we used a longitudinal study design to examine possible effects of exposure variables on the epidemic trend of the disease. Longitudinal study designs are relatively stronger than cross-sectional ones. Third, data on climate and ambient air pollutants were collected for urban areas of each geographical area, which may not have accurately represented area's climatic patterns. Fourth, although we used data before the emergency declaration in the seven main infected areas, our results may have had a possible influence of behavioral patterns before the declaration. The postponement of the 2020 Tokyo Olympic and Paralympic Games was released on March 24, 2020 (TOCOPG, 2020). Tokyo Governor called for voluntary stay at home for Tokyo residents on March 25, 2020. However, we used the data of the nationwide 28 geographical areas in Japan. The effect of this bias would be limited because the number of COVID-19 cases has clearly decreased after the emergency declaration. Fifth, we could not consider host factors, such as immunity or susceptibility, which play an important role in

Table 4
Multivariable regression models on the association with epidemic growth of COVID-19.

Variable	Ratio unit	Model 1		Model 2		Model 3	
		Adjusted RRR (95% CI)	*p* value	Adjusted RRR (95% CI)	*p* value	Adjusted RRR (95% CI)	*p* value
Male inhabitant	1%	1.05 (0.92–1.20)	0.473	1.02 (0.95–1.10)	0.587	1.03 (0.95–1.10)	0.485
Inhabitants aged ≥65 years	1%	1.00 (0.95–1.06)	0.949	0.98 (0.93–1.02)	0.350	0.98 (0.94–1.02)	0.403
Urban density	1000 inhabitants/km^2	0.95 (0.91–1.00)	0.038*	0.93 (0.90–0.97)	<0.001**	0.93 (0.90–0.97)	<0.001**
Taxable income	1,000,000 JPY/inhabitant	0.85 (0.52–1.38)	0.512	0.90 (0.64–1.28)	0.556	0.94 (0.66–1.33)	0.719
Health expenditure	1000 JPY/inhabitant	1.00 (0.99–1.01)	0.686	1.00 (1.00–1.01)	0.756	1.00 (1.00–1.01)	0.681
Life expectancy at birth	1 year	1.10 (0.87–1.40)	0.426	1.02 (0.83–1.26)	0.850	1.00 (0.81–1.24)	0.989
Mean temperature	1 °C	1.05 (1.01–1.08)	0.013*	1.04 (1.01–1.08)	0.018*	1.03 (1.00–1.07)	0.048*
Sunshine hours	1 h	1.02 (1.00–1.04)	0.039*	–	–	–	–
NO_2	1 ppb	–	–	1.01 (0.99–1.02)	0.468	–	–
SPM	1 μg/m^3	–	–	–	–	1.02 (0.99–1.04)	0.144

Values are expressed as ratios of rate ratios (95% CIs) and 2-sided *p* values. Significant at * $p < 0.05$, ** $p < 0.01$. Abbreviations: JPY, Japanese Yen; CI, confidence interval; RRR, ratio of rate ratio; NO_2, nitrogen dioxide; SPM, suspended particulate matter.

disease transmission and testing. Finally, although we considered the effects of several demographic factors in the multivariable analyses, the virus transmission is a complex. An interdisciplinary, multi-dimensional approach to understand the epidemic growth of COVID-19 will be also required (Bontempi, 2020b; Bontempi et al., 2020).

In conclusion, the epidemic growth of COVID-19 was not associated with precipitation, wind speed, humidity, NO, NO_2, Ox, and $PM_{2.5}$. Conversely, it was significantly associated with increase in daily temperature or sunshine hours during the study period. This suggests that an increase in person-to-person contact due to increased outing activities on a warm and/or sunny day might promote the transmission of COVID-19. Our results also suggested that short-term exposure to suspended particles might influence respiratory infections caused by SARS-CoV-2. However, further research with a well-controlled animal study or an *in vitro* study is recommended. Our findings suggest that weather is likely to play an indirect role in the transmission of COVID-19. However, the most important thing is that people should have knowledge and understand that SARS-CoV-2 is mainly transmitted human-to-human through close contact, respiratory droplets, fomites, and contaminated surfaces and that daily adequate preventive behavior decreases its transmission.

Credit author statement

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Ethical considerations on human subjects or experimental animals: study approval

Not applicable because we used only published data and did not use any personal information.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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