

Environmental toxicities might encourage susceptibility to COVID-19 pandemic: A brief commentary

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COVID 19 or Novel Coronavirus is a near unstoppable killer and is an emerging and rapidly evolving medical emergency situation across the globe. This gigantic viral outbreak was declared to be a Public Health Emergency of an international concern on January 30, 2020. World Health Organization (WHO) has declared the novel coronavirus disease, COVID-19 (2019- nCoV) to be a global pandemic on March 11, 2020 and until April 8, 2020, 5:30 GMT 5:30, it has reported 1, 317, 130 confirmed cases of SARS-COV 2 infections worldwide with 74, 304 confirmed deaths and 212 countries, areas and territories affected by the viral outbreak of unprecedented nature. This apocalyptic global public health emergency scenario started with a reporting of pneumonia with an unknown cause in WHO country office located in Wuhan, Hubei province in People's Republic of China (PRC) on December 31, 2019. The clinical characteristics of the infection are very similar to viral pneumonia. Respiratory sample analysis by PRC Centers for Disease Control (CDC) confirmed that the infection is related to Novel Coronavirus Pneumonia (NCP) and was caused by Coronavirus (Huang, et al., 2019). WHO officially named this viral outbreak as COVID-19 and International Committee on Taxonomy of Viruses (ICTV) ascribed it as SARS-COV-2, the abbreviation for Severe Acute Respiratory Syndrome Coronavirus-2, a member of large β – coronavirus family widely prevalent in nature. The extremely high transmissibility and infectivity despite of comparatively low mortality rates makes SARS-COV-2 a unique member of the family with SARS and MERS (Liu, et al., 2020). The crude mortality ratio (the number of reported deaths divided by the number of reported cases) is between 3-4% while the infection mortality rates (the number of reported deaths by the number of infections) is comparatively lower (COVID-19 Situation Report- 46, WHO). COVID-19 and influenza viruses have similar disease representation but the speed of transmission is entirely different between the two. Influenza has shorter median incubation period (time from infection to appearance of

symptoms) and shorter serial interval of just three days (the time between successive cases) in comparison to COVID- 19 with a serial interval of five to six days. The basic reproductive number R_0 (the number of secondary infections generated from a single individual in completely susceptible populations without any interventions) is much higher in COVID-19 (2-2.5) with respect to influenza. However, (Wu, et al., 2020) estimated R_0 of SARS-CoV-2 to be (2.47-2.86) while that of SARS-CoV is (2.2-3.6) (Lipsitch, et al., 2003) and MERS-CoV is (2.0-6.7) (Majumder, et al., 2014). This indicates high transmissible character of (2019 n-CoV). The median age of population susceptible to SARS-COV-2 is 47.0 years however the numbers are rapidly changing worldwide as new areas are being covered by the viral outbreak (Guan, et al., 2020; Wu, et al., 2020). Source of infection, routes of transmission and susceptibility are three major epidemiological parameters of Coronavirus family (Barreto, et al., 2006) and finds no exception in COVID 19. The nature and pathogenic representations between these epidemiologically linked viral diseases are contextual and time-specific making direct comparisons an uphill task for researchers worldwide. Genome analysis conclusively claimed that novel coronavirus (SARS-COV-2) has emerged from bat SARS Coronavirus (SARSr-CoV-RaTG13) with complete genome recognition rates of 79.5% and 96% respectively (Chen, et al., 2020). This finding finds basis as the detection of Group 1 Coronaviruses in bats were initially observed in North America by (Dominguez, et al., 2007). SARS-CoV-2 isolated from pangolins and the viral strains currently infecting humans show 99% similarity as per macrogenomic sequencing analysis performed by (Xu, et al., 2020). Emerging diseases such as COVID- 19 are majorly zoonoses caused by ss-RNA viruses (Woolhouse, 2002; 2005). They lack proof-reading activity and show spontaneous mutation and sporadically jump across the species defying all rules of evolutionary principles. The case in evidence is the COVID-19 infection of big cats (tigers and lions) of Bronx Zoo from the zookeeper who tested positive. Human to animal routes of viral transmission is not only rare but striking. Pathogenic mechanisms of SARS-CoV-2 reveal uncanny similarities with SARS-CoV. Receptor Binding Domain (RBP) instigates SARS-COV-2 to bind with Angiotensin Converting Enzyme 2 (ACE2) exactly in the same manner as SARS-CoV (Hoffman, et al., 2020). However, structural model analysis conclusively confirms the binding affinity of SARS-CoV2 to be ten times more than SARS (Wrapp, et al., 2020). Coronavirus recognizes the corresponding receptor on target cell through S protein on its surface and enters the cell switching on the pathogenic cytotoxicity. The high binding affinity of SARS-

CoV-2 with ACE2 might help solving the crucial puzzle in using soluble ACE2 as a potential candidate for COVID-19 epidemiological treatments. In-depth annotation analysis of novel coronavirus (2019-nCoV) genome has revealed significant differences between 2019-nCoV and severe acute respiratory syndrome (SARS) or other members of beta-coronavirus family. Comparisons reveal 380 amino acid substitutions between these coronaviruses, which may have caused functional differences, pathogenic divergence and increased infectivity of 2019-nCoV (Wu, et al., 2020). The global viral outbreak targets elderly male patients with chronic underlying health complications such as (diabetes, hypertension, coronary heart diseases, lung complications, cancers and kidney failures) more than their female counterparts (Chen, et al., 2020). The commonest clinical symptoms include fever (87.9%), cough (67.7%), fatigue (38.1%), diarrhea (3.7%) and vomiting (5.0%). However these are major symptoms and might be compounded with several other minor symptoms as developed in patients with different epidemiological fates (Guan, et al., 2020; Yang, et al., 2020). ARDS (Acute Respiratory Distress Syndrome) is common among COVID-19 patients (Huang, et al., 2020; Chen, et al., 2020) and need not be confused with any other parallel epidemiological phenomenon. Other manifestations include abnormal neurological functions (Mao, et al., 2020), renal and hepatic anomalies (Huang, et al., 2020; Li, et al., 2020; Wang, et al., 2020). Detection of viral nucleic acid (ss-RNA) is the only non-invasive procedure of COVID-19 diagnosis which includes collection of swab samples from nose and throat. (PRC NHCot, 2020) has laid down the 2019 n-CoV pneumonia diagnosis and treatment plan. Maintenance of personal hygiene and safety, social distancing, self-isolation, quarantine of suspected individuals and treatment of infected ones with aggravated epidemiological risks with supplementary oxygen and mechanical ventilator support forms the basic pathway to contain COVID-19 infections globally in absence of specific vaccine and medicine to treat COVID-19. Remdesivir, 1'-cyano-substituted adenosine nucleotide analogue is an intravenous drug with broad spectrum antiviral activity that inhibits viral replication through premature termination of RNA transcription and has shown prominent in-vitro activity against SARS-CoV-2 as well as other members of beta-Coronavirus family as per preliminary investigations conducted by US National Library of Medicine, National Institute of Health, Health and Human Services as well as per a report published by (Amirian, et al., 2020). Some potential success results regarding critical patient treatments have also been achieved with usage of drugs like Hydroxychloroquine and Azithromycin in Jaipur, India but conflicting

research reports are published by French researchers (Gautret, et al., 2020; Gautret, et al., 2020; Molina, et al., 2020).

The scientific investigations connecting the dots between environmental and epidemiological links of COVID-19 infections are still in its infancy and require systematic, holistic and global research networking during the Post COVID-19 emergency. Environmental dynamics including changing climate scenarios across the world and associated anthropogenic stress factors play a crucial role in pathogenicity of macroparasites such as mosquitoes, flies, ticks, bugs etc. It has been mentioned in scientific investigations too (Remais, et al., 2010). The impact of changing climate and anthropogenic factors on microorganisms however is not well documented (Chakravorty, et al., 2020). Strong correlations between COVID 19 infections in susceptible populations and anthropogenically derived environmental toxicity affecting global populations cannot be ruled out and needs immediate understanding through global research networking in a Post-COVID 19 world. This will give us impetus in fighting global pandemics more scientifically and holistically in coming times unlike the ongoing COVID-19 pandemic trauma that grips mankind.

Environmental toxicants leave behind unimaginable environmental damage and human health hazards of unmanageable proportions. Toxicants include broad range xenobiotic such as pesticides, radioactive elements, chemicals, drugs and heavy metals which are non-biodegradable and persistent in ecosystems even under extreme conditions. Heavy metal toxicity in the environment is a globally emergent issue that is ubiquitous across all ecosystems on this planet (Tchounwou, 2012). Recent years have seen ever increasing ecological and global public health concern associated with environmental contamination by heavy metals such as Lead, Cadmium, Chromium and Mercury. These metals have known toxicological effects and epidemiological implications on human health. Lead, for example causes known poisoning effects on almost every organ systems of human body (Flora, et al., 2012; Wani, et al., 2015) and has been long regarded as one of the most dangerous environmental contaminant (Mahaffy, et al., 1990). Similar toxicological reports have been generated for Cadmium, Chromium and Mercury. Potential health risk of Cadmium has been well highlighted in scientific literature since long and researchers worldwide have expressed deep concerns against health hazards that might lead to fatal complications. Groundwater contaminated with Arsenic and Cadmium was revealed in China long back (Wang, et al., 2011). This study further opines that although the arsenic and

cadmium concentrations in groundwater sources are well below the recommended limits of Water Quality Standards for Drinking Water (GB5749-1006) in China but the residents served by almost all centralized drinking water sources face significant health complications including Cancer. Immunocompromised patients including people with respiratory ailments, HIV patients, transplant recipients and urban patients with health complications have shown increased tendency of viral infections (Englund, et al, 2011). This include respiratory syncytial virus (RSV), Influenza and parainfluenza viruses (PIVs), adenoviruses, rhinoviruses (RhV) and coronaviruses have been detected worldwide in transplant recipients and people with opportunistic infections; two third of which include acquired heavy metal toxicities. Newly identified viruses such as human metapneumoviruses (HMPV) (Peret, et al., 2002; Bolivin, et al., 2002), new strains of Coronaviruses (Milano, et al., 2010), and bocaviruses have also been detected in symptomatic transplant recipients (Schenk, et al., 2007). Community Acquired Respiratory Viruses (CARV) has significant health complications leading to morbidity and mortality among immunocompromised patients across all geographies of the world. Similar findings were substantiated during the recent COVID-19 outbreak. Upper Respiratory Tract Infections (URTI) and Lower Respiratory Tract Infections (LRTI) are commonly reported in CARV dominated patients, a similar observation was also reported from victims of COVID-19 across the globe.

Environmental toxicity acquired through air pollution in populated and heavily commuted cities of the world such as New York, London, Hong Kong, Shanghai, Beijing, New Delhi, Tokyo, Kolkata, Moscow shows opportunistic health complications in both adults and children exposing them more to the risk of emerging and rapidly evolving pandemics under global climate change scenarios. Heavy metal such as Chromium finds way to human health hazards through vehicular pollution, industrial fumes and Cigarette smoking. Chromium is a potent carcinogen primarily through inhalation exposure in occupational settings (Costa and Klein, 2006). Hexavalent Cadmium toxicity is majorly caused by Cigarette smoking and bad air pollution causing unparalleled damage to respiratory and cardiac systems making COVID-19 infections more susceptible. The most important toxic effects, after contact, inhalation, or ingestion of hexavalent chromium compounds include dermatitis, allergic and eczematous skin reactions, skin and mucous membrane ulcerations, perforation of the nasal septum, allergic asthmatic reactions, bronchial carcinomas, gastro-enteritis, hepatocellular deficiency, and renal oligo anuric

deficiency. The underlying health issues open doors to various other secondary epidemiological conditions including increased susceptibility towards viral infections including COVID-19. It is observed that majority of smoking populations with COVID 19 infections have to swim upstream in their life battle against the viral pathogenicity.

Mercury is a silent killer and most toxic of all heavy metals found commonly in several industrial, agricultural, domestic and technological applications. Increased human exposure to heavy metals such as Mercury has resulted in exponential increase induced toxicities such as neurological disorders, reproductive ailments, male sterility, teratogenicity, lung ailments and dermatological complications. Increased cases of child mortality and miscarriage among urban women is a result of such secondary toxicities that do not find proper clinical investigations due to lack of awareness, low or no reported forensic cases and ofcourse socio-economic as well as political inequalities. Approximately, 20,000 tons/year of mercury is added by anthropogenic activity (Hansen and Dasher, 1997). It is estimated that the mercury emissions will increase at a rate of 5% a year (Zhang, et al., 2002). Low dose mercury toxicity in human health is well documented by (Zahir, et al., 2005). Multiple pathways of mercury operate in the ecosystem including soil, air, water and almost all elements of biosphere thus further complicating the problem of mercury toxicity. Mercury toxicity is well prevalent in industrial areas (Panda, et al., 1992) and also in freshwater ecosystems across the world; our main source of potable water (Sharma and Bhattacharya, 2016). Several researches reconfirmed the presence of Lead, Cadmium, Chromium and Mercury in vegetables, food crops and fishes (Dutta, et al., 2017; 2018; 2019). Climate Change induced acidification has aggravated the detrimental effects of the heavy metals in human health and ecosystems in general (Dutta, et al., 2020). Experimental findings from East Kolkata Wetlands (EKW), a prominent Ramsar Site and a wetland of international importance conclusively proves the bioaccumulation pattern of heavy metals both in ambient media (water and soils) as well as in harvested crops and fishes which form a major food basket for the people of Kolkata. Thus, we are consuming poison every day and exposing our health systems to opportunistic infections and viral outbreaks such as COVID 19. Any sustainable strategy to combat COVID 19 must ensure bioremediation of heavy metals from our ecosystems as well as a cleaner environment for all of us to live and breathe. Else, we must prepare ourselves for many such COVID-19 pandemic disasters in times to come. Global phenomena of climate change, varying weather conditions, anthropogenic stress factors, an

immunocompromised body, poison in our plates and dangerously polluted air, water and soil would only make all the biotic components on earth including humans vulnerable to such viral outbreaks. Pre and Post COVID-19 world would be very different due to changing socio-economic-political scenarios and post disaster situations. The utter chaos, psychological trauma, economic recession, joblessness, food insecurity and most importantly unthinkable poverty in meeting basic resource needs would lead to cacophony and pandemonium of humongous proportions. Environmental Management and most importantly handling and usage of xenobiotic in our daily life must not take a backseat and is to be included in Post COVID19 disaster mitigation plan for every country in the globe under the leadership of World Health Organization and other competent authorities with global presence. Sustainable management of environment would only ensure a most powerful battle against all diseases, not only viral outbreaks. With global climate change issues hovering over us, environment and human health must be the subject of our primary and pivotal concern. Natural selection accepts the most tolerant of all species, neither the strongest and nor the weakest, as Darwin's theory goes. Our only way out from the evolving and emerging crisis situation is fulfillment of the sustainable development goals. This would help us to get back in track winning over the crisis situations exposed by natural disasters, anthropogenic pollution and other stress factors, disease outbreaks and several other underlying health conditions on a global scale.

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