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Review article

Influence of airborne transmission of SARS-CoV-2 on COVID-19 pandemic. A review

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ABSTRACT

In recent years, a number of epidemiological studies have demonstrated that exposure to air pollution is associated with several adverse outcomes, such as acute lower respiratory infections, chronic obstructive pulmonary disease, asthma, cardiovascular diseases, and lung cancer among other serious diseases. Air pollutants such as sulfur oxides, nitrogen oxides, carbon monoxide and dioxide, particulate matter (PM), ozone and volatile organic compounds (VOCs) are commonly found at high levels in big cities and/or in the vicinity of different chemical industries. An association between air concentrations of these pollutants and human respiratory viruses interacting to adversely affect the respiratory system has been also reported. The present review was aimed at assessing the potential relationship between the concentrations of air pollutants on the airborne transmission of SARS-CoV-2 and the severity of COVID-19 in patients infected by this coronavirus. The results of most studies here reviewed suggest that chronic exposure to certain air pollutants leads to more severe and lethal forms of COVID-19 and delays/complicates the recovery of patients of this disease.

1. Introduction

Since March 2020, a number of investigations have pointed out that the progression of COVID-19 was more important in cities/areas/regions where certain air pollutants were being detected at comparatively high levels. In the 2000s, a positive association between air pollution and case fatality of SARS-CoV-1 was already observed in the Chinese population during the epidemic caused by that coronavirus (Cui et al., 2003). Cui et al. (2003) were focused on particulate matter (PM), nitrogen dioxide, carbon monoxide, sulfur dioxide and ground-level ozone. These environmental contaminants, as well as volatile organic compounds (VOCs), which derive mainly from vehicular traffic and industrial emissions, have been also suggested to contribute potentially to the severity of COVID-19. They would affect directly the lung ability to clear pathogens, and also indirectly, by exacerbating underlying cardiovascular and/or pulmonary diseases (Brandt et al., 2020). Thus, for example, the relationship between biomass uses and COVID-19 has even raised a novel concern due to exposure to air pollution of biomass smoke, which would be especially affecting those populations living in the most fragile conditions (Thakur et al., 2020). Regarding the transmission of SARS-CoV-2, it could be influenced not only by temperature and humidity, but also by food, water, and sewage, among other potential factors (Bashir et al., 2020a; Eslami; Jalili, 2020; Qu et al., 2020). With respect to COVID-19 vulnerability, in a recent review, Godri Pollitt et al. (2020) have highlighted possible genetic determinants of COVID-19, as well as the contribution of aerosol exposure as a potentially important route of transmission of SARS-CoV-2.

2. Ways of contagion of respiratory viruses

The main routes of person-to-person transmission of respiratory viruses are the following: a) the direct or indirect contact with an infected subject; b) the large droplets emitted by coughing/sneezing that can reach an uninfected subject; and c) the inhalation of small airborne particles remaining in the air (Eissenberg et al., 2020; Qu et al., 2020). In relation to the latter, Morawska and Cao (2020) have strongly suggested that the SARS-CoV-2 has been spreading through the air. In this same line, Frontera et al. (2020a) have hypothesized that the presence of air pollutants – together with certain climatic conditions – might mean a long permanence of the viral particles in the air, which – in turn – could promote the indirect diffusion of the SARS-CoV-2. Coccia (2020) has suggested that the transmission dynamics of COVID-19 could be due to

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air pollution-to-human transmission, rather than the direct human-to-human transmission. This author, using pollution and infected individual data of 55 Italian province capitals, has reported that the quick and vast diffusion of COVID-19 in Northern Italy showed a high association with the number of days exceeding the PM_{10} threshold. Coccia (2020) also highlighted that polluted cities in hinterland with low speed of wind had a high number of infected individuals than coastal cities. Based on this results, it was suggested that the prevention of future epidemics must be also based on sustainability and environmental sciences. In turn, Riccò and co-workers (2020) have reported that an appropriate way in dealing with, and understanding the potential relationship between air pollution and SARS-CoV-2 infection incidence rates, could be based on comparing geographical areas, which are characterized by similar socio-economic development, but strikingly different environmental status; for example, highly polluted areas vs. zones with low pollution concentrations.

The World Health Organization (WHO, 2014) has defined airborne transmission "*as the spread of an infectious agent caused by the dissemination of droplet nuclei, which remain infectious when suspended in air over long distances and time*". According to this definition, the rapid spread of the SARS-CoV-2 would suggest that, in addition to the transmission person-to person, other ways – like airborne – can be also involved in the transmission of this coronavirus (Hadei et al., 2020). Anyhow, despite these clear indications, the determination of the relative weight of air pollution, as well as the identification of the main pollutants potentially responsible of the airborne transmission of SARS-CoV-2, are issues that need still to be widely investigated (Contini and Costabile, 2020; Lewis, 2020).

3. Air pollution and COVID-19/SARS-CoV-2

We next summarize the scientific information that is currently available in the databases Pubmed (https://pubmed.ncbi.nlm.nih.gov/) and Scopus (https://www.scopus.com/), using "air pollution/pollutants" and "COVID-19/SARS-CoV-2" as keywords. The last search in these databases was carried out in June 15, 2020. Paper focused on assessing air quality changes in large cities, regions or countries during the COVID-19 lockdowns were excluded because to assess the air quality during the lockdowns was not the objective of the current review. As expected, all papers selected in the present review have been published since March 2020. Most available studies have been conducted in Northern Italy, a region in which at the beginning of the pandemic, the number of infected people and the severity of the COVID-19 were especially relevant. The first information on this topic was the Position Paper launched on March 16 b y the SIMA (Italian Society of Environmental Medicine), in which a potential link between the high levels of particulate matter (PM2.5 and PM10, which are known to negatively affect human health) in various regions of Northern Italy, and the high impact of COVID-19 in those areas, was hypothesized. Several Italian studies on this issue have been published in the last weeks. Most authors agree that air pollution is a risk factor for COVID-19 (Fattorini and Reggoli, 2020; Martelletti; Martelletti, 2020; Sciomer et al., 2020; Zoran et al., 2020).

Specifically, Setti et al. (2020a) have analyzed up to 34 samples of outdoor/airborne PM_{10} from an industrial site of Bergamo Province, the epicenter of the Italian COVID-19 epidemic from February 21 to March 11, 2020. The authors have shown that SARS-CoV-2 can be present on outdoor PM in conditions of atmospheric stability and high concentrations of PM_{10}, being this the first experimental evidence that this coronavirus can be found on PM (Setti et al., 2020b; Distante et al., 2020). Thus, the presence of SARS-CoV-2 on PM_{10} outdoor air samples might potentially mean an early indicator of COVID-19 (Setti et al., 2020b). Confirmations of this preliminary evidence are currently ongoing in Milan and Naples (Italy), Madrid, Barcelona and Tarragona (Spain), Bruxelles (Belgium), and New York (USA), under the RESCOP (Research group on COVID-19 and Particulate Matter) International Research Initiative (Setti et al., 2020a). Similar conclusions have been also obtained by Conticini et al. (2020) in a study conducted in Lombardy and Emilia Romagna, Italian regions with the highest levels of virus lethality in the world. Interestingly, both regions were among the most polluted areas of Europe. People living in areas with high concentrations of air pollutants are more prone to develop chronic respiratory conditions and more sensitive to any infective agent. On the other hand, a prolonged exposure to air pollution leads to a chronic inflammatory stimulus, even in young and healthy subjects. Thus, Conticini et al. (2020) concluded that the high level of pollution in these regions of Northern Italy should be considered an additional co-factor of the high level of lethality recorded in these areas. In another investigation also conducted in Northern Italy (Po valley), Frontera et al. (2020b) have concluded that a link between SARS-CoV-2 infection and air pollution would be plausible, which could mean a strong impact on the high rate of infection and mortality. The areas investigated had high concentrations of various air pollutants, especially $PM_{2.5}$ and NO_2. It is known that chronic exposure to $PM_{2.5}$ causes the overexpression of the alveolar angiotensin-converting enzyme 2 (ACE-2) receptor, which can increase the viral load in patients exposed to air pollutants. In turn, this would deplete ACE-2 receptors, impairing host defenses. In addition, high atmospheric levels of NO_2 can provide a second hit, causing a severe form of SARS-CoV-2 in ACE-2 depleted lungs, resulting in a worse outcome. According to the above preliminary results, the internationally recommended interpersonal distance of 1.5–2 m would be considered an effective protection only if individuals are also wearing face masks in their daily life activities (Setti et al., 2020c).

In contrast to the suggestions/conclusions above summarized, Bontempi (2020a) has reported that direct correlations between high levels of particulate matter and the diffusion of the SARS-CoV-2 are not evident. To reach this conclusion, Bontempi (2020a) analyzed the available data about PM_{10} concentrations and infections cases in Lombardy and Piedmont. It was found that the cities of Torino and Alessandria, which were suffering the most severe event of PM_{10} pollution in the 20 days before the sanitary crisis, had low infections cases (0.01% and 0.03%, evaluated on total population, respectively, on March 12). However, in Bergamo, where the limit of 50 $\mu g/m^3$ for PM_{10} concentrations was exceeded only few times, showed the highest number of infectious cases. In order to clarify some potentially confusing information related to airborne diffusion mechanisms of SARS-CoV-2. Bontempi (2020b) have suggested that parameters other than environmental pollution accounting for pollution-to-human transmission mechanisms (e.g., commercial exchanges in human-to-human mechanisms) should be considered to understand the differences in the initial diffusion of the virus in Italy. In a very recent study, Bontempi et al. (2020) have suggested that while initial conditions can respond to preexisting economic and environmental factors, the unfolding of contagion is more non-linear and depends on measures, health care system's efficiency, and other factors, which might explain different results (e.g., the different mortality rates in Veneto vs. Lombardy, for example). In summary, Bontempi et al. (2020) have concluded that the current pandemic's diffusion patterns are caused by a multiplicity of environmental, economic and social factors.

The results of studies aimed at establishing the correlation between air pollution and COVID-19 in countries abroad Europe are – in general terms – in the same line than most of the above reviewed investigations. In a study conducted in California (USA), Bashir et al. (2020b) used Spearman and Kendall correlation tests to analyze the association of $PM_{2.5}$, PM_{10}, SO_2, NO_2, Pb, VOCs and CO, with the COVID-19 cases in that American State. It was found that, at least PM_{10}, $PM_{2.5}$, SO_2, NO_2, and CO levels showed a significant correlation with the COVID-19 epidemic in California. On the other hand, Wu et al. (2020) assessed whether long-term average exposure to $PM_{2.5}$ in the USA was associated with an increased risk of COVID-19 deaths. COVID-19 death counts were collected for more than 3000 counties (representing 98% of the population) across the country up to April 22, 2020. It was observed that an increase of only 1 μg/m^3 in $PM_{2.5}$ was associated with an 8% increase in the COVID-19 death rate, being the results statistically significant and robust to secondary and sensitivity analyses. Liang et al. (2020) also in the USA, carried out a cross-sectional nationwide study in order to assess the potential association between long-term county-level exposure to NO_2, $PM_{2.5}$ and O_3, and county-level COVID-19 case-fatality and mortality rates. A total of 3122 counties were included in that study. Statistically significant positive associations between long-term exposure to NO_2 and COVID-19 case-fatality rate and mortality rate, were found, independently of the concentrations of $PM_{2.5}$ and O_3. It was concluded that prolonged exposure to NO_2, an urban traffic-related air pollutant, may be an important risk factor of severe COVID-19 outcomes.

In England, Travaglio et al. (2020) have investigated the potential links between major air pollutants related to fossil fuels and SARS-CoV-2 mortality in that country. It was found that the levels of multiple markers of poor air quality, including nitrogen oxides and sulfur dioxide, were associated -after adjusting for population density-with an increased number of COVID-19-related deaths across England. In China, Li et al. (2020) investigated whether air quality index (AQI), four ambient air pollutants ($PM_{2.5}$, PM_{10}, NO_2 and CO) and five meteorological variables (daily temperature, highest temperature, lowest temperature, temperature difference and sunshine duration) could increase COVID-19 incidence in Wuhan and XiaoGan between January 26 and February 29, 2020. It was noted that AQI, $PM_{2.5}$, NO_2, and temperature could promote the transmission of the coronavirus and the increase of COVID-19. Based on this finding, a conclusion of the study was that personal protective devices, mainly facial masks, are suggested for coronavirus protection, especially for those subjects residing in highly polluted regions. With respect to the effects of AQI, Xu et al. (2020) collected daily data of COVID-19 confirmed cases, air quality and meteorological variables of 33 Chinese locations for the outbreak period between January 29 and February 15, 2020. The results suggest an enhanced impact of AQI on the COVID-19 spread under low relative humidity. In turn, Zhu et al. (2020) assessed the relationship between ambient air pollutants and the infection caused by SARS-CoV-2 in 120 Chinese cities. The association of $PM_{2.5}$, PM_{10}, SO_2, CO, NO_2 and O_3 with confirmed cases of COVID-19 was investigated. It was found that a 10-μg/m^3 increase in $PM_{2.5}$, PM_{10}, NO_2, and O_3 was related with a 2.24, 1.76%, 6.94% and 4.76% increases in the daily counts of confirmed cases, respectively. By contrast, a 10-μg/m^3 increase in SO_2 was associated with a 7.79% decrease of cases.

On the other hand, Ogen (2020a) have assessed the contribution of a long-term exposure to NO_2 on COVID-19 fatality. For it, three databases were combined: the tropospheric concentration of NO_2, the atmospheric condition as expressed by the vertical airflow, and the number of fatality cases. Data were obtained from 66 regions of France, Germany Italy and Spain. The Sentinel-5P satellite data showed two main NO_2 hotspots over Europe located in Northern Italy and the Madrid metropolitan area, respectively. Among the 4443 fatality cases included by Ogen (2020a) in his study, up to 78% corresponded to five regions located in these two areas. It was concluded that chronic exposure to NO_2 could be an important contributor to the high COVID-19 fatality rates observed in both areas. However, this conclusion was questioned by Chudnovsky (2020), who raised that only two months of exposure to NO_2 could not be considered as a long-term/chronic exposure. Chudnovsky (2020) also indicated that in countries like Taiwan - with much higher air concentrations of NO_2 - had low fatality cases. The response of Ogen (2020b) was that his results simply showed that the highest number of cases was observed in highly polluted areas of Europe, with very important cultural differences with respect to Taiwan, which would make hard a comparison of the results.

In another vein, recently Tsatsakis et al. (2020) have discussed how long-term exposure to thousand chemicals in mixtures, mostly fossil fuel derivatives, exposure to PM, metals, ultraviolet (UV)–B radiation, ionizing radiation, and lifestyle contribute to immunodeficiency observed in the contemporary pandemics, such as COVID-19. The authors have noticed that environmental-related diseases (e.g., energy-metabolism-immune mediated obesity, type II diabetes, metabolic syndrome and cancers) and infectious diseases (e.g., parasitic, influenza or coronavirus-related epidemic or pandemic) share the same pathogenic mechanisms at the molecular level, particularly the AhR pathway. The immunotoxicity risk of vulnerable groups, taking into account biochemical and biophysical properties of SARS-CoV-2 and its immunopathological implications, were discussed and the common mechanisms by which xenobiotics and SARS-CoV-2 act at the cellular and molecular level was underlined.

4. Conclusion

The results of most of the studies hereby reviewed suggest/conclude that chronic exposure to certain air pollutants might lead to more severe and lethal forms of COVID-19 and delays/complicates recovery of patients suffering this disease. This suggestion/conclusion, which is obviously new for the SARS-CoV-2, seems to follow a similar pattern as other respiratory viruses. Thus, a notable evidence supports a clear association between concentrations of various air pollutants and human respiratory viruses interacting to adversely affect the respiratory system (Domingo and Rovira, 2020).

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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