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Correlation between Air Pollution and the Spread and Development of COVID-19 Related Disease

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Potential correlation of exposure to polluted air and the spread and co-development of COVID-19 and severe acute respiratory syndrome, caused by SARS-CoV-2, was examined. The emphasis was given on polluted air in the form of suspended particulate matter or liquid particles in gas or air (so-called dust particles). This study was structured as a systematic literature review of multiple research projects carried out across the globe. Impact of the polluted air particles on the virus spread was examined from the temporal and spatial spread. Furthermore, overall impact of particulate matter and COVID-19 disease on human health human was investigated on a microbiological level.

Despite some ambiguity, through systematic literature review effect of the polluted air on the increased spread of various viruses was demonstrated. Longer exposure to contaminated airborne dust particles has a negative effect on the human immune system and in the case of infection with COVID 19, may even overload it. This can lead to serious consequences for human health or even cause death.

This review article also provides an insight into a more comprehensive analysis of possible correlation between the spreading the virus (SARS-CoV-2) by means of particulate matter and other meteorological variables (such as air temperature and humidity, weather events and climate).

Keywords: air pollution, coronavirus (COVID-19), particulate matter, morbidity, meteorological parameters, air quality

Highlights

- *A strong relationship was found between air pollution and the spread of COVID-19 pandemic in the EU, China and the US.*
- *Particulate matter was found to contribute to morbidity and mortality due to COVID-19.*
- *Higher temperature and humidity have a negative effect on the spread of the SARS-CoV-2.*

0 INTRODUCTION

Coronaviruses are a family of enveloped positive-stranded RNA viruses, which cause a variety of diseases, from mild colds to severe respiratory problems [1]. New SARS-CoV-2, causing COVID-19 disease, was identified on 7th of January 2020. On 11th of March 2020, the World Health Organization announced a pandemic of global dimensions [2]. From the very beginning of the novel virus identification a great emphasis was given on the investigation of virus characteristics and transmission by various research groups, with goal of limiting the virus spread.

Past studies researching the transmission of respiratory virus (RSV) [3] and acute respiratory syndrome (SARS-CoV) [4] in the air, have found that various viruses spread in the form of drip aerosols transmitted by coughing, sneezing, talking or breathing and by physical contact and transmission through contaminated surfaces.

Research of transmission of respiratory viruses based on ribonucleic acid as a genetic material (RNA) has shown that the virus expelled by coughing is present in both larger drip aerosols (> 5 μm) and smaller particles (< 5 μm) [5]. In exposed people, the (previously exhaled or coughed) drip aerosol of larger dimensions (> 5 μm) is lodged in the upper airways (areas of the nose and throat), while drip aerosol of smaller dimension (< 5 μm) can penetrate all the way to the lower respiratory tract (bronchi and alveoli in the lungs) [6].

SARS-CoV-2 is mostly transmitted from a distance of a few centimeters if there are larger aerosols present, to few meters if there are smaller aerosols. If there are drip aerosols of larger size (> 5 μm) it can take a few minutes for them to land on the ground. Aerosols of smaller sizes (< 5 μm) can remain in the air for several hours before they are deposited in the human body or on another surface in the area where the infected subject moves [7]. The distance of transmission of the virus and the persistence of the virus and its infectivity depends on the force of the individual person coughing or sneezing, the transmission procedure (the size of the coughed air cloud) [8], parameters of the internal or external environment and the type of surface [9] on which the drip aerosols are retained, before the infected person passes them on or they enter into another host body through his/her activity. The survey [10] showed that under similar meteorological conditions (air temperature from 21 ºC to 23 ºC and relative humidity 40 %) different types of surfaces can affect the temporal and effective stability of SARS-

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CoV-2: plastic (up to 72 h), stainless steel (up to 48 h), cardboard (up to 24 h) and copper (up to 4 h).

However, the recent review [11] showed that outdoor SARS-CoV-2 concentrations are very low and often under detection limits so that airborne transmission could eventually be limited to crowded sites and small indoor environments with poor ventilation. On the other hand, that one of the first paper [12] addressing the problem of studying correlations among COVID-19 cases and mortality with pollution mentioned that long-term exposure could eventually make susceptible individuals more prone to have strong effects of COVID-19 and even mortality. The correlation with number of cases is not indicating a causal relationship because there are a large number of confounding factors that needs to be taken into account such as population density, transmissibility that induces spatial autocorrelations, movement of people that influence both probability of contagion.

1 IMPACT OF METEOROLOGICAL PARAMETERS

The spread of coronaviruses in the external environment is influenced by several meteorological parameters (air temperature, air humidity, air movement and solar radiation).

1.1 Air Temperature

Survey of meteorological variables and disease rates for COVID-19 in 190 countries [13] showed a clear association of air temperature with the spread of viruses. When temperature rises from 5 ºC to 11 ºC, the risk of COVID-19 disease is reduced by up to 28 %. In their time series study (carried out between 23rd January 2020 and 13th April 2020 at 415 locations in 190 countries) an increase of air temperature from 7 ºC to 22 ºC was associated with the decrease of 25 % in the cumulative risk of the COVID-19 incidence over a 14-day period [14]. The study [14] found that with the formation of seasonal influenza and the lowering of temperatures, the lipid-containing virus envelope (including SARS-CoV-2 [15]) stabilizes and contributes to the persistence of the virus. Low air temperature inhaled through the nasal canal by cooling the nasal epithelium (avascular tissue) inhibit the production and transport of mucus. Low temperature reduces phagocytic ability of cells in the upper respiratory system, which may increase the amount of virus in the body [16].

1.2 Air humidity

Various studies have shown a clear association between air humidity and the spread of viruses, which is not unique. As the relative humidity of the air increases by up to 72 %, the risk of COVID-19 disease also increases [13].

When the virus is clinging to a drop of water, lowering relative air humidity leads to the crystallization of the salt, which consequently lowers the salt concentration in the water thereby stabilizing ineffective virus (virion) [17]. transmission rate will be increased due to lower air humidity levels and evaporation, which retains the virus in/on smaller particles in the liquid state and makes it harder for particles to drop on the floor. A review of viability of the virus in different climates [9] came to a similar conclusion. It says that at the same time lower temperatures (6 ºC) and relative humidity (50 %) of the air (moderate climate belt) virus is nevertheless more stable than in higher temperatures (20 ºC) and relative humidity (80 %) of the air.

1.3 Wind Speed

When the wind blows faster (above 6 m/s), the virus's ability to spread is reduced [13]. In outside spaces, the virus is more easily dispersed due to its own low weight and stronger movement of the air mass.

1.4 Solar Radiation

Stronger solar radiation is credited for a faster rate of virus decay in/on the medium through which it is transmitted. The survey [18] concluded that the average virus decomposition time, found in the medium (saliva), is halved when compared with the intensity of the simulated light between early autumn/ winter/summer. The theory [19] assumes, that only UV-B spectrum of electromagnetic radiation from sunlight hits the RNA of the virus and damages it, is not sufficient enough to justify results [20] thus leaving space to a greater role of UV-A spectrum of light.

2 IMPACT OF AIR POLLUTION

Air pollution is caused by releasing gaseous, liquid or solid pollutants into the air naturally or due to human factor. Viruses are most easily spread by particulate matter that can differentiate based on the state of matter, chemical composition, size and shape. Particulate matter (dust particles) most commonly originate from bare surfaces (e.g. deserts), by transmission of seawater by natural fires [21]. They can also originate from anthropogenic activity as a by-product of the following activities: the production of electricity and heat from fossil fuels and wood chips, transport based on fossil fuels and industrial activities such as petrochemical, metallurgical, ceramic, pharmaceutical and other activities as evidenced by reports from Slovenia [22] and the EU [23]. Particulate matter polluted air is found in urban centers, where most of the industrialized world population lives, which is also credited with the highest share of emissions in history [24] next to recently emerging large countries (China and India), as shown in a survey [25].

Study [26] examined the impact of particulate matter concentration in Italian municipalities, where it argued that prolonged pre-COVID exposure to, and contemporary levels of particulate matter can play a positive and significant role. Particulate matter concentration impact on daily deaths between the first COVID-19 outbreak in Italy and the previous five years was studied and the findings showed a positive and significant effect of botch components.

The virus-laden aerosol particles eventually present in atmosphere are dry residual of evaporated droplets (i.e. droplet nuclei) rather than agglomerate with pre-existing particles. There is a small, but not negligible, probability that virus-laden aerosol could act as a sink of ultrafine particles (around 0.01 µm in diameter). However, this will not change significantly the dynamics of the virus particles or their permanence time in atmosphere. Therefore, the probability of airborne transmission due to respiratory aerosol is very low in outdoor conditions, even if it could be more relevant for community indoor environments [27].

Weather and climatic conditions favorable for increased deposition of submicron aerosols (and infectious aerosols) due to supersaturation in the airways, can be linked to seasons of respiratory infections and an increase in the respiratory symptoms of asthma and chronic obstructive pulmonary disease (COPD). Thus, while all available evidence in favor of the critical role of air humidity, and decrease in air temperature, and supersaturation in the airways increasing the risk of developing respiratory symptoms is circumstantial [28].

Unfortunately, premature and unsubstantiated claims that SARS-CoV-2 coagulates (creates clusters) with outdoor particulate matter (PM_{10}) in the air, and that SARS-CoV-2 can be transported by air pollutants, have been widely circulated and cited by many researchers as fact, as a result of the misinterpretation of statistical data and misuse of specific terminology. The current work shows that these mistakes have resulted in the creation of a new epidemiological myth [29].

2.1 Particulate Matter

Particulate matter transport different chemical components and micro-organisms and may be inhaled through the mouth or nose and, due to their different sizes, are deposited in different areas of human body (Fig. 1).

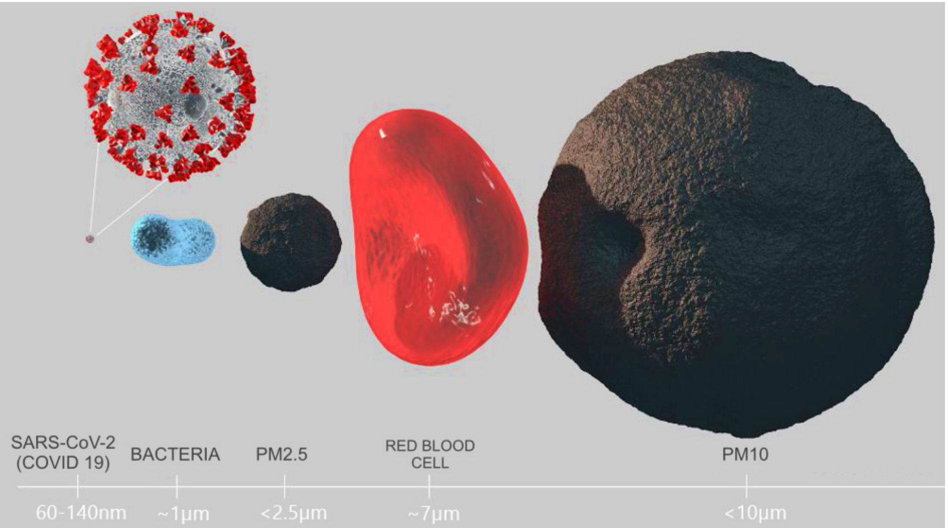

Fig. 1. *Comparison of particles (PM2.5 and PM10) sizes and SARS-CoV-2 virus size* [30]

Larger particulate matter (> 10 μm) are usually deposited in the oral and nasal cavity and throat. Breathing through the nose is usually safer due to the successful filtering of particulate matter because of nose hair and greater change in direction through which inhaled air flows and consequently stops particles. Bigger particles which do not stop in these parts of the respiratory system may also penetrate the trachea. There they can be removed through mucus, or they enter the body. Smaller particles can penetrate all the way to the pulmonary follicles. Only 1 % of 10 μm particles can access the pulmonary follicles, according to the World Health organization (WHO) [31], while particles of 2 μm have a higher chance of penetration. Particles of less than 2 μm (about 0.5 μm) on average do not exceed 10 % to 15 % ability due to the respiratory system exhalation. Meanwhile, ultrafine particles (0.1 μm) are much more likely to remain in the system. They enter the bloodstream and internal organs via diffusion [32].

Exposure to particulate matter in polluted air is in itself are problematic from the standpoint of the impact on the human health in the form of diseases [31], [33] and [34] such as:

- lung disease caused by accumulation of dust in the lungs,
- cancer that may develop due to inflammation of the lung tissue,
- cardiovascular disease,
- blood, kidney and central nervous system poisoning due to body absorbing toxic,
- chemicals that trigger reactions in other organs,
- infectious diseases,
- skin reactions,
- neurodegenerative disorders,
- deterioration of other diseases such as asthma.

Burnett et al. estimate that in 2015 there was around 8.9 million deaths due to long-term exposure to particulate matter in ambient air and subsequent development of the aforementioned diseases [35] requiring assumptions about equivalent exposure and toxicity. We relax these contentious assumptions by constructing a $PM_{2.5}$-mortality hazard ratio function based only on cohort studies of outdoor air pollution that covers the global exposure range. We modeled the shape of the association between $PM_{2.5}$ and nonaccidental mortality using data from 41 cohorts from 16 countries - the Global Exposure Mortality Model (GEMM). The number of deaths is comparable to 10.3 million due to nutrition and 6.3 million smoking-related deaths (as a separate parameter) which are two of the largest causes of death respectively. As a result, many describe the consequences of air pollution as a 'silent epidemic' of large dimensions [36].

3 PARTICULATE MATTER AND SARS-CoV-2

3.1 Temporal and Spatial Impact of Particulate Matter

The likelihood of interactions of pre-existing particulate matter in the atmosphere and virus-laden aerosols was studied in the cities in Italy [27] but the relative importance of airborne transmission is still controversial. Probability of outdoor airborne transmission depends on several parameters, still rather uncertain: virus-laden aerosol concentrations, viability and lifetime, minimum dose necessary to transmit the disease. In this work, an estimate of outdoor concentrations in northern Italy (region Lombardia. The maximum probability of particulate matter merging with viral aerosols is when particles are approximately 0.01 μm (ultrafine particulate matter) in size. However, due to the reduced overall presence of concentrations of genetic material in ambient air (excluding crowds of people) this would not contribute to the significant spread through space and time. Chemical analyses of PM_{10} concentration samples from Bergamo in Italy [37], confirmed the presence of SARS-CoV-2 genetic material, but did not confirm infectiveness. A similar study was conducted in the Lombardy region in Italy [38], where they analyzed the relationship between PM_{10} concentrations and the number of cases of infected cases in different regions. Direct correlation could not be established as the maximum number of cases appeared in some provinces that did not have the highest PM_{10} concentrations. Due to the uncertainty of faster virus spread, focus was given on studies which investigated correlation of long-term exposure to particulate matter and the negative impact of COVID-19 disease on human health.

3.2 Impact on COVID-19 Disease and Mortality

Research review [39] of negative effects of particulate matter on human health and the exploitation of them by SARS-CoV-2 showed that the virus at the cellular level typically exploits the vulnerability of cells that have been damaged by long-term exposure to air pollution (different sizes and chemical compositions) through oxidative stress and inflammation of cells.

Oxidative stress occurs when harmful substances are present in the organism. These substances cause a state of imbalance between free radicals (chemically reactive molecules containing oxygen with free electrons) and antioxidants in the human body. The right amount of these compounds (free radicals) occurs with normal oxygen metabolism and contributes to the defense mechanism against different microbes. Harmful substances cause production of free radicals in large quantities which, when neutralization has not been successful, cause damage to cellular structures in the human body or limit the defense mechanisms against harmful viruses [40].

Particulate matter shows an intrinsic oxidant generating capacity that is correlated with the physical-chemical characteristics of the particles, such as their surface properties and their chemical composition. In [41] the analysis of the oxidative potential of PM_{10} was integrated with PM_{10} characteristics. These results support the idea that the oxidative potential of PM could be an indicator of cytotoxicity of PM. When acellular and cellular assays of oxidative potential are compared, it seems that cellular assays are more representative of cytotoxicity. However, these results should be validated with further studies done in different seasons (at the same site) and different sites (for example urban and industrial areas).

Cell inflammation due to particulate matter exposure eventually weakens the immune system response and causes impairment of the ability of white blood cells, such as macrophages to successfully perform phagocytosis process to disable microorganisms [42]. In [43] it was shown, that the human immune system responds to COVID-19, also by producing interleukin (e.g., Interleukin-6, IL-6), which contributes to the defense by stimulating a more vigorous immune response. If the immune system response is too strong (as in the case of cytokine storms) and immune cells produce too much interleukin (IL-6) the effect is the reverse. Immune system response is so vigorous that it starts to attack or harm microbes as well as healthy cells through various products that should eliminate attack of microbes. In patients with severe symptoms of COVID-19, inflammation can be limited by inhibiting interleukin access (IL-6) to IL6R receptors and limit the development COVID-19 disease itself [44] but after review, treatment was liberalized to patients with lower oxygen requirements. Patients were divided into two groups: those requiring ≤ 45 % fraction of inspired oxygen (FiO_2). The immune system responds similarly to particulate matter i.e., by secreting IL-6 [45]. Due to these processes, it is evident that a long-lasting presence of particulate matter in the human body and a consecutive infection with COVID-19 disease, may overload the human immune system. In a longitudinal study [46] it was also suggested that particulate matter further stimulates the response of the immune system when already dealing with COVID-19 and can overload it, which can result in higher mortality.

In [47] the contribution of air pollution to COVID-19 disease in England, while taking into account socio-economic, demographic and health-related characteristics of the population, it was determined that the increase in long-term exposure to concentrations of $PM_{2.5}$ to 1 μg/μm³ was associated with a 12 % increase in the number of COVID-19 cases. When examining the correlation between air pollution and the increase in COVID-19 deaths in three French cities [48], the researchers were able to establish the levels of particulate matter concentrations ($PM_{2.5}$ and PM_{10}) above which the number of deaths due to COVID-19 could be significantly increased. To mitigate the number of deaths related to COVID-19, the concentration level should be lower than 17.4 μg/μm³ for $PM_{2.5}$ and 29.6 μg/μm³ for PM_{10} in Paris, from 15.6 μg/μm³ for $PM_{2.5}$ and 20.6 μg/μm³ for PM_{10} in Lyon and from 14.3 μg/μm³ for $PM_{2.5}$ and 22.04 μg/μm³ for PM_{10} in Marseille. Study in Germany [49] confirmed the link between environmental pollutants ($PM_{2.5}$, PM_{10}, O_3, NO_2), meteorological indicators and cases of disease and death due to COVID-19. Germany presents an unique case as it at the time faced a relatively high number of infectious cases of disease, but very low COVID-19 mortality. The concentration between particulate matter ($PM_{2.5}$ and PM_{10}) present in Germany has a high compliance with the number of cases of disease but does not have such significant association with the number of deaths due to COVID-19. Data analysis thus supports the fact that a lower level of environmental pollution presents a known contribution to the fight against coronavirus, as Germany has high quality health services, with a high proportion of renewable energy sources in the electricity generation sector [50].

Similar link was established in a study in the United States where research was conducted [51] across more than 3,000 counties. Very strong correlation between long-term exposure to air contaminated was shown with $PM_{2.5}$ particles and death by COVID-19. The study further highlights that COVID-19 mortality also depends on other variables such as: population size, age of population, population density, socioeconomic status of people, number of hospital beds available, behavioral patterns.

In China an extensive survey of 49 cities [52] and 14 cities [53] the extent of this effect requires further investigation. This study was designed to investigate the relationship between long-term exposure to air pollution and the case fatality rate (CFR demonstrated that long-term exposure to contaminated air with $PM_{2.5}$ and PM_{10} increases the vulnerability of the population to the SARS-CoV-2 and the impact of the development of COVID-19 disease. Negative impact of long-term exposure to different pollutants in the air and its connection to COVID-19 morbidity was also demonstrated in the [54]. Statistical analysis showed that increases in $PM_{2.5}$, PM_{10}, NO_2 and O_3 by 1 μg/μm³ may result in 1.95 %, 0.55 %, 4.63 % increase and 2.05 % reduction in morbidity for COVID-19. Whereas the analysis did not show a morbidity increase due to the combined impact of COVID-19 and particulate matter, significant association between COVID-19 morbidity and long-term exposure to SO_2 and CO was observed.

In India results of air pollution study related to COVID-19 pandemic in 741 counties studies [55] indicated that a 1 % increase in long-term exposure to solid particles ($PM_{2.5}$) leads to increase in COVID-19 deaths by 5.7 %. However, a survey in Chennai (India) [56] especially the particulate matter (PM found that the areas of cities exposed to prolonged excessive concentrations of PM particles ($PM_{2.5}$ and PM_{10}) also present the highest (initial) proportion (including up to 90 %) of COVID-19 sufferers. Later measures against the COVID-19 pandemic (reduction in industrial production, transport) lowered concentrations of air pollution (including by 80 %), which moderated the effects of SARS-CoV-2.

Based on the presented studies, we can observe that particulate matter together with SARS-CoV-2 disease pose an additional hazard. The particulate matter itself causes damage and have adverse effects on human health.

4 DISCUSSION AND CONCLUSION

Various studies [39] show that increased exposure to air polluted by particulate matter has a negative effect on a person's immune system and may, while fighting COVID-19 disease, overload immune system. Overloading the immune system can lead to serious consequences for human health or even to death. In order to better understand the development of the disease itself, it would be necessary to further study how various disease development mechanisms function in relation to other with other factors mentioned. Due to the proven correlations between polluted air, which in itself harms human health and the spread of the virus and the development of COVID-19 diseases, there is also an urgent need for air quality control. This could be done by performing air quality measurements at a large number of locations in cities and rural areas, regular improvement of atmospheric dispersal models and building more effective communication routes, thus making the public more aware of current air quality and expected air quality in the near-future. In order to improve air quality, it would make sense to perform short-term solutions such as: limiting containment around the source of pollution, technical systems to improve the quality of internal [57] however, were debated, especially regarding quantitative recommendations. The answers to \"what is the safe distance\" and \"what is sufficient ventilation\" are crucial to the upcoming reopening of businesses and schools, but rely on many medical, biological, and engineering factors. This study introduced two new indices into the popular while perfect-mixing-based Wells-Riley model for predicting airborne virus related infection probability - the underlying reasons for keeping adequate social distance and space ventilation. The distance index Pd can be obtained by theoretical analysis on droplet distribution and transmission from human respiration activities, and the ventilation index Ez represents the system-dependent air distribution efficiency in a space. The study indicated that 1.6 m to 3.0 m (5.2 ft to 9.8 ft and ambient air, the use of fuels with lower emissions of particulate matter for heating households and propelling individual and public transport. Long-term measures to address the reduction of air pollution include investments in installations that are not based on fossil fuel for the production of heat and electricity in households, refurbishment of the external layer of buildings making them more energy-saving, investment projects for the technologies that have low or zero particulate emissions in transport and major energy promoting activities which are not based on excessive air pollution.

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