



Impacts of environmental pollution on infection humans by COVID-19

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ABSTRACT

The industrial progress that occurred during the past two centuries (given the huge increase in the number of people) led to the emergence of pollution in all ecosystem types. It is likely that the common cold evolved into flu viruses which mutated into severe acute respiratory syndrome coronavirus (SARS-CoV), then Middle East respiratory syndrome coronavirus (MERS-CoV), and finally coronavirus disease 2019 (COVID-19) with its all strains under pollution conditions. This study can be contributed to a better understanding of COVID-19 evolution and its relationship with environmental pollution. Environmental pollution led to a lot of damage to plants, animals, and finally human health. This can represent the indirect cause of the transformation of the flu virus into COVID-19 over the long term. The cumulative effects of environmental pollution over several centuries contributed largely to the COVID-19 virus emergence. Re-assortment of viral genomes of COVID-19 derived from incubation of different flu strains with SARS-CoV by using overloaded iron (Fe^{2+}) can represent the mysterious role in the evolution of flu to COVID-19 over a long period. As pollution propagation through the food chain, humans will suffer from the concentration of pollutants in their bodies and will be the entrance to viral evolution in the future.

Keywords: COVID-19, Environmental pollution, Heavy metals, Diet system, Ecosystem

INTRODUCTION

Respiratory problems are caused by respiratory viruses over the world. In the past, human coronaviruses were considered unimportant pathogens, which led

to the infection of healthy people with a common cold. A large host range is related to coronaviruses including humans. Although there are four types of influenza viruses (A, B, C, and D) that can cause flu that has negative effects on a healthy person, this person can be given a higher risk of severe illness from COVID-19. The host cell is attached by the influenza virus to penetrate the membrane of the cell. Frequent antigenic variations cause influenza virus evolution. The main difference between the flu and COVID-19 is the speed of transmission. COVID-19 virus has a longer incubation period (the period from infection to symptom onset) than the flu virus. Also, COVID-19 is characterized by a longer sequential period (the time between successive cases where the sequential interval for COVID-19 virus is estimated to be five-six days, while for flu virus, the sequential interval is three days. In this concern, **Liu et al. (2021)** showed that the proportion of leukopenia for COVID-19 patients was 12.00% compared with 31.71% for flu patients. They added that the COVID-19 virus leads to higher creatinine and creatine kinase percentages than flu patients. Many precautionary measures and controls, the most important of which are masks and gloves, were taken daily in order to prevent the transmission of COVID-19 from one human to another. There are still many unresolved inquires regarding viral invasion, pathogenesis, and clinical features for COVID-19 patients. If COVID-19 spreads in your family, you should look around and think seriously about how to protect yourself from this disease?. A used vaccine against COVID-19 may not be highly effective in a person, but it may be effective in another depending on his surrounding environment, diet, and health conditions.

SARS-CoV and COVID-19 target human Angiotensin 1 converting enzyme 2 receptor, while the dipeptidyl peptidase-4 (DPP-4) receptor is the cellular target of MERS-CoV (**Jia et al., 2005 and Raj et al., 2013**). Meanwhile, **Zou et al. (2014)** revealed that Angiotensin-converting enzyme 2 is pivotal in acute lung injury resulting from influenza viruses. In general, SARS's average latency is slightly shorter than COVID (**Arora et al., 2020**). According to **Chan et al. (2020)**, the proportion of genomic characterization of COVID-19 is nearly 80% of the SARS-CoV genome, with additional gene regions. So, it is likely that a chain of genetic mutations that resulting from the mixing of genes from different flu strains with each of SARS-CoV and MERS-CoV occurred in reservoirs of wild animals (bats in particular) to form COVID-19 genome due to an overload of iron (Fe^{2+}). Imbalanced Fe^{2+} , zinc (Zn^{2+}) and magnesium (Mg^{2+}) can be involved in this mechanism. All types of pollution had a negative impact on the surrounding environment with all organisms. There are several possibilities that can be assumed about the reproduction of COVID-19 within the blood, it depends mainly on the diet for a long period (exceeding about three months or more). With respect to

foods, it can increase or reduce the efficiency of Fe^{2+} , Zn^{2+} , or Mg^{2+} absorption in human blood over its normal level. This possibility increases in the presence of polluted food, and chronic diseases such as diabetes, obesity, and chest allergies. So, the objective of this study was to evaluate the cumulative effects of environmental pollution from several centuries to the emergence of the COVID-19 virus.

MATERIALS AND METHODS

A systematic literature search was performed in several well-known databases related to computer science and health science, such as Elsevier, Scopus, Healthline, PMC, Webmd, and Nature using "COVID-19 and its relations with environmental pollution" as a keyword. At first, there were more than 550,000,000 papers queried from all databases. A quick skimming of the title and abstracts of each article was conducted to exclude irrelevant articles that focused more on technical details and hardware rather than the use of this technology for intervention. This selection process was also done to remove duplicate articles across all databases. To review the selected papers, three important aspects were suggested for comparing results from all studies.

RESULTS and DISCUSSION

When Italian explorer Christopher Columbus reached the Americas (New World) in 1492, the new world was divided into North America, Central America, and South America. Meanwhile, the old world included Africa, Asia, and the European continents. Thomas Malthus in the 18th century stated that a growing population would become a problem for food production in the future but did not mention that industry might become a greater danger to humans. The cold or flu virus can mutate into a super virus through genetic mutation and genetic recombination by increased co-contamination as reported by **Zhou *et al.* (2003)**. Particularly, **Tong *et al.* (2013)** revealed that there is a long-term association between host viruses and new world bats as a result of these bats containing more genetic diversity of flu virus than all other mammals and birds. Also, they indicated that bats formed a diverse pool of flu viruses. The industrial revolution began in the middle of the 7th century (AD), when the world's population was about to return to its normal levels, which had been affected by the deaths caused by the black plague that killed 75 million people in 1300 AD. Because of it, the number of the Earth's population rose to one billion in the year 1800, and then to double that in the year 1926. The basic factor in changing the balance in the world of energy was the use of coal, which changed the way people deal with industry and energy generation. Knowing that man had used coal since the 13th (AD), but its use in the industrial

movement was not until the year 1800 AD. At the beginning of the twenty-first century, the number of the population had approached six billion.

A food chain is a group of organisms that interact with each other within an ecosystem, and in turn one of the species feeds on the other. Once the upper species fed on a contaminated lower rank, the contaminated substance will be accumulated within the upper species. Pollution leads to changes in the structure and function of ecosystems, where it is a result of human-caused activities. It is not easily observed exposure to small pollutants per day; this can lead to serious health issues for a long time. At the beginning of the 19-first century, the main impacts resulting from the industry come in four forms, and they are effects on air, water, soil, and agricultural fields. All ecosystem types were exposed to the negative effects of air pollutants (**Lovett et al., 2009**). The United Nations Environmental Protection Organization regulates the emissions of more than 80 toxic substances found in industrial processes, including asbestos, dioxin, lead, and chromium. However, factories remain among the worst sources of air pollution in the world. The biggest problem is air pollution resulting from gaseous emissions from the process of burning petroleum products. Air pollutants include several pollutants such as nitrogen oxide (NO₂), carbon monoxide (CO), sulfur dioxide (SO₂), ozone (O₃), and heavy metals. NO₂ is one of the important elements of smog caused by fossil fuels. **Su et al. (2019)** showed that the risk of flu-like illness may be increased by air pollutants such as particulate matter (PM), CO and SO₂. The most important indicator of environmental pollution is SO₂ level (**Kukkola et al., 1997**). Particularly, SO₂ exposure-related respiratory symptoms were observed by **Iwasawa et al. (2009)**. Of course, atmospheric air pollution has had a negative effect on the ecological system. **Wong et al. (2009)** found that significant effects of O₃ on flu modifications. When O₃ was increased at ground level, this environmental situation affected the respiratory and cardiovascular systems (**Manisalidis, 2020**).

For a long period, air pollution can be reduced lung functioning. Hence, humans are exposed to less airborne PM than birds because humans have a lower respiratory rate compared with birds in the open air. In this concern, **Llacuna et al. (1993)** observed that there was an increase in the mucus which covers the tracheal epithelium in passerine birds due to atmospheric air pollutants. Insects have many biological properties that make them useful in biomonitoring because they are ubiquitous. Insects are one of the main organisms were affected by pollution. Since they are at or near the bottom of the food chain, environmental pollution in insect populations will affect the rest of the food chain. Insects that feed on plants (herbivores) return plant nutrients to the soil, which are food for reptiles, mammals, wild birds and various insects. Hence, insects are an important part of the world

where we live in; it is a basic factor in the healthy functioning of ecosystems. In this concern, **Zvereva and Kozlov (2002)** reported that air pollution may have negative effects on herbivores and their natural enemies, thus altering population dynamics. Additionally, the quality of soil and water bodies was influenced by polluting precipitation, falling into water and soil environments due to air pollution (**Kjellstrom et al., 2006**). Accordingly, **Karan et al. (2020)** showed that air pollution led to the emergence of Spanish flu in 1918, and SARS-1 in 2003 which reflected in strong human sensitivity to respiratory infections. They added that there was a relationship among acute respiratory distress syndrome, air pollution, and ozone. Hence, air pollution can lead to infant mortality or chronic disease in adulthood as mentioned by **Kelishadi and Poursafa (2010)**. Based on the above, it is clear that air pollution had a considerable impact on the evolution of the flu virus into COVID-19 by polluting the functioning of ecosystems.

Food is correlated with water, and, in turn, water pollution or irrigated with contaminated water can reflect in the food of these areas. Water pollution is mentioned, especially in areas where there are factories next to natural water sources. Water pollutants come in many forms: solid, liquid, and gaseous pollutants. In USA, **Gale et al. (1976)** showed that the Susquehanna River (in Pennsylvania) is heavily polluted by acidified mine tailings where the river contained about 38.5 mg/l of Fe^{2+} . In Italy, a study was carried out by **Berbenni et al. (1993)** in the region of Lombardy (northern Italy) and stated that the main cause of groundwater pollution was the intrusion of industrial wastewater in the province of Mantua. Meanwhile, **Zhu et al. (2002)** suggested that the main cause of pollution in the Pearl River Delta is the sewage water of southern China. A report by the provincial environmental protection bureau found that nearly 70 percent of the 116 river sections tested in Guangdong met the second to third grade water quality standards, making them clean enough for human consumption. However, about ten percent of these rivers still have pollution and cannot be suitable for human consumption where water pollution led to an increase in the infected human with serious diseases such as stomach and liver cancer (**BSR, 2009**). Although the importance of lakes for irrigation systems intended for drinking, agriculture, and industry, aquatic insects are rarely used as a biomarker to assess the quality of this water (**Priawandiputra et al., 2017**). The destruction or decreasing numbers of insects in freshwater will affect vertebrate predators such as fish and waterfowl that feed on them.

Thus, water pollutants can lead to health problems in humans, such as blood vessels and heart disease. A mother's consumption of polluted fish or shellfish resulted from methylmercury, can adversely affect a baby's growing brain and nervous system (**Environment, 2014**). In India, **Kumar et al. (2017)** found the

maximum levels of Fe^{2+} were 3820 and 6294 ppb in the groundwater and the surface water samples, respectively, meanwhile the permissible limit is 300 ppb. On the other hand, **Martí (2019)** mentioned that about half of Spain's groundwater reserves are polluted, according to the Ministry of Ecological Transition in Spain. He added that the World Health Organization (WHO) reported that NO_2 in drinking water should not exceed 50 milligrams per liter to avoid negative effects in the short term. There are several negative effects of NO_2 on insect's growth (**Campbell and Vallano, 2018**). **Brancolini (2021)** reported that Bergamo and other picturesque towns in the Po River valley in northern Italy have suffered from air pollution in Europe for decades that has been a direct cause of cancer as a result of factories and busy truck highways. Usually, fish are at the top of the aquatic food chain. It is known that the evaluation of fish is used in determining the quality of aquatic systems. **Pujin et al. (1990)** and **Kargin (1996)** observed higher levels of Mg in the muscles of freshwater and marine fish. Polluted aquatic organisms are eaten by fish then those fish are eaten by larger fish, birds, and animals until reach humans. Particularly, **Rajkowska and Protasowicki (2013)** showed that high levels of Zn^{2+} were found in the digestive tract and gills. They added that high amounts of Fe^{2+} were accumulated in the spleen, kidneys, and liver in some fish species and tissues. So, it is suggested that polluted aquatic organisms led to disorders in the immune system's control that contributed largely to higher reproduction of the COVID-19 virus. Biomagnification is a process that reflects the concentration of a contaminant increases within the food chain. When an organism absorbs a toxic substance, bioaccumulation can occur at a rate greater than that at which the substance is lost.

The most common causes of soil pollution are industrial activities and the applied agricultural chemicals. The industry in the agricultural field is one of the largest consumers of water. Incalculable relationships were developed between organisms and their environment over several centuries. According to **Clark (1981)**, industrial activities and the applied agricultural chemicals influenced the abundance of bats. Some smaller bats are feeding on small insects such as *Chironomidae* are the main source of heavy metals accumulation (**Racey and Swift, 1985**). In China, water and soil pollution led to more people at risk of carcinogenic diseases (**Lu et al., 2015**). Soil is a natural habitat for many microorganisms. The function of the soil microbial community forms not only the belowground ecosystem but also the aboveground ecosystem (**Tate, 2000**). Consequently, the expected yield of a crop can be affected negatively by soil pollution as a result of impairing plant metabolism due to fluctuations in soil microorganisms. The natural ecosystem, surface water, groundwater, and greenhouse gas emissions are defected by nitrogen (N) accumulation and nitrate

pollution (**Ward, 2009**). N use efficiency is ranged from 30 to 50% for most plant species, while the rest of N is consumed in different forms as soil microbes, leaching, and volatilized nitrous oxide (**Wuebbles, 2009**). Accordingly, microorganisms can be reacted to each other very quickly in polluted soil, which leads to the unavailability of different soil nutrients.

Moreover, often farmers apply N fertilizers to their crops excessively to increase the growth of crops and therefore their yields. The toxicity of nitrate reflects carcinogens (**Walker, 1990**). Cereals such as rice, wheat, and maize need the most N fertilizers followed by fruit and vegetable crops (**IFA, 2011**). Plants can pick up some of the chemicals deposited such as NO₂, SO₂, and some heavy metals. As such, several heavy metals can have toxicity consequences for the human body after long-term accumulation. Considerable doses of Fe²⁺, Mg²⁺, and Zn²⁺ may cause acute or chronic toxicities. Negative effects on human health due to using N fertilizers have been observed in several studies. In this concern, **Jones et al. (2016)** reported that ingestion of nitrate-contaminated drinking water and excessive diets of root and leafy vegetables can be considered major sources of human exposure to N fertilizers. Thus, pollutants from agriculture contain high N amounts, creating toxins that kill fish through dead zones (lack of dissolved oxygen 'O₂'), and thereby seabirds and marine mammals, as well as human health. Additionally, pesticides are used to protect agricultural production from various pests. It is chemical or biological substances or even a mixture made of them. Several studies revealed that the high concentrations of pesticides in some birds resulted in debilitated egg shells, their young dying, and populations decreased which affected natural enemies. Pesticide residues were accumulated in most vegetables, fruits, and in turn, meat, birds, fish, and dairy. After exposure to pesticides, red blood cell (RBC) and platelet counts were increased (**Azmi et al., 2009**).

Based on diet's effects on public health, different diseases should be taken into account when studying the evolution of flu to the COVID-19 virus. Pollution of food represents the main danger to the organisms on the globe, instead of food being a source of energy and health; it has become a source of diseases and epidemics. Sources of food contamination are physical, chemical, or biological. Also, food should have its natural role to build and preserve life, not be a source of human misery and disease. In this concern, **Gonçalves et al. (2020)** showed that SARS-CoV-2 has been found in wastewater, which can reflect in food contamination. Also, **Domingo (2016)** revealed that diet and lifestyle are clearly associated with five of the ten leading causes of death, namely coronary heart disease, certain types of cancer, stroke, non-insulin-dependent diabetes, and atherosclerosis. It is known that a diet-related to environmental pollution that

accumulating in humans has formed their food chain, which indicates the concentration of a pollutant increases within the food chain. Moreover, **Schreinemachers and Ghio (2016)** reported that the cell is forced to receive more Fe^{2+} necessary for its survival by activating Fe^{2+} -responsive proteins and increasing Fe^{2+} import. Fe^{2+} homeostasis is altered in the exposed cells due to a new balance being created between the cells that require Fe^{2+} and the inappropriate chelate (contaminated). In another study, **Lin et al. (2018)** found that acute and sub-chronic exposure to certain specific pollutants alters the behavior of the angiotensin-converting enzyme 2 (ACE2) receptor, which help the SARS-CoV-2 virus to control the respiratory system.

The influenza A viruses led to four pandemics emergence, and the last of them was known as the novel influenza A virus resulted in about one hundred thousand to five hundred thousand deaths from 2009 to 2010 in the world (**Shieh et al., 2010**). Particularity, **CDC (2010)** mentioned that influenza A and B viruses are evolving which lead to 3000–48 000 deaths each year in the USA alone. Moreover, severe influenza infection resulted in the progression of atherosclerosis and related cardiovascular disease (**Phrommintikul et al., 2011**). According to **Shao et al. (2017)**, the influenza A viruses are characterized by high mutation rates due to antigenic drifts and shifts. Influenza A has a high ability to adapt with its antigenic sites to escape from the host immune system and vaccination (**Doyle et al., 2019**). Meanwhile, SARS-CoV emergence in November 2002 and resulted in about seven hundred deaths before this novel A virus (**Peiris et al., 2003**). Therefore, we expect that flu viruses that infected bats in the past have mutated into the modified fierce virus as a result of the pollution of environmental conditions. Particularly, the original reservoir host of SARS-like CoV is Chinese Horseshoe bats (**Lau et al., 2005**). Also, **Han et al. (2006)** showed that antibodies that were used against ACE2 have a high ability to block SARS-CoV infection. Hence, **Guan et al. (2003)** reported that bats transferred SARS-CoV to humans through fecal contamination of food sources, and also by intermediate hosts (palm civets and raccoon dogs). In China, SARS-CoV-1 caused a victim rate estimated at 9.6% in 2002 as reported by **Mann et al. (2020)**.

Once pollutants enter the body, they remain for a long time as a result of their chemical stability and ability to be penetrated by different tissue. Diet can lead to oxidative stress that causes disordering levels of Fe^{2+} , Mg^{2+} , and Zn^{2+} in the blood, and this negative effect is increased by pollution. Thus, it should be taken into consideration the significance of these elements in this biological disorder. Fe^{2+} is necessary for the synthesis of dopamine and is a major cofactor of tyrosine hydroxylase (**Wigglesworth and Baum, 1988**). Also, increased Fe^{2+} can affect negatively serum hepcidin levels. Moreover, Zn^{2+} regulates dopamine transport

(Arnold and DiSilvestro, 2005). It is considered as a cofactor that is important for enzymes involved in cell membrane stabilization or required for the metabolism of neurotransmitters, melatonin, and prostaglandins (Dodig-Curkovic *et al.*, 2009 and Robberecht *et al.*, 2020). Meanwhile, Mg^{2+} plays important roles in the desaturase enzymes implicated in hyperactive behavior due to its ability to convert essential fatty acids to omega-6 and omega-3 polyunsaturated fatty acids (Antalis *et al.*, 2006). Most viruses can enhance increased Fe^{2+} deposition in the host cells. We, therefore, hypothesize that the risk of severe influenza virus infection is highly similar to COVID-19 symptoms, at least partly due to chronic diseases related to diet. In this concern, Kawabata *et al.* (2005) reported that Fe regulatory proteins will be degraded when the intracellular Fe^{2+} concentration is high which reflect in increased ferritin synthesis. According to Lopes (2009), Fe^{3+} binds with transferrin and then circulates in the plasma. Increased ferritin in the pulmonary epithelium can result from tissue Fe sequestration. Moreover, increased Fe^{2+} levels above normal can affect negatively DPP-4 inhibitors which lead to defective erythropoiesis. Further, Fe^{2+} metabolism and low oxygen (O_2) supply can furnish the Fenton oxidative reaction which helps in COVID-19 replication evolution (Schmidt, 2020 and Eren and Tuzkaya, 2021).

The main reason for the COVID-19 virus to attack a person is the overloaded Fe^{2+} content in his blood as mentioned by Abdel-Wahab *et al.* (2020a) so that we would be expected there is a hidden attraction between the virus and this person. The disordering levels of Fe^{2+} , Mg^{2+} , and Zn^{2+} in the blood can furnish an imbalanced biological situation to facilitate penetration of the COVID-19 virus (Abdel-Wahab *et al.*, 2020b). So we can say that increased Fe^{2+} levels above normal affected negatively not only Mg^{2+} and Zn^{2+} levels but also the angiotensin hormone activity when flu infection for a long period. Consequently, it is expected that this biological situation will lead to increased blood pressure due to vasoconstriction. Hence, eating wild animals (bats in particular) was the incubating environment for COVID-19 development inside human blood characterized by an overload of Fe^{2+} (Abdel-Wahab and Adel "a" theory, 2020). Thus, it is likely that when Fe^{2+} , Zn^{2+} , and Mg^{2+} are disordering, it contributes largely to the amino acid substitution at different antigenic sites in flu involved in the pathogenicity. This biological situation can form adaptive genetic variations of different flu strains with SARS-CoV that might provide viral genomes of COVID-19 by glycan specificity and major antigenic sites some antigenically special clades. Consequently, it is likely that irregularity in some overall-folded proteins can occur, reflecting negatively on RBC agglutination and fetuin-binding properties. Thus, it seems that the diet system contributed mainly to the evolution of the flu

virus to COVID-19, and this effect is enhanced by food contamination compared to other environmental factors.

CONCLUSION

The industrial progress formed an environmental hazard that led to an imbalanced ecosystem which reflects on the evolution of flu into COVID-19. Indirectly, industrial progress furnished the perturbation of blood metabolites in humans and, in turn, the emergence of the COVID-19 virus. Governments of developed countries should take concrete steps to minimize environmental pollution to constrict viral evolution in the future.

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CONFLICT OF INTEREST

We have no competing interests

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