AIR POLLUTION LINKED WITH HIGHER MORTALITY RATE BY COVID-19

Saja.M.Shareef¹, Zinah.E.hameed², Saba.N.Abbas³, Khulood.M.Al saraf⁴
¹²³Assistant lecturer, Department of pharmacy, College of pharmacy, Al- Esraa University, Baghdad, Iraq
⁴Assistant Professor, Head of Pharmacy Department, College of pharmacy, Al- Esraa University, Baghdad, Iraq

ABSTRACT:
Coronavirus (COVID-19), is an infectious disease recognized in late December, 2019, in Wuhan city of China, was established as a pandemic by the World Health Organization. Most countries have declared some lockdown to diminish the effects of COVID-19 and terminate the transmission of novel coronavirus. Novel study shows that long-term exposure to air pollution could contribute to higher numbers of COVID-19 fatalities. According to the World Health Organization, 4.6 million individuals die annually from diseases and illnesses directly related to poor air quality. Meteorological conditions may also have a significant role in air pollution–virus interactions. Previous studies have suggested that ambient air pollutants are risk factors for respiratory infection by carrying microorganisms to make pathogens more invasive to humans and affecting the body's immunity to make people more susceptible to pathogens.

Key words: - Corona virus, air pollution, NO2, O3, Particulate matter

I. INTRODUCTION
Coronavirus diseases-2019 (COVID-19) was found in Wuhan district of China in the month of December, 2019 for the first time; COVID-19 has been announced a pandemic by the World Health Organization (¹). After that, the coronavirus was rapidly transmitted and affected several people within a month. Various studies have been conducted to control the spread of COVID-19, and to explore important factors affecting the transmission of SARS-CoV-2 (²). SARS-CoV-2 can cause mild symptoms, including fever, dry cough, and sore throat. However, sometimes could cause severe and even fatal complications such as Acute Respiratory Distress Syndrome (ARDS) (³).

Home isolation, constant hand washing, increasing awareness and individual immunity are very important steps for prevention from infection (⁴).

Poor prognosis in elderly patients and comorbidities have consistently been reported, younger patients lacking the risk factors are similarly being admitted to intensive care, albeit to a less sever and with a different range of symptoms (⁵).

Comorbidities may consist of obesity, hypertension, diabetes, cardiovascular disease, chronic kidney disease, COPD, and malignancy. The Symptoms, when present, is relatively variable, reflecting systemic involvement, including symptoms of lower respiratory tract infection (e.g. cough, fever and dyspnea), neurological deficit, or gastro-intestinal issues, especially in the elderly (⁶).

New suggestion made by the Emerging epidemiological and experimental data relating the involvement of air pollution to COVID-19-related outcomes. Air pollution is a mixture of particulate constituents and gaseous compounds that differ both spatially and temporally (⁷). COVID-19-linked epidemiological studies have explored impacts established on particulate matter (PM) of two sizes, e.g. particles that are inhalable (this with a 50% cut-off aerodynamic diameter of 10 µm (PM10)) and the second are fine particles (particles with a 50% cut-off aerodynamic diameter of 2.5 µm (PM2.5)). It is likewise worthwhile mentioning here that both PM10 and PM2.5
are a proxy for ultrafine particles (diameter <0.1 \text{µm}) \(^{(7)}\). Until now, no official indices for ultrafine particles and nanoparticles, unfortunately. It is possible to know the “order of magnitude” if we put in mind that the amount of particulate matter that can accumulate yearly in a polluted area is in the order of hundreds of tons per 10,000 m\(^2\) (per hectare) \(^{(8)}\).

![Figure 1: The deposition of particulate matter on a biological surface. Colors indicate the ranges of particles dimension: red, \(\varnothing < 1 \text{µm}\); yellow, \(\varnothing \sim 4 \text{µm}\); light blue, \(\varnothing \sim 8 \text{µm}\); blue/dark blue, \(\varnothing \sim 11.5 \text{µm}\). Dimensional bar = 20 µm. Photo courtesy of Professor G. Lorenzini (University of Pisa, Italy), kindly acknowledged](image)

The World Health Organization has exposed that the maximum tolerable limits of PM10 and PM2.5 must not be over the annual average of 20\(\mu\text{g}\) and 10 \(\mu\text{g m}^{-3}\) of air, respectively; and 50\(\mu\text{g m}^{-3}\) and 25 \(\mu\text{g m}^{-3}\) of air in 24 h, respectively \(^{(8)}\). In the European Union and in Italy, the limits are as follows (Legislative Decree 155 of 13/8/2010 and EU Directive 2008/50/EC):

PM10: 40\(\mu\text{g m}^{-3}\) not to be exceeded as annual mean, and 50\(\mu\text{g m}^{-3}\) not to be more than 35 times per year as daily mean.

PM2.5: 25 \(\mu\text{g m}^{-3}\) not to be exceeded as annual mean, with the aim of not exceeding 20 \(\mu\text{g m}^{-3}\) as a yearly mean starting from 1 January 2020\(^{(8)}\).

The final destination inside the respiratory tract or bloodstream and the PM transportability detected by the size and depends on its source, PM can have many different compositions. The carbonaceous particulate matter from coal, wood, or fuel combustion is the most dangerous. It is accountable for several chronic diseases, such as cardiopulmonary and metabolic diseases, cancer, and low birth weight \(^{(9,10)}\). The population-level discovered the gaseous pollutants in correlation to COVID-19 and other respiratory viruses include ozone (O\(3\)) and nitrogen oxides (NO\(x\)). Nitrogen dioxide is a significant air pollutant in urban environments, primarily rise from traffic, particularly from diesel cars, and associated with asthma, COPD, bronchiolitis, and cardiovascular diseases \(^{(11)}\). The tropospheric ozone levels depend on other released pollutants, such as nitric oxide and volatile organic compounds VOCs, climate parameters, and increased cardiopulmonary mortality and morbidity \(^{(8)}\). The spread of COVID-19 was conducted by several studies that explore the essential factors affecting the transmission of SARS-CoV. Ambient temperature has shown an association with the infection of COVID-19 by a recent study. However, the impact of short-term exposure to air pollution lacks careful consideration.

It is interesting to explore the effect of air pollution on COVID-19 infection Since COVID-19 is a respiratory disease and SARS-CoV-2 could remain viable in aerosols for hours. The most common pollutants are particulate air pollution - from traffic emissions, industrial pollution and forest fires \(^{(8)}\).

These molecules are very small - about 3\% of the width of a human hair. It is interesting to explore the impact of air pollution on COVID-19 infection Since COVID-19 is a respiratory disease and SARS-CoV-2 could remain
viable in aerosols for hours. The most common pollutants are particulate air pollution - from traffic emissions, industrial pollution and forest fires. These molecules are very small - about 3% of the width of a human hair. In fact, the poor quality of air may be more vulnerable to this disease to people who live in that area, and airborne particulate matter may help to spread the virus. But world leaders now have a chance to plot a different, cleaner future.

**Links between air pollution and COVID-19: Based on studies**

Among the research addressing the temporary effects of air pollution, novel one displays that long-term exposure to air pollution could be accountable for higher COVID-19 mortalities, and were the first to notice a link between the number of Italian provinces with daily averaged PM10 concentrations beyond the European limit values of 50 µg·m−3 and the subsequent number of COVID-19.

Significant links were found between mean concentrations of PM2.5 through February 2020 and the overall number of Italian COVID-19 cases on 31 March 2020.

A study in the century after the Spanish Influenza Pandemic reported that cities that used more coal had tens of thousands of extra flu deaths compared to cities that used less coal, consider the confounders such as socio-economic and baseline health status. Long-term exposure to air pollution-related to the increased influenza mortality in the USA.

Current research done by researchers at Harvard University – they collect air quality data from 3,000 counties in the US, with analysis on every death and confirmed case of COVID-19 in the US up until April 4. The results exposed that long-term exposure to air pollution increases susceptibility to experiencing the most severe COVID-19 outcomes. This statistically found significant evidence that an increase of 1 g/m3 in long-term PM2.5 (microscopic particulate matter in the air with a diameter of fewer than 2.5 micrometers) exposure is related to a 15% increase in COVID-19 mortality rate. This type of particulate forms by burning fossil fuels; additionally, it is linked to high rates of premature deaths due to lung problems, heart attack and cancer.

Daily confirmed COVID-19 cases were examined in more than 70 cities. In China, city-specific effects of PM10 and PM2.5 on them, Short-term lagged (7 and 14 days) increases in PM2.5 were related to the daily COVID-19 confirmed cases, and the magnitude of the effect was more significant for PM2.5 compared to PM10.

Another study in China searches the short-term levels of six different pollutants (PM2.5, PM10, SO2, CO, NO2 and O3) in 120 cities to determine their association with daily COVID-19 confirmed cases. The study investigated an approximate 2% increase in daily COVID-19 cases for every 2-week lagged 10 µg·m−3 increase in PM2.5 and PM10.

A pre-print study also determined a positive association between NO2 levels measured with a 12-day time-lag and the spread of COVID-19 (estimated with the primary reproduction number R0) in 63 Chinese cities, after adjustment of temperature and humidity.

Concerning the role of longstanding exposure to air pollution, an Italian study stated that (the mean levels of NO2, O3, PM2.5 and PM10 during the past four years, as well as the day’s number that higher than the limit values well-known by the European Commission through the past three years, were both linked with the number of COVID-19 cases in Italy.

Participants, including COVID-19 confirmed cases, that adjusted the models for confounding variables, reported significant positive associations of PM2.5 and PM10 with SARS-CoV-2 infectivity.

**How does air pollution affect COVID-19 comorbidities?**

Many studies showed that prolonged exposure to air pollution, especially Nitrogen dioxide (NO2), a toxic component, may cause many diseases. NO2 pass the atmosphere as a result of anthropogenic activity (mainly fossil fuel combustion from vehicles and power plants) and natural processes (lightning and soil processes). Long term exposure to NO2 associated with hypertension, heart and cardiovascular diseases, increased rate of hospitalization, chronic obstructive pulmonary disease (COPD), significant deficits in the growth of lung function in children, poor lung function in adults or lung injury and diabetes.
Also, other studies have focused on the immune system's response to NO2 exposure. Blomberg et al., 1999, found that exposure to NO2 causes an inflammatory response in the airways (26), and Devalia et al., 1993, showed that these exposures might induce the synthesis of proinflammatory cytokines from airway epithelial cells, which consequently play an essential role in the etiology of airway disease (27).

**The interaction between air pollution and COVID-19 in the human body**

Experimental studies have investigated the effect of concomitant exposure to air pollutants and respiratory viruses suggested that there is an impact of air pollution on COVID-19 comorbidities at the population level in addition to that air pollutants may also reduce the immune response and facilitate respiratory virus replication (28).

**Human studies**

A study included children announced that those who live close to an electronic waste area with high PM2.5 concentrations had remarkably lower the levels of salivary agglutinin (one of the primary antimicrobial proteins and peptides) compared to children who live in a less polluted area (29).

In a randomized double-blind study in which volunteers were introduced to either ambient air or air with elevated levels of NO2 in an environmental chamber, analysis of broncho alveolar lavage has determine that macrophages were less effective in inactivating the influenza virus when individuals were previously exposed to NO2 compared to ambient air (30).

In another randomized double-blind study, nonsmoking volunteers were introduced to wood smoke particles or filtered air before nasal inoculation with a vaccine dose of live attenuated influenza virus. When introduced to smoke particles, nasal lavage showed low levels of interferon-γ-induced protein-10, which may cause a decrease in immune response to viral infection, as interferon-γ-induced protein-10 is involved in the recruitment of cytotoxic lymphocytes (31).

In another double-blind randomized study involved both healthy volunteers and volunteers with allergic rhinitis, nasal inoculation of live attenuated influenza virus was demonstrated after 2h of exposition to diesel exhaust or clean air and come up to that diesel exposure may cause eosinophil activation and elevate viral replication in the allergic group, highlighting the fact that diesel exhaust promotes inflammation and lowers virus clearance in allergic patients (31, 32).

**How nitrogen dioxide (NO2) levels acts as a contributing factor to coronavirus (COVID-19) fatality?**

Nitrogen dioxide NO2 is a gas that mainly released from cars, trucks, power plants and some industrial plants; it is a well-established traffic emissions tracer and linked to multiple adverse health outcomes (33).

Increased levels of NO2 concentration is remarkably linked to respiratory mortality (34). In addition to its responsibility for generating some harmful secondary pollutants such as nitric acid (HNO3) and ozone (O3) (35). WHO has announced that the health risks may potentially occur due to the presence of NO2 or its secondary products. Accordingly, the WHO knows that the health issues arising from NO2 suggest that the world population should protect from exposure to this pollutant (36).

**How do weather-linked conditions affect the air pollution - virus interaction?**

Weather-related conditions may also encompass in air pollution–virus interactions as well as, a current study did not find any evidence of a relationship between solar UV radiation and COVID-19, many studies found that UV radiation has antibacterial and antiviral effect, both through a direct effect and through the formation of O3 and reactive oxygen species (37,38). Air pollution, especially PM, can decrease UV penetration, as determine by several studies which announced that air pollutants such as PM significantly decrease the amount of UVB received by the body and thus, lead to lower vitamin D synthesis (39,40).

In the high concentrations, Ozone can also filter UVB and can cause reduction of vitamin D levels. Vitamin D has an antioxidant effect, which has protective effects against respiratory viral infections and against oxidative stress due to air pollution (41,42). Also, studies announced that vitamin D modulates the inflammatory response to viral infections, regulates the RAAS and that decreased levels of vitamin D may have assisted in the severity of COVID-19 (43, 44).
As viral droplets contain water, humidity may assist in evaporation and rehydration of viral aerosols, and thus be part of viral stability, but its activity in viral transmission and viral activity remains unknown \(^{(45)}\).

Additionally, there is no consensus on the subject, it seems likely that a reduction in humidity which leads to dehydration of macro droplets into smaller droplets which have capacity to stay in suspension in the ambient air, while an increasing in humidity may cause elevation in water content of viral droplets, and thus elevate weight, enabling them to fall to the ground faster \(^{(28)}\).

**FIGURE 2:** Air pollutants- virus association according to climate state \(^{(28)}\).

Humidity have a role in the desiccation or hydration of viral droplets thus, have impact on the droplet size and the persistence of respiratory viruses in the air. Solar ultraviolet (UV) radiations have in vitro antiviral activity and raise the level of vitamin D synthesis. Atmospheric air pollutants may decrease UV penetration which lead to reduction in vitamin D synthesis. Temperature affects the size of the viral droplet. In addition, low temperatures decrease the functioning of airways ciliated cells, while high temperatures may have antiviral activity. Droplet nuclei refer to viral droplets \(\leq 5\mu m\), and it is also called viral airborne or viral aerosol. In addition to the expected effect of air pollutants, which lead to a decrease in respiratory, immune defense, particulate matter (PM) may be implicated in respiratory virus transport. AMP: antimicrobial proteins and peptides; ELF: epithelial lining fluid; RASS: renin-angiotensin-aldosterone system; AT1R: angiotensin II receptor type 1.

**II. CONCLUSION**

Major negative effects on the social and surrounding environment have been reported due to COVID-19, however positive effects have also been observed with respect to air quality. The results of the researches also suggest that long-term exposure to this pollutant may be one of the most important contributing factors to the death caused by COVID-19 in these regions and possibly around the world. Many studies have some implications to control and prevent infection by COVID-19 and the first one is that, governments and the public should pay more attention to regions with high concentrations of PM2.5, PM10, CO, NO2 and O3, since these regions may suffer more serious COVID-19 epidemic. In other words, reducing air pollutants could be a useful way to control COVID-19 infection, to protect human health both during and after the Covid-19 crisis. The choice is ours to act accordingly. Some Studies have some limitations as Harvard researchers admit that they were unable to calculate the differences that would have been available in medical resources on mortality rates, due to lack of data. Although there is a need for more specific studies exploring interactions between air pollutants and SARS-CoV-2 in the

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ambient air and their impact on human health, this review highlights that both short- and long-term exposures to air pollution may be important aggravating factors for SARS-CoV-2 transmission and COVID-19 severity and lethality through multiple mechanisms. Future studies should also examine the role of indoor air pollution, in particular biomass and tobacco smoke, in COVID-19. The fact that both biology and atmospheric chemistry are separately implicated suggests that a more holistic approach to disease management and mitigation is necessary both in addressing the current COVID-19 pandemic and future viral epidemics. We cannot ignore that our surrounding environment may be exacerbating not only chronic disease, but infectious disease as well. In the light of these relationships between air pollution and COVID-19, and by virtue of the precautionary principle, we recommend the reduction of air pollution from all sources, especially that from road traffic and heat generation, through the reinforcement of public health policy.

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