Associations between Air Quality and Covid-19 Infection

Yuye Chen[a]
Department of Chemistry, University College London, London WC1E 6BT, U.K.

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Abstract: Air pollution has been an urgent trouble for many regions. The clear relationship between various types of air pollution and COVID-19 cases has not been well understood. The particulate matter (PM), as an air pollutant, was found to act as a potential carrier of the SARS-CoV-2 virus. It might also cause higher angiotensin-converting enzyme 2 (ACE2) activation when inducing airway inflammation, and eventually increase the risk of COVID-19 infection. By concluding some of the existing studies, the statistical correlations between air pollutants and COVID-19 infection can be visualised, such as positive correlations found between $PM_{2.5}$, PM_{10}, NO_2, etc. and COVID-19 infection, while negative correlations with SO_2, as well as some controversial findings on O_3, etc. Further research is required to address possible mechanisms of how PM might facilitate the spreading of COVID-19. Monitoring air pollution levels and applying comprehensive models for analysing associations between COVID-19 infection and air pollution appear to be useful for further studies.

1 INTRODUCTION

COVID-19 has caused a worldwide pandemic. Over 200 countries have suffered from the SARS-CoV-2 virus. As of 10th September 2021, over 200 million infection cases and 4 million deaths have been reported to World Health Organization (Geneva: World Health Organization, 2020). COVID-19 patients usually undergo fever, cough; and fatigue, with congestion, sore throat, etc. also could be seen in some cases (Fu et al. 2020). Coronaviruses (CoVs) are enveloped viruses with a positive single-stranded RNA genome inside each virus. COVID-19 is caused by the SARS-CoV-2, a very pathogenic form of virion (Borisova and Komisarenko 2021) that enters the host cell via binding through the angiotensin-converting enzyme 2 (ACE2) receptor (Naqvi et al. 2020), which is a membrane enzyme found in the lungs, arteries, heart, kidney, and intestines' cells (Lin et al., 2018).

Research has found that countries such as China (Zhu et al. 2020, Hou et al. 2021, Yao et al. 2021) and Italy (Bontempi 2020, Fattorini and Regoli 2020) that reported a high incidence of COVID-19 together with high levels of air pollution. For example, a study of China with an average daily COVID-19 confirmed cases of 12.94 calculated during the observation period found that average daily concentrations of $PM_{2.5}$, PM_{10}, CO, NO_2, and O_3 (46.43 $\mu g/m^3$, 62.97 $\mu g/m^3$, 0.85 mg/m^3, 19.28 $\mu g/m^3$ and 78.22 $\mu g/m^3$, respectively) were significantly positively related to COVID-19 confirmed cases (Zhu et al. 2020). Moreover, among these air pollutant particles, the mechanism of how PM (particulate matter) might facilitate the infection of COVID-19 was recently investigated (Comunian et al. 2020). Previous studies found that PM_{10} may cause airway inflammation (Choi et al. 2020) and $PM_{2.5}$ collected in China largely enhanced the levels of expression of the inflammatory genes (Bekki et al. 2016). In the case of inflammation caused by PM, ACE2 as an anti-inflammatory peptide generator is overactivated, leading to an increased likelihood of COVID-19 entering the cells (Hayashi et al. 2010).

This review introduces the possible mechanism of COVID-19 infection facilitated by PM, as well as summarizes and discusses the correlation between the number of COVID-19 infection cases and air pollution. The different models chosen for the various studies are also mentioned, which would give references to the model constructions in further studies.

[a] https://orcid.org/0000-0003-3813-2466

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2 GENERAL MECHANISMS

2.1 Interaction between PM Particles and COVID-19 Virus

PM as the global environmental issue is known to cause irregular inflammatory and coagulation responses through the whole body (Choi et al. 2020). There are many sources of PM classified by their diameters. For example, PM_{10} and $PM_{2.5}$ stand for particulate matter with diameters no more than 10 micrometers and 2.5 micrometers respectively (Comunian et al. 2020). Certain types of PM were found to be able to interact with the plasma membrane of nerve cells (Borisova and Komisarenko 2021). COVID-19 virus has an envelope that can contain lipid components of host neuron cells as well as membrane fragments of infected cells (Borisova and Komisarenko 2021). Evidence has shown that some fine/ultrafine PM was be able to interact with the plasma membrane of nerve terminals in brains (Borisova and Komisarenko 2021). Therefore, these water-suspended PM particles in turn forms complexes with the COVID-19 virus that contains membrane segments of brain nerve cells. The complexes, when dried, then serves as carriers of the COVID-19 virus in the transmission (Borisova and Komisarenko 2021). The viruses are immobilized to the surfaces of these particles, leading to possible changes in the characteristics of the original virus. For example, the virus becomes more stable when grouping with these PM. Moreover, these SARS-CoV-2-PM complex possibly may enter the cells without binding to the ACE2 receptor (Borisova and Komisarenko 2021).

2.2 PM Activating ACE2 Causing COVID-19 Infection

ACE2 is a receptor on the cell membrane that binds to the spike-like proteins on the surface of the COVID-19 virus. It can regulate blood pressure by catalyzing the breaking of vasoconstrictor peptide, angiotensin 2 and turn them into angiotensin 1-7 (Comunian et al. 2020). ACE1 and ACE2 cooperating in the renin-angiotensin system could lead to the protection of organs and blood vessels by anticoagulant, anti-inflammatory, anti-oxidative stress activity, etc. (Gemmati et al. 2020). As SARS-CoV-2 depends on ACE2 to enter the host cell, various pathological conditions that could further activate ACE2 have been listed as possible hazards for COVID-19 (Wang et al. 2021). One of the possible mechanisms could be inflammation. Due to the anti-inflammatory function of angiotensin 1-7 peptide, ACE2 can make lung impairment from hyperoxia less severe by inhibiting the inflammatory response. Therefore, when there is inflammation, the activity of ACE2 would increase (Comunian et al. 2020). Chronic $PM_{2.5}$ exposure was found to increase the risk of systemic inflammation and oxidative stress in the lung epithelial cells (Pun et al. 2017). Also, research showed that exposure to PM particles can cause an inflammatory response, which might activate ACE2 and thus facilitate the infection of COVID-19 (Comunian et al. 2020). Therefore, PM may increase the risk of COVID-19 infection via ACE2 expression, as shown in Fig.1. In addition, the increased inflammation may also aggravate lung injury (Tung et al. 2021).

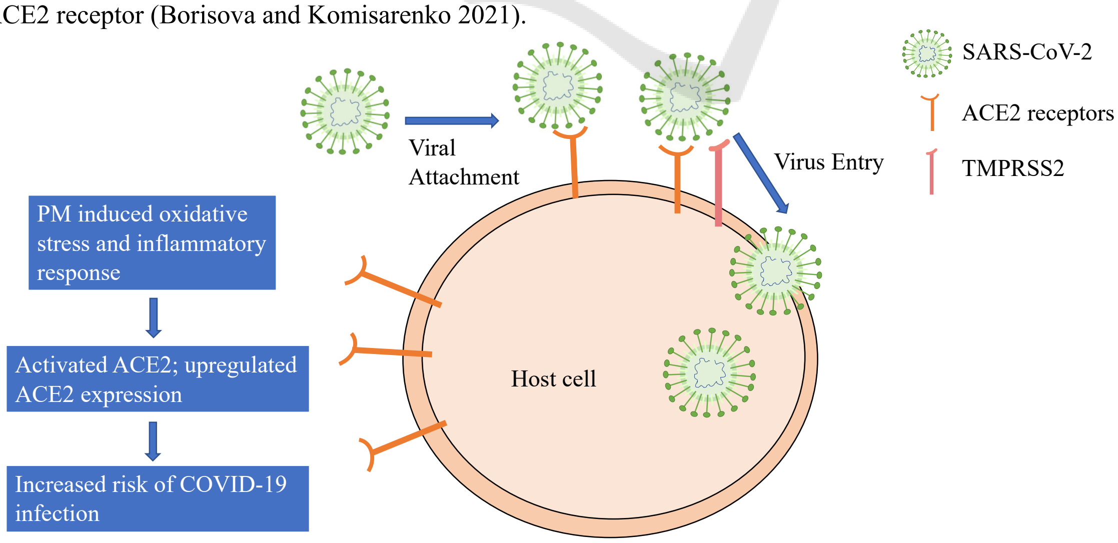

Figure 1: PM facilitating SARS-CoV-2 binding to ACE2 receptors to enter the host cell.

2.3 Nose-to-brain Entering Pathways of PM Particulates and CoronaVirus and Their Influence on Brain Nerve Terminals

PM, the inhalable corpuscles, can lead to various health problems because of their small size (Comunian et al. 2020). For example, the water-suspended smoke PM was found to affect exocytosis in nerve terminals (Borisova and Komisarenko 2021). The air pollution PM influenced exocytosis in nerve terminals, which in turn changed the transfer activity of CoVs between neurons. Air pollution PM and CoVs can be inhaled through the same nasal cavity path, pass through the axon of olfactory nerves, and eventually reach the brain (Borisova and Komisarenko 2021). They can then act separately and/or as a SARS-CoV-2-PM complex. Their neurological effects can meddle and intensify each other, being additive or even synergetic. When acting as a complex, the SARS-CoV-2-PM may disturb synaptic vesicle recycling in the process of exo-/endocytosis due to their larger size (Borisova and Komisarenko 2021).

3 AIR QUALITY CHANGES DURING COVID-19 LOCKDOWN

Results for a study in China showed that the significant decreases in NO_x and other air pollution emissions in the lockdown period due to COVID-19 contributed to considerable increases in O_3, which induced elevated atmospheric oxidizing ability and boosted the forming of secondary PM in eastern China (Huang et al. 2021). Another study of America found that the CO concentration fell more rapidly than NO_2 and $PM_{2.5}$ concentrations during the COVID-19 situation, while NO_2 emissions dropped over places of main power plants and rose over densely populated residential regions, especially those functioning as transportation centres at the junctions of national highways (Liu et al. 2021). A study in Korea found that from January 2020 to April 2020, monthly mean concentrations of $PM_{2.5}$, PM_{10}, NO_2, and CO were significantly lower than those in the three previous years (Ju et al. 2021). Another study of the Bangkok Metropolitan Region found that NO and the AQI declined during the COVID-19 lockdown. By comparison, CO, NO_2, SO_2, O_3, and $PM_{2.5}$ increased considerably during the lockdown period compared to the corresponding period of last year (Sangkham et al. 2021). Another study in China also witnessed a sharp reduction in the concentrations of air pollutants during the COVID-19 outbreak. In contrast to the same period in 2019 (from December 2018 to April 2019), the concentration of ambient air pollutants decreased 9.31%, 14.49%, 11.54%, and 13.89% for $PM_{2.5}$, SO_2, NO_2, and CO respectively. However, PM_{10} and O_3 concentrations increased 0.57% and 6.90% (Zhang et al. 2021).

4 STATISTICAL CORRELATION BETWEEN COVID-19 CASES AND AIR QUALITY MEASUREMENTS IN DIFFERENT REGIONS

Many studies have been investigating the long-term (over one year) and short-term (less than one year) relationships between the number of COVID-19 infection cases and air quality with several models. For example, a study of Italy summarized their data using the number of confirmed cases against the detection date and the correspondent PM_{10} concentration values (Bontempi 2020), and another study in China focused on the percentage change of daily COVID-19 infectors with a unit rise (10 $\mu g/m^3$ rise in $PM_{2.5}$, PM_{10}, SO_2, NO_2, O_3 and 1 mg/m^3 in CO) in pollutant concentration among six different pollutants (Zhu et al. 2020). Though different conclusions were also drawn from these studies. Hence, this review is to compare these differences and analyse the possible reasons for proposing a new possible model for further studies.

4.1 Short Term Studies

An Italian study (from 10th February 2020 to 27th March 2020) focused on the PM_{10} concentration in Lombardy cities, as well as some Piedmont cities, though no overall relationship was found (Bontempi, 2020). This study compared the pattern of PM_{10} concentration changes with the increase in COVID-19 confirmed cases about 20 days later. In some Lombardy cities like Bergamo and Brescia, the high PM_{10} concentration (over 50 $\mu g/m^3$/day) from 22nd to 26th of February, was corresponding to the increase in COVID-19 cases on the 11th and 12th of March. However, there were other cities, such as Pavia and Cremona, that also experienced high concentrations of PM_{10}, but reported a limited number of infection cases throughout the whole period. In some adjoining piedmont cities that also experienced high levels of pollution, no close relationship was found between

PM_{10} and COVID-19 cases. The lack of a direct contribution owing to PM_{10} acting as carriers for COVID-19 spreading was suggested in this study. One possible reason was that COVID-19 cases remained undetected for the investigated period, resulting in delayed countermeasures (Bontempi 2020).

A short-term study in China witnessed a clear correlation between the daily increase in COVID-19 cases from 23rd January 2020 to 29th February 2020, and the concentration of six pollutants: $PM_{2.5}$, PM_{10}, SO_2, NO_2, CO, and O_3. Except for SO_2, the other five pollutants all showed significant positive correlations with reported COVID-19 infectors (Zhu et al. 2020).

A brief California study using the dataset from 4th March 2020 to 24th April 2020 found that ambient air pollutants were remarkably related to COVID-19 cases and mortality. PM_{10}, $PM_{2.5}$, SO_2, CO, and NO_2 had significant associations with the total number of cases and deaths for both Spearman and Kendall models, with higher magnitudes resulted for PM_{10}, $PM_{2.5}$, SO_2, and NO_2 using the Spearman model (Bashir et al. 2020). The limitations of this study include not accounting for socio-economic indicators, social distancing, and personal hygiene.

In another study for Saudi Arabia, the degrees of air pollution for the three pollutants (PM_{10}, NO_2, and O_3) investigated from 9th March 2020 to 19th November 2020 were all positively related to the number of daily COVID-19 infectors. Other meteorological parameters like temperature and wind speed were also investigated in the study, revealing a significant association with the daily number of COVID-19 infections (Ben Maatoug et al. 2021).

4.2 Long Term Studies

A study of Italy that analysed the average concentrations of O_3, NO_2, $PM_{2.5}$, and PM_{10} for a long period from 2016 to 2019 suggested a significant correlation between a long-term, chronic exposure to air pollutants and the enhanced spreading of the COVID-19 virus (Fattorini and Regoli 2020). However, this study did not consider other crucial factors of COVID-19 incidence and mortality, for example, age structure, lifestyle factor, and the duration of the confinement.

A significant positive relationship between COVID-19 infections and the number of people exposed to SO_2, NO_2, and PM_{10} showed that pollution-related morbidity induced the COVID-19 infection across Mumbai (Chattopadhyay and Shaw 2021). This research suggested that Mumbai as a subtropical city having high temperature and humidity probably had not undergone the ill effect of PM_{10} during the COVID-19 situation. They also revealed a low-low association between air pollution and COVID-19 in the southern areas, which could be owing to a smaller quantity of industries, the predominance of corporate offices, defence areas, etc., and partially for its location of facing the open sea in both west and east parts where the wind could flow freely (Chattopadhyay and Shaw 2021).

The long-term association between exposures to common air pollutants and the COVID-19 case fatality rate (CFR) in China was investigated (Hou et al. 2021). The relationships between CFR and air quality indicators (air quality score, AQI, and $PM_{2.5}$ concentration) in the past 1,3, and 5 years were examined, and the results showed that the CFR of COVID-19 infectors rose for higher levels of long-term AQI, $PM_{2.5}$, and PM_{10}. However, there was no statistically significant association between the CFR and the levels of SO_2, NO_2, and O_3 found (Hou et al. 2021). Limitations of this study include those specific patient comorbidities, ethnic characteristics, and social factors, such as access to care and pollution density, as well as the relatively small sample size which may affect the CFR for this population-level study.

A study in the Netherlands focused on the period 2015-19 (Cole et al. 2020) found that $PM_{2.5}$ concentrations had a statistically significant positive correlation with COVID-19 cases, hospital admissions, and deaths. For NO_2, a statistically significant positive association was found between the number of COVID-19 cases and deaths but was not associated with hospital admissions. For SO_2 a trend of positive relationship was also found with COVID-19, but not statistically significant. A further application of the Fisher combination test suggested that both $PM_{2.5}$ and NO_2 significantly affect the overall COVID-19 outcomes, but SO_2 did not. The results indicated that, with other conditions under control, a district with 1 $\mu g/m^3$ extra $PM_{2.5}$ concentrations than another would on average report 9.4 and 15.1 more COVID-19 infections, varying from the model used. It would also result in from 2.9 to 4.4 more COVID-19 hospital admissions and from 2.2 to 2.8 more COVID-19 deaths. In this study, it was also found that average household income was inversely related to COVID-19 infection, while the average household size and the share of small housing were both positively correlated with COVID-19 spreading.

4.3 Combination of Both Short-term and Long-term Models in One Study

Both single-year and five-year average models at subregional and individual levels were discussed in an England study; the two models (subregional and individual) have significantly different patterns (Travaglio et al. 2021). In the individual model, $PM_{2.5}$ and PM_{10} were the most significant contributors to the higher incidence of COVID-19, with similar statistics in both long-term and short-term studies. Nitrogen oxides and dioxides were also positively related, while ozone showed a lack of relevance with COVID-19 infection. However, in the subregional study, only nitrogen oxides and nitrogen dioxides had infectivity rate ratios over 1 for both the single-year and multi-year models. $PM_{2.5}$, PM_{10}, and O_3 were negatively related to the infectivity of COVID-19. It was proposed that the inverse correlations between O_3 levels and the number of COVID-19 cases and deaths may be because less nitrogen oxide converted to ozone in metropolitan regions, a phenomenon that had been declared in regions with heavy traffic. In addition, due to the high reactivity of ozone, the negative association between O_3 levels and COVID-19 cases is compatible with extended nitric oxide scavenging nearly reaching levels of emissions.

Another study in China (Yao et al. 2021) focused mainly on the correlation between NO_2 concentration and spreading capability (basic reproductive number, R0) of COVID-19 in 63 cities in China. R0 was positively related to the average NO_2 level from 2016 to 2019 with adjusted temperature and relative humidity. Moreover, no significant relationships were found between the other examined air pollutants (SO_2, CO, O_3, $PM_{2.5}$, and PM_{10}) and R0. The study also investigated the daily R0 values for 11 cities in Hubei (except Wuhan) and normalized the data based on daily R0 value in Wuhan to exterminate the influences by other covariates. 11 Hubei cities (except Xianning City) reported significantly positive association for NO_2 with R0, indicating a positive correlation between daily NO_2 concentration and COVID-19 diffusion on the transient scale.

Table 1: Correlation between air pollutant particles and COVID-19 cases.

Country/Region	Short-term/long-term study	Pollutant(s)	Type(s) of the model used	Association with COVID-19 infection	Reference
Italy (Lombardy and Piedmont)	Short term (from 10th February 2020 to 27th March 2020)	PM_{10}	Confirmed infection cases against the detection day and corresponding PM_{10} concentration values	No clear association	(Bontempi 2020)
China (120 cities)	Short term (from 23rd January 2020 to 29th February 2020)	$PM_{2.5}$, PM_{10}, SO_2, NO_2, CO, and O_3	Generalized additive model, including both single-pollutant model and two-pollutant model	Significant positive associations with $PM_{2.5}$, PM_{10}, CO, NO_2, and O_3; negative association with SO_2	(Zhu et al. 2020)
California	Short term (from 4th March 2020 to 24th April 2020)	VOC, Pb, PM_{10}, $PM_{2.5}$, SO_2, CO, and NO_2	Spearman and Kendall correlation tests	Significant associations with PM_{10}, $PM_{2.5}$, SO_2, CO, and NO_2	(Bashir et al. 2020)
Saudi Arabia	Short term (from 9th March 2020 to 19th November 2020)	PM_{10}, NO_2, and O_3	Poisson and binomial negative models	Positive associations with PM_{10}, NO_2, and O_3	(Ben Maatoug et al. 2021)
Italy	Long term (from 2016 to 2019)	O_3, NO_2, $PM_{2.5}$, and PM_{10}	Average concentrations of NO_2, $PM_{2.5}$, and PM_{10} and number of days exceeding the controlled limits (averages of the last 3 years) for	Significant associations with O_3, NO_2, $PM_{2.5}$, and PM_{10}	(Fattorini and Regoli 2020)

			O_3 and PM_{10} versus the number of COVID-19 confirmed cases		
Mumbai	Long term (from 2017 to 2019)	SO_2, NO_2, and PM_{10}	Ordinary Least Square model, spatial lag model, spatial error model, and spatially adjusted regression model	Significant positives association with SO_2, NO_2, and PM_{10}	(Chattopadhyay and Shaw 2021)
China	Long term (from 2015 to 2020)	$PM_{2.5}$, PM_{10}, SO_2, NO_2, and O_3	Shapiro–Wilk test, Pearson correlation, and Spearman test	Positive associations with $PM_{2.5}$ and PM_{10}; no significant associations with SO_2, NO_2, and O_3	(Hou et al. 2021)
Netherlands (355 municipalities)	Long term (from 2015 to 2019)	$PM_{2.5}$, NO_2, and SO_2	Fisher combination test, negative binomial count model, Operational Priority Substances dispersion model, spatial econometric models	Significant positive associations with $PM_{2.5}$ and NO_2; not significant positive association with SO_2	(Cole et al. 2020)
England	Both short term (2018) and long term (from 2014 to 2018)	$PM_{2.5}$, PM_{10}, NO, NO_2, and O_3	Negative binomial regression model, binomial regression model, including both subregional and individual models	Individual model: positive associations with $PM_{2.5}$, PM_{10}, NO, and NO_2; lack of association with O_3 Subregional model: positive associations with NO and NO_2; negative associations with $PM_{2.5}$, PM_{10}, and O_3	(Travaglio et al. 2021)
China	Both short term (from 1st January 2020 to 8th February 2020) and long term (from 2016 to 2019)	NO_2, $PM_{2.5}$, PM_{10}, SO_2, CO, and O_3	Linear regression model	Significant positive association with NO_2; no significant associations with $PM_{2.5}$, PM_{10}, SO_2, CO, and O_3	(Yao et al. 2021)

4.4 General Trends in the 10 Selected Studies

Table 1 represents the correlation between air pollutant particles and COVID-19 infectivity. From the 10 studies, $PM_{2.5}$, PM_{10}, and NO_2 showed a significant positive correlation with COVID-19 cases in both long and short terms. It was, therefore suggested that concentrations of pollutants like NO_2 should be monitored, especially in urban areas (Bashir et al. 2020). Moreover, colder regions of the world should adopt stricter measures (Iqbal et al. 2021). Similarly, the significance of $PM_{2.5}$ and PM_{10} suggested that reducing air pollutants could be a useful way to control COVID-19 infection (Zhu et al. 2020), and the adoption of green environmental policies should be further promoted (Bashir et al. 2020). In addition, the burning of fossil fuels is the main source of NO_2 emissions. Therefore, variations in NO_2 levels can be applied to show alternations in human activity and population movement due to the COVID-19 lockdown (Yao et al. 2021). SO_2 was under debate. For the association discussed in 6 of the studies, three of them indicated a lack of significance with COVID-19 infection (Hou et al. 2021, Yao et al. 2021, Cole et al. 2020), two of them found significant association (Bashir et al. 2020, Chattopadhyay and Shaw 2021), while one study showed a negative association with COVID-19 cases (Zhu et al. 2020). Similar trends can be found with O_3, which showed significant association (Zhu et al., 2020, Ben Maatoug et al. 2021), no significant relevance (Hou et al. 2021, Yao et al. 2021, Travaglio et al. 2021), or negative association, which may be due to less nitrogen oxide converting to ozone in urban areas (Travaglio et al. 2021). Hence, more laboratory research needs to be carried out to clarify the underlying mechanism (Zhu et al. 2020). CO has not been frequently discussed in these studies and the potential associations remain unclear.

5 CURRENT EFFORTS IN CONTROLLING COVID-19 AND FUTURE EXPECTATIONS

Along with the research about the possible ways of COVID-19 spreading and infection, efforts have been done for the prevention and treatment of COVID-19. Preventions involve the use of personal protective equipment including masks, gloves, and googles (Qu et al. 2021). Vaccines have also been applied widely. As of 5th September 2021, a total of 5,352,927,296 vaccine doses have been administered as reported to WHO (Geneva: World Health Organization 2020). Studies are working on developing antiviral therapeutics. A recent study focusing on the nsp14 MTase activity suggested that development in this field would be viable for the COVID-19 pandemic treatment (Devkota et al. 2021). Another research targeting the SARS-CoV-2 Nsp13 Helicase also drew the same conclusion that potential inhibitor compounds could be identified and applied (White et al. 2020). On the other hand, it was proposed that the COVID-19 epidemic could not only be resolved through medicinal analysis and experiment, but also be promoted through environment-related sustainable research (Iqbal et al. 2021). Future research could involve a more in-depth study of characterization of SARS-CoV-2 virion's sorption onto atmospheric particulate matter (Duval et al. 2021) and thus find methods to alleviate the spreading of COVID-19 virus through air pollution.

6 CONCLUSIONS

An increasing amount of data are available to illustrate the correlation between COVID-19 infectivity and exposure to air pollutants. This review summarized the results of multiple studies, including information about country/region, length of data collected, pollutants, type(s) of the model used, and associations between the pollutants and COVID-19 infection, as shown in Table 1. In the selected research, $PM_{2.5}$, PM_{10}, and NO_2 were found to have the most significant positive association with COVID-19 confirmed cases. Different perspectives were oriented for SO_2 and O_3 among different studies, while CO was not frequently discussed in these studies. COVID-19 lockdown also showed significant association with the air quality changes in the same period. These statistics also suggested a possible mechanism of PM facilitating the spreading of SARS-CoV-2. Studies have found that PM would lead to COVID-19 infection by introducing inflammation and thus increasing the activity of the ACE2 receptor, the binding site of SARS-CoV-2. PM in water surrounding can also bind with the coronavirus, forming the SARS-CoV-2-PM complex, which could serve as carriers of the COVID-19 virus or disturb synaptic vesicle recycling if entering the brain. Further research in this area may involve more complex models and focus on the multifaceted conditions including weather, age groups, income level, population density, etc.

REFERENCES

BASHIR, M. F., MA, B. J., BILAL, KOMAL, B., BASHIR, M. A., FAROOQ, T. H., IQBAL, N. & BASHIR, M. 2020. Correlation between environmental pollution indicators and COVID-19 pandemic: A brief study in Californian context. *Environmental research,* 187, 109652.

BEKKI, K., ITO, T., YOSHIDA, Y., HE, C., ARASHIDANI, K., HE, M., SUN, G., ZENG, Y., SONE, H., KUNUGITA, N. & ICHINOSE, T. 2016. PM2.5 collected in China causes inflammatory and oxidative stress responses in macrophages through the multiple pathways. *ENVIRON TOXICOL PHAR,* 45, 362-369.

BEN MAATOUG, A., TRIKI, M. B. & FAZEL, H. 2021. How do air pollution and meteorological parameters contribute to the spread of COVID-19 in Saudi Arabia? *Environmental science and pollution research international,* 28, 44132-44139.

BONTEMPI, E. 2020. First data analysis about possible COVID-19 virus airborne diffusion due to air particulate matter (PM): The case of Lombardy (Italy). *Environmental research,* 186, 109639.

BORISOVA, T. & KOMISARENKO, S. 2021. Air pollution particulate matter as a potential carrier of SARS-CoV-2 to the nervous system and/or neurological symptom enhancer: arguments in favor. *Environmental science and pollution research international,* 28, 40371-40377.

CHATTOPADHYAY, A. & SHAW, S. 2021. Association Between Air Pollution and COVID-19 Pandemic: An Investigation in Mumbai, India. *Geohealth,* 5, e2021GH000383-n/a.

CHOI, J., SIM, J. K., OH, J. Y., LEE, Y. S., HUR, G. Y., LEE, S. Y., SHIM, J. J., MOON, J.-Y. & MIN, K. H. 2020. Relationship between Particulate Matter (PM10) and Airway Inflammation Measured with Exhaled

Nitric Oxide Test in Seoul, Korea. *Canadian respiratory journal,* 2020**,** 1823405-7.

COLE, M. A., OZGEN, C. & STROBL, E. 2020. Air Pollution Exposure and Covid-19 in Dutch Municipalities. *Environmental & resource economics,* 76**,** 581-610.

COMUNIAN, S., DONGO, D., MILANI, C. & PALESTINI, P. 2020. Air pollution and covid-19: The role of particulate matter in the spread and increase of covid-19's morbidity and mortality. *International journal of environmental research and public health,* 17**,** 1-22.

DEVKOTA, K., SCHAPIRA, M., PERVEEN, S., KHALILI YAZDI, A., LI, F., CHAU, I., GHIABI, P., HAJIAN, T., LOPPNAU, P., BOLOTOKOVA, A., SATCHELL, K. J. F., WANG, K., LI, D., LIU, J., SMIL, D., LUO, M., JIN, J., FISH, P. V., BROWN, P. J. & VEDADI, M. 2021. Probing the SAM Binding Site of SARS-CoV-2 Nsp14 In Vitro Using SAM Competitive Inhibitors Guides Developing Selective Bisubstrate Inhibitors. *SLAS DISCOVERY: Advancing the Science of Drug Discovery (2021) (In press).*

DUVAL, J. F. L., VAN LEEUWEN, H. P., NORDE, W. & TOWN, R. M. 2021. Chemodynamic features of nanoparticles: Application to understanding the dynamic life cycle of SARS-CoV-2 in aerosols and aqueous biointerfacial zones. *Advances in colloid and interface science,* 290**,** 102400.

FATTORINI, D. & REGOLI, F. 2020. Role of the chronic air pollution levels in the Covid-19 outbreak risk in Italy. *Environmental pollution (1987),* 264**,** 114732.

FU, L., WANG, B., YUAN, T., CHEN, X., AO, Y., FITZPATRICK, T., LI, P., ZHOU, Y., LIN, Y.-F., DUAN, Q., LUO, G., FAN, S., LU, Y., FENG, A., ZHAN, Y., LIANG, B., CAI, W., ZHANG, L., DU, X., LI, L., SHU, Y. & ZOU, H. 2020. Clinical characteristics of coronavirus disease 2019 (COVID-19) in China: A systematic review and meta-analysis. *The Journal of infection,* 80**,** 656-665.

GEMMATI, D., BRAMANTI, B., SERINO, M. L., SECCHIERO, P., ZAULI, G. & TISATO, V. 2020. COVID-19 and individual genetic susceptibility/receptivity: Role of ACE1/ACE2 genes, immunity, inflammation and coagulation. might the double x-chromosome in females be protective against SARS-COV-2 compared to the single x-chromosome in males? *International journal of molecular sciences,* 21**,** 3474.

GENEVA: WORLD HEALTH ORGANIZATION. 2020. *WHO COVID-19 Dashboard* [Online]. Available: https://covid19.who.int/ [Accessed 2021].

HAYASHI, N., YAMAMOTO, K., OHISHI, M., TATARA, Y., TAKEYA, Y., SHIOTA, A., OGURO, R., IWAMOTO, Y., TAKEDA, M. & RAKUGI, H. 2010. The counterregulating role of ACE2 and ACE2-mediated angiotensin 1-7 signaling against angiotensin II stimulation in vascular cells. *HYPERTENS RES,* 33**,** 1182-1185.

HOU, C. K., QIN, Y. F., WANG, G., LIU, Q. L., YANG, X. Y. & WANG, H. 2021. Impact of a long-term air pollution exposure on the case fatality rate of COVID-19 patients—A multicity study. *Journal of medical virology,* 93**,** 2938-2946.

HUANG, X., DING, A., GAO, J., ZHENG, B., ZHOU, D., QI, X., TANG, R., WANG, J., REN, C., NIE, W., CHI, X., XU, Z., CHEN, L., LI, Y., CHE, F., PANG, N., WANG, H., TONG, D., QIN, W., CHENG, W., LIU, W., FU, Q., LIU, B., CHAI, F., DAVIS, S. J., ZHANG, Q. & HE, K. 2021. Enhanced secondary pollution offset reduction of primary emissions during COVID-19 lockdown in China. *National science review,* 8.

IQBAL, W., TANG, Y. M., CHAU, K. Y., IRFAN, M. & MOHSIN, M. 2021. Nexus between air pollution and NCOV-2019 in China: Application of negative binomial regression analysis. *Process Safety and Environmental Protection,* 150**,** 557-565.

JU, M. J., OH, J. & CHOI, Y.-H. 2021. Changes in air pollution levels after COVID-19 outbreak in Korea. *The Science of the total environment,* 750**,** 141521.

LIN, C.-I., TSAI, C.-H., SUN, Y.-L., HSIEH, W.-Y., LIN, Y.-C., CHEN, C.-Y. & LIN, C.-S. 2018. Instillation of particulate matter 2.5 induced acute lung injury and attenuated the injury recovery in ACE2 knockout mice. *INT J BIOL SCI,* 14**,** 253-265.

LIU, Q., HARRIS, J. T., CHIU, L. S., SUN, D., HOUSER, P. R., YU, M., DUFFY, D. Q., LITTLE, M. M. & YANG, C. 2021. Spatiotemporal impacts of COVID-19 on air pollution in California, USA. *The Science of the total environment,* 750**,** 141592.

NAQVI, A. A. T., FATIMA, K., MOHAMMAD, T., FATIMA, U., SINGH, I. K., SINGH, A., ATIF, S. M., HARIPRASAD, G., HASAN, G. M. & HASSAN, M. I. 2020. Insights into SARS-CoV-2 genome, structure, evolution, pathogenesis and therapies: Structural genomics approach. *Biochimica et biophysica acta. Molecular basis of disease,* 1866**,** 165878-165878.

PUN, V. C., KAZEMIPARKOUHI, F., MANJOURIDES, J. & SUH, H. H. 2017. Long-Term PM2.5 Exposure and Respiratory, Cancer, and Cardiovascular Mortality in Older US Adults. *AM J EPIDEMIOL,* 186**,** 961-969.

QU, J.-M., CAO, B. & CHEN, R.-C. 2021. Chapter 6 - Prevention and disease control of COVID-19. *In:* QU, J.-M., CAO, B. & CHEN, R.-C. (eds.) *COVID-19.* Elsevier.

SANGKHAM, S., THONGTIP, S. & VONGRUANG, P. 2021. Influence of air pollution and meteorological factors on the spread of COVID-19 in the Bangkok Metropolitan Region and air quality during the outbreak. *Environmental research,* 197**,** 111104.

TRAVAGLIO, M., YU, Y., POPOVIC, R., SELLEY, L., LEAL, N. S. & MARTINS, L. M. 2021. Links between air pollution and COVID-19 in England. *Environmental pollution (1987),* 268**,** 115859.

TUNG, N. T., CHENG, P.-C., CHI, K.-H., HSIAO, T.-C., JONES, T., BÉRUBÉ, K., HO, K.-F. & CHUANG, H.-C. 2021. Particulate matter and SARS-CoV-2: A possible model of COVID-19 transmission. *The Science of the total environment,* 750**,** 141532.

WANG, M., BU, X., FANG, G., LUAN, G., HUANG, Y., AKDIS, C. A., WANG, C. & ZHANG, L. 2021.

Distinct expression of SARS-CoV-2 receptor ACE2 correlates with endotypes of chronic rhinosinusitis with nasal polyps. *Allergy (Copenhagen),* 76**,** 789-803.

WHITE, M. A., LIN, W. & CHENG, X. 2020. Discovery of COVID-19 Inhibitors Targeting the SARS-CoV-2 Nsp13 Helicase. *The journal of physical chemistry letters,* 11**,** 9144-9151.

YAO, Y., PAN, J., LIU, Z., MENG, X., WANG, W., KAN, H. & WANG, W. 2021. Ambient nitrogen dioxide pollution and spreadability of COVID-19 in Chinese cities. *Ecotoxicology and environmental safety,* 208**,** 111421.

ZHANG, X., TANG, M., GUO, F., WEI, F., YU, Z., GAO, K., JIN, M., WANG, J. & CHEN, K. 2021. Associations between air pollution and COVID-19 epidemic during quarantine period in China. *Environmental pollution (1987),* 268**,** 115897.

ZHU, Y., XIE, J., HUANG, F. & CAO, L. 2020. Association between short-term exposure to air pollution and COVID-19 infection: Evidence from China. *The Science of the total environment,* 727**,** 138704.