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COVID-19 pandemic through perspective of surface science

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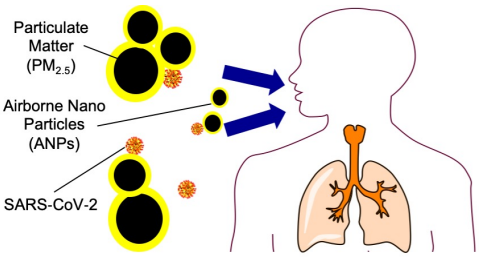
COVID-19 pandemic is once in a century viral outbreak, which has severely affected lives of millions worldwide. The case fatality rate or case-fatality ratio (CFR) for the COVID-19 is in-between 3 to 15 for the countries with low air pollution levels. In contrast, countries severely affected by air pollution have CFR less than 3. Further, the infected COVID-19 cases per 100 thousand people in least air polluted countries far exceeds than those with relatively poor air quality. These number indicate direct link between air pollution and COVID-19 pandemic. However, the observed trends are contradictory to recent research reports, which suggest that the air pollution will worsen the COVID-19 pandemic. Such reports are negatively influencing policy makers and world agencies to devise strategy to deal with the COVID-19 pandemic. The surface science of virus interaction with different available airborne particles such as: particulate matter (PM) and airborne nano particles (ANPs) or nanoparticles (NPs) help us to explain lower CFR numbers and lower deaths per 100,000 population in countries severely affected by air pollution.



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1. Introduction

Coronavirus pandemic have caused severe distress worldwide as available medicines along with several adopted policies by individual governments have failed to halt the wide spread of infection. Many governments worldwide are being forced to take unprecedented steps such as lockdown, international travel ban etc. to control rapid spread of the disease.[1] Further, unavailability of proper medicine and cure has left doctors and researchers to try several combinations of potent drugs, which may or may not address the problem.[2] There is increased effort to design new vaccine, which may end this pandemic.[3] Recent scientific reports show direct link between air pollution and COVID-19 infection.[4-8] It seems a section of researchers are fully convinced that air pollution can influence the rapid spread of virus, however data suggests otherwise. Close look into data compiled by coronavirus recourse center of the Johns Hopkins University shows that many developed countries or countries with lower air pollution levels (with few exceptions) have high case fatality rate (CFR) as well as deaths per 100,000 population.[9] CFR number for a particular country reflects the deaths due to COVID-19 compared to the total number of people diagnosed with COVID-19 for a particular period.

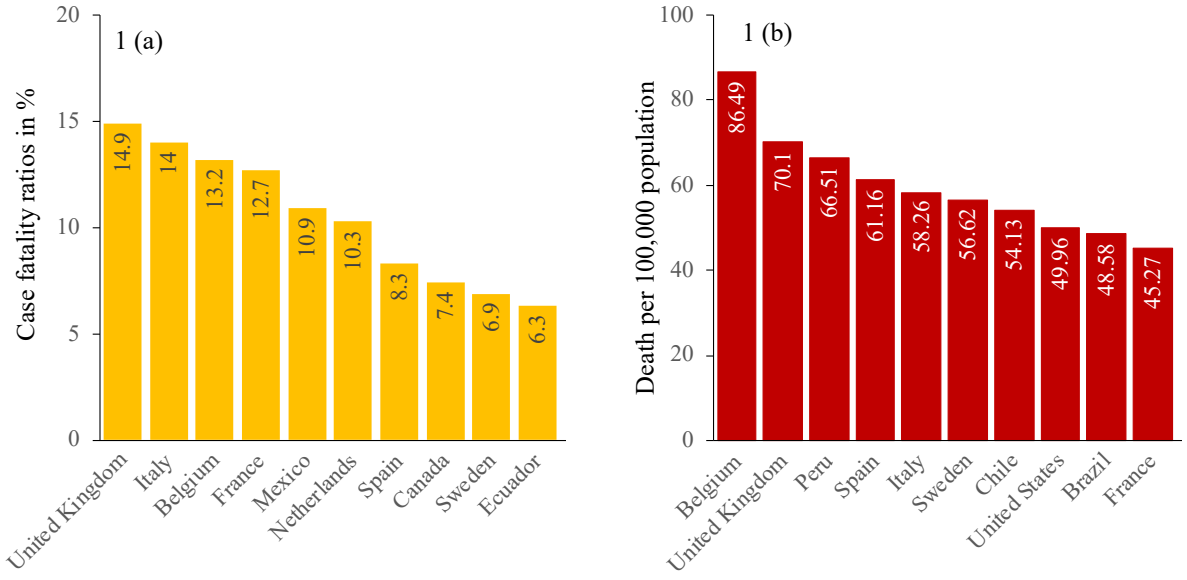

Figure 1. (a) Highest case fatality ratios countries due to COVID-19. (b) Countries with highest death per 100,000 population due to COVID-19. The countries with minimum COVID-19 deaths of 5000 are considered for compiling the data.

Figure 1 (a) shows countries with high CFR and figure 1 (b) shows highest number of deaths due to COVID-19 per 100,000 population for individual countries. Only those countries are considered for compiling the data where deaths due to COVID-19 has crossed 5000 mark. Certainly, the countries with the best medial facility in the world (with the few exceptions) and good air quality have highest CFR and deaths per 100,000 of population. General perception as well as some recent research reports suggest that people living in developing countries will be severely affected by COVID-19 pandemic due to bad air quality. This is supported by the fact that people living in developing countries are significantly exposed to PM and ANPs along with other gaseous pollutants because of rapid industrialization and unrestricted rapid increase in air pollution level.[10] However in contrast, the people living in cleaner environment with low PM and ANPs levels are more severely impacted by COVID-19 pandemic as CFR as well as deaths per 100 thousand population is many times higher in the countries with low air pollution levels. Recent research findings have shown correlation between gaseous nitrogen dioxide (NO2) – an air pollutant for deaths in regions located in north Italy and central Spain.[11] However the report does not completely explain high infection rate as well as mortality rate in other developed parts of the world with low air pollution levels. Countries like United States, United Kingdom, France, Netherland, Belgium, Brazil etc., with significantly lower PM and ANPs levels are the worst affected by this pandemic. Surprisingly people living in Indian subcontinent countries like India, Pakistan, Bangladesh, Nepal that are worst impacted by air pollution having significantly higher PM and ANPs levels, are least impacted countries by COVID-19 pandemic as these countries have lower CFR and lower number of deaths per 100 thousand of their population. According to the IQAir Company, which specializes in providing technology to protect people from airborne pollutants. The top ten most air polluted countries in the year 2019 were: (1) Bangladesh (2) Pakistan (3) Mongolia (4) Afghanistan (5) India (6) Indonesia (7) Bahrain (8) Nepal (9) Uzbekistan and (10) Iraq.[12] Furthermore, half of these mentioned countries are densely populated. Certainly, data show that the most polluted countries are least impacted by COVID-19 pandemic if we consider CFR as well as deaths per 100 thousand population for individual countries. If the month wise data of COVID-19 spread is rigorously scrutinized, a very alarming trend is visible. Developed nations like United States, United Kingdom, France, Spain, Italy, Netherland, Belgium, Germany, Canada, Ireland, Sweden and Switzerland accounted almost 85% of the total COVID-19 deaths at the end of April 2020. These countries accounted for only less than 10% of the total world population and have overall best air quality in the world. Surprisingly people living in majority of developing nations with dense population and comparatively polluted environment at that particular point of time were the least impacted by this pandemic. However, by the end of March 2020 and in April 2020 many developing countries implemented strict lockdowns, this resulted in significant decrease in air pollution levels due to limited economic and industry activity in these parts of the world. Lockdowns led to decrease in air pollution levels with corresponding increase in COVID-19 cases in developing nations.

The perfect example is countries in Indian subcontinent where surge in COVID-19 cases were only recorded after lockdowns were lifted and air quality of these countries improved. So now the question arises what mechanism is controlling the rapid spread of the COVID-19 pandemic or what mechanism is responsible for slow spread of COVID-19?

Dealing with such an infectious virus requires us to understand COVID-19 pandemic via interdisciplinary approach. This requires us to understand this virus in terms of surface science in addition to biological science. Often entry of any virus into host cells involves some biological mechanism, which may be endocytosis or other processes. However the infectious virus must attach to the host cells before it can be taken up by host cell by biological process. What if virus gets adsorbed over external micro and nano surfaces and becomes inactive in outer environment before it is inhaled and taken up by host cell?

2. Role of Surface Science in Containment of COVID-19 Pandemic in the Environment

The COVID-19 has shown tremendous ability to transmit and unlike normal virus it is easily transmitted from infected person to healthy person. One of the modes of transfer is when healthy person inhales coronavirus particles released through sneezing and coughing by infected person as respiratory droplets.[13] What if some external surface is available to virus when it is released as respiratory droplets by infected person? The adsorption of viruses to solid surfaces in contact with water is a well investigated research area.[14-21] Although we have limited information about COVID-19 virus and its survival on different surfaces,[22] however research have established that viruses can only survive for limited time frame on different surfaces.[23] Adsorption of virus over different surfaces can also cause permanent damage to virus structure rendering it ineffective to infect host cells.[24,25] Research findings have also established how some bacteriophages becomes inactive at air-water-solid interface.[26] At molecular level, proteins strongly interact with PM[27] and NPs,[28] which is one of the most abundantly available surfaces present in the environment as air pollutant in developing nations. Thus, virus surface which is composed of membrane proteins can easily get adsorbed over the surface of PM and ANPs by physical forces of interaction. Recent scientific findings suggest that molecular proteins can be easily oxidized and degraded by PM.[29] There are also several studies, which indicate protein-NPs interactions significantly induce changes in protein structure.[30,31]

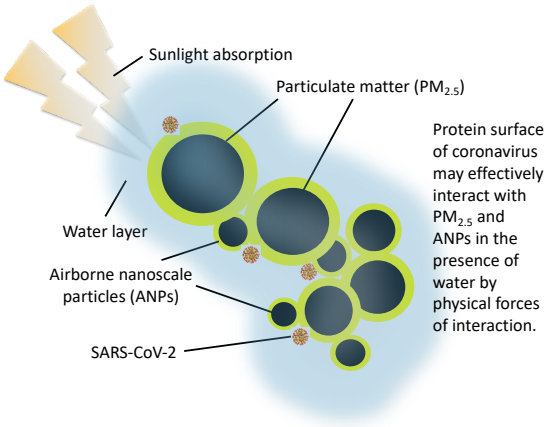

Figure 2. Graphic representation showing possible adsorption of SARS-CoV-2 over solid−water interface. The heterogenous chemical interactions involving water molecules, traces of atmospheric gases, ions etc. along with light absorption by PM or ANPs can bring permanent irreversible damage to virus structure.

ANPs also have higher surface energy compared to relatively larger PM particles and hence larger surface energy of ANPs allows them to attract different types of biomolecules on their surface.[32-34] Therefore, protein outer layer of viruses may interact with PM and ANPs in outer environment as well as inside human body. Research as also established how sunlight[35] and heat[36] could inactivate viruses in environment. Strong absorption of sunlight by PM or ANPs can cause permanent damage to SARS-CoV-2 adsorbed over their surface by either heating or photochemical reaction, rendering it incapable to cause infection (Figure 2). Research findings by Kaan and Hegele have also shown how virus exposed to particulate matter is less infectious as it losses it affinity to infect host cell.[37]

3. Role of Surface Science in Inhibiting or Slowing COVID-19 Virus Replication Process inside Human Host Cell

PM and ANPs present in environment as air pollutants gets free access to the cells of the airway and intracellular components.[38,39] PM and ANPs deposition in the alveolar spaces of the lung also responsible for several diseases as they interfere with normal functioning of cells.[40,41] These fine particles have greater tendency to get deposited depending upon their respective sizes.[42] Recent scientific report suggests that finer $PM_{2.5}$ randomly distributes in lung and extrapulmonary organs even if exposure is for short duration of time.[43] People living in many developing countries are being severely exposed to such particulate matter due to air pollution caused by number of factors including vehicular pollution, rapid industrialization, crop burning, power plants, fossil fuels, dust etc. Certainly this has led deposition of PM in external cell surface and significant ANPs deposition inside the host cell.

The deposited ANPs can interact with wide range of biomolecules and particularly proteins present in cells and such interaction are very common when NPs are introduced to biological fluid.[44] Nanoparticle interaction with proteins and formation of protein corona is a well-established branch of nanoscience and currently being extensively explored for designing new generation of nano-medicines.[45] NPs are able to significantly interact with biological proteins and form NPs-protein corona complexes.[46] NPs-protein corona complex formation involves absorption of proteins onto NPs surfaces in a physiological environment.[47] NPs interact with the proteins present in biological systems in different ways.[48] Initially the proteins present in biological system weakly adsorb to the NPs via non-covalent interactions to form a *soft corona* and eventually the weakly bound proteins are displaced by more tightly binding proteins to form a *hard corona*.[49]

The pre-deposited ANPs present in the host cells of people living in developing nations due to long time exposure to different air pollutants such as metal ions, mineral dust, carbon etc. causes several health hazards because these deposited ANPs significantly interfere with the normal functioning of cells.[40] However the important point to be considered here is: if the pre-deposited NPs present in the host cells causes compromised functioning of normal biological pathways due to strong interactions of NPs with biological molecules present in cell. What will happen if

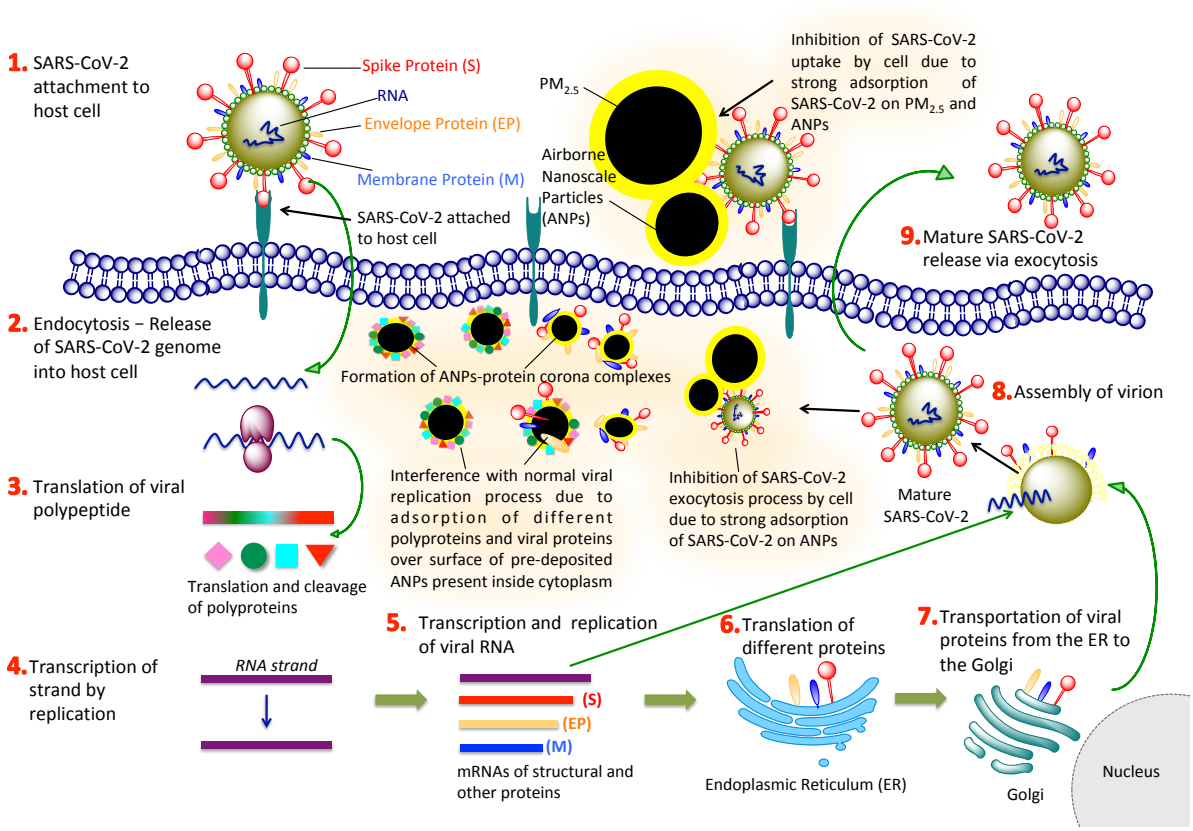

Figure 3. Probable compromised SARS-CoV-2 replication process in host cells exposed to significant level of PM and ANPs.

SARS-CoV-2 infects such system and tries to replicate itself by hijacking host biological pathways? Since NPs have capability to adsorb proteins from biological fluids and form protein layer over its surface called protein corona. Certainly the pre-deposited NPs present in the host cells will significantly affects its replication process in the host cells as viral replication process will be highly compromised due to adsorption of different polyproteins and viral proteins formed at different stages of the viral replication process in the host cells (Figure 3).

4. Surface Science Hypothesizes Counterview Explanation on Impact of Air Pollution on COVID-19 Pandemic

Recent report suggest that exposure to air pollution could increase vulnerability and have detrimental effects on the prognosis of patients affected by the COVID-19.[50] Another scientific report has linked large number of COVID-19 cases during initial spread of infection in China and Italy to $PM_{2.5}$ levels. The report suggested that the $PM_{2.5}$ levels of the areas severely affected by COVID-19 outbreaks in these countries exceeded the hourly standard of 75 μg/m^3.[5] Similar views about negative effect of air pollution on COVID-19 spread has been put forward by other researchers.[51] However it must be noted that $PM_{2.5}$ levels in many big cities of Indian subcontinent as well as in some of the cities of China were twice to five times to this mentioned value at similar point of time and there was limited travel restriction at that point of time. So question arises why infection does not rapidly spread in these parts of world at initial stage of pandemic? Countries of Indian subcontinent like Bangladesh, Pakistan, India

etc. with abnormally high level of $PM_{2.5}$ levels are least affected by COVID-19 pandemic (if we consider CFR numbers and death per 100,000 population in these countries). Also it must be noted that the air quality of the major cities of Australia was very bad during initial months of the year due to Australian bush fire. $PM_{2.5}$ levels in Australian cities crossed alarming level but still Australia is one of the least impacted countries by COVID-19 pandemic. However in recent months the air quality of major Australian cities significantly improved. This has led to some surge in COVID-19 cases in Australia. Our research group has presented a counterview on impact of air pollution on COVID-19 pandemic based on principles of surface science. The SARS-CoV-2 may strongly associate with external micro and nano surfaces present in the environment in the form of air pollutants such as PM and ANPs by the process of adsorption. Physical forces of interaction such as electrostatic interactions along with contributions from the hydrophobic effect, Van der Waals interactions and hydrogen bonding govern the adsorption of viruses to solid surfaces in contact with water.[52] Strong adsorption phenomena may inactivate viruses in external environment and hence countries with high $PM_{2.5}$ levels has low CFR and death per 100,000 population compared to countries with lower $PM_{2.5}$ levels. Also the ANPs deposited in the host cell due to exposure to higher PM or ANPs levels interfere with the viral replication process due to strong interaction of deposited NPs and viral proteins leading to formation of NPs-protein corona complex. The compromised viral replication process may eventually results in lesser viral load in host body and people living in developing world may remain in asymptomatic condition.

5. Direct Relation between COVID-19 Deaths and Air Pollution Levels, and Future Implications

The available data shows direct relation between COVID-19 deaths and air pollution level. Countries with average $PM_{2.5}$ level below 20 μg/m³ (based on average pollution levels in 2019),[12] which can be classified as good air quality level have CFR above 3 and high death per 100,000 population. Table 1 shows list countries with best air quality and data related to total COVID-19 related deaths in these countries.

Table 1. List of countries with best air quality and data related to total COVID-19 related deaths in these countries.

Country*	Total COVID-19 Deaths	Case Fatality Rate (CFR %)	Death per 100,000 Population
United States	163463	3.2	49.96
Brazil	101752	3.3	48.58
United Kingdom	46611	14.9	70.10
Italy	35209	14.0	58.26
France	30327	12.7	45.27
Spain	28576	8.8	61.16
Russia	14,973	1.7	10.36
Colombia	13154	3.3	26.49
Belgium	9879	13.2	86.49
Germany	9203	4.2	11.10

On the other hand, countries which are severely affected by air pollution with average $PM_{2.5}$ level ranging from 38 μg/m³ to 100 μg/m³ (based on average pollution levels in 2019),[12] shows CFR below 3 (with few exceptions) and low death per 100,000 population (Table 2).

Table 2. List of countries with poor air quality and data related to total COVID-19 related deaths in these countries.

Country*	Total COVID-19 Deaths	Case Fatality Rate (CFR %)	Death per 100,000 Population
India	45257	2.0	3.35
Pakistan	6097	2.1	2.87
China	4689	5.3	0.34
Indonesia	5765	4.5	2.15
Bangladesh	3438	1.3	2.13
Afghanistan	1328	3.6	3.57
Kuwait	482	0.7	11.65
UAE	357	0.6	3.71
Bahrain	163	0.4	10.39
Nepal	79	0.3	0.28

Air pollution and particularly airborne particles has sharply dropped to unprecedented levels in major global cities during coronavirus lockdowns.[53] Based on the hypothesis of surface interaction and working principles of interface science, developing nations saw surge in COVID-19 cases in recent months. This may be explained on the basis of decrease in available micro and nano surfaces in external environment due to decrease in air pollution levels. This resulted in increased pathogenicity of SARS-CoV-2. The deactivation mechanism of SARS-CoV-2 that was previously working in favor of countries with bad air quality is now missing. However, people living in some of the worst affected areas by airborne pollutant particles will show some resistance to SARS-CoV-2 infection due to long exposure and deposition of ANPs in their cells. They may become infected but will remain asymptomatic. Therefore there may be net increase in COVID-19 cases in developing nations but the CFR numbers and death per 100,000 of population is expected to remain low.

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