

A first review to explore the association of air pollution (PM and NO₂) on severe acute respiratory syndrome coronavirus (SARS-CoV-2).

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Abstract

A new coronavirus (SARS-CoV-2) have determined a pneumonia outbreak in China (Wuhan and Hubei) on December 2019. While pharmaceutical and non-pharmaceutical intervention strategies are strengthened worldwide, the scientific community has been studying the risk factors associated with SARS-Cov-2, to enrich epidemiological information. For a long time, before the industrialized era, air pollution has been a real and big health concern and it is today a very serious environmental risk for many diseases and anticipated deaths in the world. It has long been known that air pollutants increasing the invasiveness of pathogens for humans by acting as a carrier and making people more sensitive to pathogens through a negative influence on the immune system. Based on scientific evidences, the hypothesis that air pollution, resulting from a combination of factors such as meteorological data, level of industrialization as well as regional topography, can acts both as an infection carrier as a harmful factor of the health outcomes of COVID-19 disease has been raised recently. This hypothesis is turning in scientific evidence, thanks to the numerous studies that have been launched all over the world. With this review, we want to provide a first unique view of all the first epidemiological studies relating the association between air pollution and SARS-CoV-2. Major findings are consistent, highlighting the important contribution of air pollution on the COVID-19 spread and with a less extent also PM₁₀.

Keywords: Air pollution; Particulate Matter; Nitrogen dioxide; COVID-19; Pandemic

1. Introduction

A new coronavirus (SARS-CoV-2) have determined a pneumonia outbreak in China (Wuhan and Hubei) on December 2019. SARS-CoV-2 is the etiologic agent of COVID-19, it is mainly spread by close contact (about 6 feet) with respiratory droplets. Symptoms are similar to other viral upper respiratory illnesses (Chavez et al., 2020) such as fever, cough, dyspnoea, and fatigue (Huang et al., 2020). The three main forms are a minor disease with the involvement of the upper airways, non-severe pneumonia, and severe pneumonia complicated by acute respiratory distress syndrome (ARDS) (Chavez et al., 2020; Chen et al., 2020). In experimental condition, it has be proven a convincing aerosol transmission of SARS-CoV-2 with the COVID 19 pathogen viable and infectious in aerosols for some hours and on surfaces up to days (van Doremalen et al., 2020), similarly with findings related to SARS-CoV-1 that is transmitted in association with nosocomial and super-diffusion events (Chen et al., 2004).

Acute respiratory distress syndrome (ARDS) is a form of non-cardiogenic pulmonary oedema, originated by injury to alveoli following an inflammatory pathway, that can beginning by lung or how systemic form (Sweeney and McAuley, 2016). In the twenty-first century we have had two new coronaviruses in humans: severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV), that are able to lead ARDS with high mortality (Martelletti and Martelletti, 2020).

For a long time, before the industrialized era, air pollution has been a real and big health concern and it is today a very serious environmental risk for many diseases and anticipated deaths in the world. (GBD 2017 Risk Factor Collaborators, 2018). It has long been known that air pollutants increasing the invasiveness of pathogens for humans by acting as a carrier and making people more sensitive to pathogens through a negative influence on the immune system (Becker and Soukup, 1999; Cai et al., 2007). One of the mechanisms by which ambient PM exerts its proinflammatory effects is the generation of oxidative stress by its chemical compounds and metals (Li et al., 2008; Signorelli et al., 2019). Many studies reported an association between short- and long-term exposures to ambient air pollutants and numerous adverse health effects (e.g. higher mortality rates, greater hospital admissions, increased outpatient visits) (Bremner et al., 1999; Cohen et al., 2017; Dockery et al., 1993). It has notably deleterious effects on asthma, bronchitis, pneumonia and COPD (Dick et al., 2014; Perng and Chen, 2017; Raji et al., 2020; Vignal et al., 2017; Yarahmadi et al., 2018). Furthermore, air pollution is a recognized aggravating factor for infection diseases caused by viral infection such as respiratory syncytial virus (RSV), influenza A and B, para influenza virus type 3, pneumonia and influenza-like illness (Carugno et al., 2018; Croft et al., 2020; Fukuda et al., 2011;

Huang et al., 2016; Huh et al., 2020; Liang et al., 2014; Lin et al., 2005; Silva et al., 2014; Somayaji et al., 2020).

Based on scientific evidences, the hypothesis that air pollution can become vector of the infection and harmful factor of the health outcomes of COVID-19 disease has been raised recently (Conticini et al., 2020; Frontera et al., 2020; Isaifan, 2020; Martelletti and Martelletti, 2020). This hypothesis is turning in scientific evidence, on the basis of the numerous studies that have been launched all over the world.

With this review, we want to provide a first unique view of all the first epidemiological studies relating the association between pollution and meteorological data with SARS-CoV-2, being aware that not all Authors had the time to study the interferences of confounding factors for obtaining a rigorous interpretation, and also, that associations were performed with very different methodologies of study.

2. Method

We selected representative original epidemiological studies on the association between severe acute respiratory syndrome SARS-CoV-2 and air pollution (PM_{2.5}, PM₁₀ and NO₂) available online by April 26th, 2020. The research of epidemiological studies was conducted in PubMed, Scopus and Google Scholar databases. This review includes articles published in their final version, but also pre-proof and not reviewed preprints. We collected a total of N. 3 papers in their final version, N.1 paper in the pre-proof form, and N.9 papers in their preprint version.

3. Results

3.1 Particulate Matter

First observations report a positive association between ambient concentrations of PM_{2.5} (Guan et al., 2020; Pansini and Fornacca, 2020; Wang et al., 2020; Wu et al., 2020; Yao et al., 2020b; Zhu et al., 2020) and PM₁₀ (Coccia, 2020; Guan et al., 2020; Pansini and Fornacca, 2020; Setti et al., 2020; Yao et al., 2020b; Zhu et al., 2020) with COVID-19 pandemic across the most affected countries: China, Italy and U.S.A. Only one research group provides different conclusions (Ma et al., 2020).

In China Zhu et al. (2020) explored the relationship between particulate matter and the infection caused by the novel coronavirus in 120 cities in China. The Authors included over 58,000 (70%) of daily-confirmed new cases in the whole of China between January 23, 2020 and February 29, 2020. They applied a generalized additive model (GAM) to examine the effects of meteorological factors

(the daily mean temperature (AT), relative humidity (RH), air pressure (AP) and wind speed (WS)) and air pollution, applying a moving-average approach to capture the cumulative lag effect of ambient air pollution. They observed a $10\text{-}\mu\text{g}/\text{m}^3$ increase (lag0–14) in $\text{PM}_{2.5}$ and PM_{10} were respectively associated with a 2.24% (95% CI: 1.02 to 3.46) and 1.76% (95% CI: 0.89 to 2.63) rising in the daily numbers of COVID-19 confirmed cases. Similarly, Wang et al. (2020) applied a generalized additive model (GAM) as well, by controlling daily ambient temperature (AT), absolute humidity (AH) and population migration scale index (MSI), to verify the combination between airborne PM pollution and daily numbers of confirmed case in 72 cities of China (excluded Wuhan city), observing more than 50 cases from January 20th to March 2nd, 2020. In cumulative lag effects, the pooled estimates of 72 cities were all significant and the strongest effects for both PM_{10} and $\text{PM}_{2.5}$ appeared in lag 014 and the RRs of each $10\text{ }\mu\text{g}/\text{m}^3$ increase were 1.47(95% CIs:1.34, 1.61) and 1.64 (95% CIs:1.47, 1.82). In addition, they found that in all included lag days the effects of $\text{PM}_{2.5}$ on daily-confirmed cases were higher than PM_{10} .

Guan et al. (2020) with a time-series analysis conducted from Jan 25th to Feb 29th 2020 a retrospective cohort study taking into account COVID-19 incidence in Wuhan and XiaoGan, two worst hit cities in China. Results obtained from the Pearson regression coefficient analysis showed the incidence positively correlated with $\text{PM}_{2.5}$ in both cities ($R^2=0.174$ and $p<0.02$; $R^2=0.23$ and $p<0.01$, respectively), and with PM_{10} only in XiaoGan ($R^2=0.158$ and $p<0.05$). Furthermore, they also found local temperature correlated with COVID-19 incidence in negative pattern, while no association was found with wind speed and relative humidity.

To determine the association between PM pollution level and the initial spread of COVID-19, an Italian study presented daily data relevant to ambient PM_{10} levels, urban conditions and virus incidence from all Italian Provinces from February 24th to March 13th. They highlighted that the Italian Northern Regions, the most affected by COVID-19, are also the regions with a high amount of PM_{10} and $\text{PM}_{2.5}$ going above the legislative standards (limit, $50\text{ }\mu\text{g}/\text{m}^3$ per day) on February 2020 (Setti et al., 2020). They highlighted how PM_{10} daily over limit value can be a significant predictor of infection.

Similarly, Coccia et al. (2020), by analyzed data on N=55 Italian province capitals, and data of infected individuals to April 7th, 2020, revealed an high association with rapid and wide diffusion of COVID-19 in Northern Italy and the air pollution measured in the days exceeding the set limits for PM_{10} in previous years. In particular, a very high average number of infected individual (about 3,600 infected individuals on 7th April, 2020) were observed in the cities having more than 100 days of air pollution (exceeding the limits set for PM_{10}) and a lower average number of infected (about 1,000 infected individuals) in the cities having less than 100 days of air pollution. The coastal cities have

an average intensity of wind speed (about 12 km/h) higher respect the hinterland cities (8 km/h) and there was a negative coefficient correlation between infected subjects and wind speed intensity.

Other studies explore the association between COVID-19 case fatality and airborne PM. Pansini and Fornacca (2020), compared both COVID-19 cases and deaths, normalised by population size (100,000 residents) and airborne PM levels of Italy, USA and China. The collected diagnosed cases and deaths up to March 23 for Italy, March 24 for China and March 29 for U.S.A. They provide Pearson and Kendall correlation matrices and the corresponding coefficients, according to the distribution type, were analysed. Comparing PM_{2.5} and PM₁₀ data form ground measures retrieved from different databases (WHO for Italy, EPA for U.S.A and University of Harvard Dataverse for China) for previous years they found strong association with COVID-19 cases in all country only for PM_{2.5} (China; tau =0.13 and p<0.01; Italy: tau=0.31 and p<0.001; U.S.A.: tau=0.08 and p<0.02), while only in U.S.A also for PM₁₀ (tau=0.14 and p<0.01). Association with COVID mortality rate was performed only for China and U.S.A and they found a strong association for both PM fractions (PM_{2.5}: tau_{China}=0.19 and p<0.001; tau_{U.S.A.}=0.14 and p<0.001. PM₁₀: tau_{China}=0.11 and p<0.01; tau_{U.S.A.}=0.13 and p<0.02).

In China, Yao et al. (2020) studied both spatial and temporal association of particulate matter pollution and death rate of COVID-19. A cross-sectional analysis was performed to explore the spatial associations of death rate of COVID-19 concentrations in 49 cities including Wuhan, other 15 cities inside Hubei and 33 cities outside Hubei with the daily PM_{2.5} and PM₁₀. They adjusted their results for temperature, relative humidity, gross domestic product (GDP) per capita and hospital beds per capita, trying a positive association between COVID-19 death rate and PM_{2.5} ($\chi^2=13.10$, p=0.011) and PM₁₀ ($\chi^2=12.38$, p=0.015). Furthermore, the authors conducted a time series analysis to look for the temporal associations day-by-day collecting both COVID-19 confirmed cases and deaths information, calculating the case fatality rate (CFR) with a 21-day lag considered from infection to death, examining also the lag effects and patterns of PM_{2.5} and PM₁₀ on CFR. They found how COVID-19 higher case fatality rate is related to increasing concentrations of PM_{2.5} and PM₁₀ in temporal scale especially with lag3 (r=0.65, p=2.8×10⁻⁵ and r=0.66, p=1.9×10⁻⁵, respectively). Contrary to Yao et al. (2020), findings of Ma et al. (2020) observed only a negative association of daily mortality with PM_{2.5} and PM₁₀. The authors collected the daily death numbers occurred from January 20th to February 26th 2020 in Wuhan, China, and used a generalized additive model to examine if there is a link between the daily death counts of COVID-19 and the effect of pollutants, temperature, humidity and diurnal temperature range on, considered the lag effects on COVID-19 death of weather conditions. Furthermore, the study demonstrated a significant positive effect on the daily mortality of

COVID-19 of the diurnal range of temperature, and a significant negative association between ambient temperature as well as relative humidity and COVID-19 mortality.

In the United States, Wu et al. (2020) investigated whether the risk of COVID-19 deaths increases, occurred up to April 04, 2020, is related to long-term average exposure to fine particulate matter (PM_{2.5}), by considering about 3,000 USA counties (98% of the population). They also adjusted their results by population size, hospital beds, number of tested subjects, weather, and socioeconomic and behavioural variables. An increase of only 1 µg/m³ in PM_{2.5} have determined a 15% increase in the COVID-19 death rate (95% CI, 5%, 25%).

3.2 Nitrogen dioxide (NO₂)

First observations report a positive association between ambient concentrations of NO₂ and COVID-19 pandemic across Europe, China and U.S.A (Guan et al., 2020; Ogen, 2020; Pansini and Fornacca, 2020; Travaglio et al., 2020; Yao et al., 2020a; Zhu et al., 2020). As well as for particulates matter, but the paper of Ma et al., (2020) provides different findings, reporting no association between NO₂ and mortality rate in in Wuhan, China.

Guan et al. (2020) and Zhu et al. (2020), by applying the same method explained for PM, observed that the COVID-19 incidence follows a positive pattern association with NO₂ in the city of Wuhan ($R^2 = 0.329$ and $p < 0.001$) and XiaoGa ($R^2 = 0.158$ and $p < 0.05$), and that a 10-µg/m³ increase (lag0–14) in NO₂ was associated with a 6.94% (95% CI: 2.38 to 11.51) increase in the daily numbers of COVID-19 confirmed cases in 120 cities of China, respectively. Pansini and Fornacca, (2020), by applying the same method explained for PM, compared also cases and deaths due to COVID-19 with tropospheric NO₂ quality information of Italy, USA and China, retrieved data from Sentinel-5 Precursor space-borne satellite. They found positive correlation between NO₂ data and COVID-19 cases in China ($\tau = 0.12$; $p < 0.01$), U.S.A. ($\tau = 0.20$; $p < 0.001$) and Italy ($\tau = 0.52$; $p < 0.001$). Association with COVID mortality rate was performed only for China and U.S.A, as for PM, and they found a strong association both in China ($\tau = 0.10$; $p < 0.02$) and U.S.A ($\tau = 0.19$; $p < 0.001$). Travaglio et al., (2020) compared up-to-date, real-time SARS-CoV-2 cases and death measurements up to April 8 2020 from public databases across over 120 sites in different regions of England, with 2018 and 2019 annual average concentrations of NO₂ and NO. They applied the Pearson correlation coefficient, for normally distributed data (NO) or Spearman correlation coefficient for non-normally distributed data (NO₂). The Authors correlate high levels of two NO_x with an increasing of mortality and spread in England by COVID-19. In particular, NO was found positive associated with both diagnosed cases and number of deaths ($R^2 = 0.67$ and $p < 0.05$, $R^2 = 0.59$ and $p < 0.05$, respectively),

while the association with NO₂ was positive but not significant ($R^2 = 0.32$ and $p = 0.20$, $R^2 = 0.50$ and $p = 0.09$, respectively).

A cross-sectional study was performed by Yao et al. (2020a) to evaluate the spatial association of NO₂ levels with R₀ of COVID-19, as well, a longitudinal study to evaluate a day-by-day association between NO₂ and R₀ across 63 Chinese cities, collecting COVID-19 confirmed case information and hourly NO₂ data from the national databases. The cross-sectional study showed a positive association of R₀ with NO₂ in all cities ($\chi^2 = 10.18$ and $p = 0 < 0.05$). The temporal association, conducted for the period between January 27 and February 26, was based on the daily R₀ of 11 cities in Hubei except Wuhan. They revealed that in all the 11 Hubei cities, but Xianning, there was a positive correlations between NO₂ (with 12-day time lag) and R₀ ($r > 0.51$ and $p < 0.005$), suggesting a time basis association between NO₂ and disease spread.

Ogen et al., (2020) in their study gave first results on the relationship between long-term exposure to NO₂ (including the months of January and February 2020 shortly before the COVID-19 spread in Europe) and novel coronavirus fatality in the most affected European countries, concluding that long-term exposure to NO₂ may be a potential contributor to mortality caused by SARS-CoV-2. He collected data concerning the fatality cases from 66 administrative regions in Italy, Spain, France and Germany and correlated mortality with NO₂ concentration in the troposphere measured by the Sentinel-5 Precursor space-borne satellite. The major tropospheric NO₂ hotspots identified was the Northern Italy. In all European regions considered, gas concentrations was between 177.1 and 293.7 $\mu\text{mol}/\text{m}^2$, with airflows directed downwards. Results show that out of the 4443 fatality cases by March 19, 2020, 3487 (78%) were in 5 regions of northern Italy and central Spain. Furthermore, by analysing mortality trends based on NO₂ concentrations it was revealed that the highest percentage of deaths were measured in geographical area where the maximum NO₂ concentration was higher than 100 $\mu\text{mol}/\text{m}^2$ (83%), with a significant decrease where the highest concentration was between 50 and 100 $\mu\text{mol}/\text{m}^2$ (15.5%), and below 50 $\mu\text{mol}/\text{m}^2$ (1.5%).

1. Conclusion

The first scientific evidences collected in the literature highlight the important contribution of air pollution on the COVID-19 spread. In particular, PM_{2.5} and NO₂ were found to be more closely related to COVID-19 spread than PM₁₀.

Nevertheless, major findings of these studies are to be better evaluated because virus vitality and/or many confounding factors are not considered and it determines important limitations for direct comparison of results, and more studies are needed to strengthen scientific evidences and support firm conclusions.

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