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Understand COVID-19 through Heavy Metals Pollution

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Review Article

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ABSTRACT

The quick spread of COVID-19 crisis and fast emergence of new variants of it , dissimilar clinical forms from silent to exaggerated ones , misunderstanding of etiologies , mode of transmission, variable effectiveness and side effects of vaccines and absence of comprehensive and efficient treatment protocols , heavy spread in certain continents and on less in others a lot of questions arise from the variables mentioned above need answer. In this review I introduced my hypothesis about origin of COVID-19 , its later variants and the main mode of transmission of the virus, the role of mutagenic heavy metals in emergence and the rising of the pandemic and explained the relationship between COVID-19 and malaria. Scattered information used to compose it. Experimental studies are required to test it.

Keywords: COVID-19; heavy metals; pollution; COVID- variants.

1. INTRODUCTION

Heavy metals are natural elements with a high atomic weight and a density more than five times that of water. Their diverse industrial, home, agricultural, medical, and technical uses have resulted in their wide distribution in the environment. Express concerns about potential

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impacts on human health and the environment [1]. Indiscriminate human activity has dramatically changed the geochemical cycle and biochemical balance, accumulating metals in plant parts containing secondary metabolites involved in certain pharmacological activities. Long-term exposure to heavy metals such as cadmium, copper, lead, nickel and zinc can adversely affect human health [2].

People are consciously or unknowingly exposed to heavy metals [3]. These pollutions are predominantly due to metal leaching from various sources such as metal mining, smelting, foundries and other metal-based industries, landfills, landfills, feces, livestock and chicken manure. It is due to the human activity that is the cause. Outflow, car and road construction. The use of heavy metals in agriculture is a secondary source of heavy metal pollution, including: B. Use of pesticides, pesticides, fertilizers, etc. Natural causes can also increase heavy metal contamination such as volcanic activity, metal corrosion, metal evaporation from soil and water and resuspension of sediments, soil erosion, geological weathering [4].

Their toxicity depends on several factors, including dose, exposure route, chemical species, and age, gender, genetics, and nutritional status of the exposed individual. Arsenic, cadmium, chromium, lead, mercury and nickel are one of the healthier metals due to their high toxicity, while mercury, lead and cadmium are of particular concern due to their long-term transport in the atmosphere [1,5].

In some countries like China, the geological background level of heavy metals is low, but human activity pollutes soil, water, air and plants with heavy metals and even affects human health through the food chain. It exerts [6].

Soils are the major sink for heavy metals released into the environment by harmful anthropogenic activities and unlike organic contaminants which are oxidized to carbon (IV) oxide by microbial action, most metals do not undergo microbial or chemical degradation, and their total concentration in soils persists for a long time after their introduction [7].

The presence of one heavy metal can affect the availability of another heavy metal in the soil and thus in the plant. In other words, there is antagonistic and synergistic behavior between heavy metals, and it has been reported that Ni and Cd (OMICRON) compete in plants for the same membrane support [8].

Organisms require different amounts of heavy metals. Humans need iron, cobalt, copper, manganese, molybdenum, and zinc. All metals are highly concentrated and toxic. Too much can damage the organism. Other heavy metals such as mercury, plutonium, and lead are toxic metals that are not known to have life-threatening or beneficial effects on living organisms and can cause serious illness when accumulated in animals. Certain elements, which are usually toxic, are beneficial under certain organisms or under certain conditions. Examples are vanadium, tungsten, and even cadmium. Heavy metals destroy metabolic function in two ways. They accumulate, thereby destroying the function of important organs and glands such as the heart, brain, kidneys, bones and liver, and moving important food minerals from their original location, thereby restoring their biological function. It hinders [2].

It was observed that higher genetic diversity was greater in the heavy metal contaminated population than in the uncontaminated population. Exposure to heavy metals can adversely affect plant growth, soil microbial diversity and activity, and clearly has a greater impact on genetic structure [9]. Currently, cadmium pollution in soil is a serious global environmental problem. occurs to varying degrees in soils in Asia, North America, and Europe (only OMICRON due to low levels of COVID19 in Africa) [10]. Bayram SS et al. [11] reported the recognition of Cd2 +, Pb2 +, Zn2 +, and Ni2 + by quenching the unique tryptophanyl fluorescence of the tobacco mosaic virus coat protein (TMV) in its natural and denatured states, which are these metals. And assumed that it could occur with the influenza virus.

Metal ions are integral part of some viral proteins and play an important role in their survival and pathogenesis. Zinc, magnesium and copper are the commonest metal ion that binds with viral proteins. Deficiency of trace metals is known to alter the genome of the viruses and the grave consequences of this may be the emergence of new infections [12]. Study done by Petukhova NV et al showed that superexpression of the influenza virus epitope M2e in plants has been developed on the basis of a recombinant Tobacco mosaic virus (TMV, strain U1) genome designed for Agrobacteriummediated delivery into the plant cell nucleus. The TMV coat protein

(CP) served as a carrier and three versions of the M2e sequence were inserted into the surface loop between amino acid residues 155 and 156. It has been suggested that cysteine residues in heterologous peptides are likely to interfere with the efficient assembly of chimeric particles [13]. Study by LiL et al. [14] showed that tobacco mosaic virus RNA invasion induces stress-induced endoplasmic reticulum autophagy in HeLa cells. Su W et al. [15].

It is well known that many of the toxic effects of cadmium (Cd) are due to their interaction with essential elements such as zinc (Zn). On the one hand, exposure to Cd leads to disturbances in Zn in vivo, while on the other hand, Zn intake with food has important effects on Cd uptake, accumulation, and toxicity. The zinc status of the body is important in relation to the development of cadmium toxicity. Large amounts of data show that increased zinc supply reduces Cd absorption and accumulation and can prevent or mitigate the adverse effects of Cd, while zinc deficiency can increase Cd accumulation and toxicity [16]. Since cadmium and zinc have the same oxidation state, cadmium can replace the zinc present in metallothionein and prevent it from functioning as a free radical scavenger in the cell. Cadmium has the ability to bind to ligands for cysteine, glutamic acid, histidine, and aspartic acid and can cause iron deficiency [17].

Zhao, X et al. [18] evaluated heavy metal pollution in China and found that water pollution was the largest at 97.87%, 92.50%, 80.51%, 76.16% and 79.46%. Metal pollution, followed by air and soil pollution. The highest exposure levels of Hg, Cd, As, and Pb were found in Wuhan (starting point of COVID.19) and were the lowest in Dalian. And the results of this study stopped me and was excited to look for possible links between these heavy metals and COVID.19.

2. DISCUSSION

A well-functioning human immune system is absolutely important to prevent infections caused by various viruses. Among the factors that can have a significant impact on the role of the immune system in the fight against these viruses, including SARSCoV2, are the significant effects of nutritional and nutritional genetic factors, including dietary supplements. In this regard, the European Safety Agency (EFSA) is essential for the proper functioning of six vitamins (A, B6, B12, C, D, folic acid) and four trace elements (zinc, selenium, copper, iron). I reported that there is. Immune system. These micronutrients affect some aspects of immune function due to clinical defects. In addition, increased susceptibility to infections and worse results. In many cases, zinc and selenium deficiency appear to play a negative role in patients with COVID19 [16], high levels of Cd reduce both zinc and selenium [19], and selenium reduces arsenic. Has also been reported. Toxicity of Cd and lead (Pb) [20]. Satarug S et al. [21] suggested that chronic exposure to low concentrations of cadmium induces zinc-copper dysregulation.

Checconi P et al. [22] show that Cd-induced oxidative stress directly increases the ability of influenza virus to replicate in host cells, and exposure to such heavy metals is dangerous for individuals with high exposure to contaminants. It suggests that it may be a factor. Increased severity of virus-induced respiratory illness. Emissions of heavy metals in ash and gas are usually particularly intense in winter, with reduced emissions of certain metals in warmer climates [23], their intensity associated with peak winter influenza virus epidemics.

Park SK et al. [24] High levels of cadmium, a chemical found in tobacco and contaminated vegetables, are associated with increased mortality in patients with influenza or pneumonia , with severe COVID 19 and other respiratory viruses. It suggests that it may increase the degree of severity.

Study done by Fourmy D and Yoshizawa S. [25], showed that PRF regions of all SARSCoV2 sequences available in GenBank and from the Global Initiative on Sharing All Influenza Data for variations. 5,156 and 27,153 sequences analyzed, respectively, the PRF regions were identical in 95.7% and 97.2% of isolates. The most common change from the reference sequence was from C to U at position 13,536, which lies in the three stemmed pseudo-knot known to stimulate frameshifting.

The influenza virus matrix protein (M1) has cysteine and histidine (CCHH) motifs in the helix 9 (H9) and adjacent regions ((148) CATCEQIADSQHRSH (162)). The CCHH motif has been proposed as a putative zinc finger motif, and zinc binding activity is involved in viral delamination, as well as transcriptional inhibition and mRNA regulation. A study by HuiEK et al. Studies conducted have suggested that zinc binding function may not be involved in viral biology. However, the fatal phenotype of the Ala

(155) mutation indicates that the H9 region of M1 provides some other important function in viral replication [26].

A study by Olejniczak M et al. [27] observed that Pb2 + experiments that cleave HIV1 TARRNA induce strong and selective cleavage of C24U25 phosphodiester bonds. Horby PW et al. [28] Studies have shown that lopinavir-ritonavir HIV drug is not an effective treatment for patients admitted with COVID 19. Stalder G. And Alberio L. A study conducted by Stalder G, Alberio L [29] suggested that ritonavir and lopinavir induced elliptosis in patients infected with SARSCoV2. The main targets of lead toxicity are enzymes involved in hem synthesis, thiol-containing antioxidants and enzymes (antioxidants such as superoxide dismutase, catalase, glutathione peroxidase, glucose-6-phosphate dehydrogenase and GSH) [30].

A study by Janicka M et al. [31] found that metals affect blood morphology, blood levels vary by age group, and that blood levels of Cd and Pb in older donors are significantly correlated. I hypothesized that these hematopoietic changes occurred in this elderly patient due to heavy metal levels (lead pb + 2) of COVID.19 structure.

A study by Feiler MO et al. [32] in children, it was suggested that there was a gender association of between blood lead levels and influenza risk. According to Jin JM et al [33] this study showed that men with COVID 19 had an increased risk of outcome and death, regardless of age, and that the number of men who died from COVID 19 was 2.4 times that of females.

The World Health Organization reported that the hospitalization rate for flu season was consistently higher among men of all ages than women. Influenza virus mortality differs between men and women Seasonal influenza virus mortality rates are most common in children (under 5 years) and the elderly (65 years and older).

Age is the most important risk factor for increased mortality from seasonal influenza, with 90% of seasonal influenza-related deaths occurring in people over the age of 65. Double infections, chronic respiratory disease, cardiovascular disease, diabetes, and obesity are important comorbidities that make patients more susceptible to increased prevalence associated with seasonal influenza.

One of the biological variables that differs between men and women and can lead to different outcomes of infection and disease development is the reaction of the immune system. For example, the innate recognition of the virus by pattern recognition receptors differs between men and women. Several genes that encode immune proteins, such as the Tlr7 gene, which encodes a receptor that recognizes single-stranded RNA viruses, including influenza virus, are located on the X chromosome and can avoid X-chromosome inactivation in women. Expression is high. Than men. The inflammatory immune response is generally higher in women than in men, with men having lower CD3 + and CD4 + T cell counts, CD4 +: CD8 + T cell ratios, and helper T cell type I (Th1) responses. Cytokine responses, including the production of interferon and interleukin, often differ between infected men and women [34]. Most of the time flu activity peaks between December and February, but activity can last as late as May [35]. For COVID19 Literature described that females compared to males have greater inflammatory, antiviral, and humoral immune responses.

In female, estrogen is a potential ally to alleviate SARSCOV2 disease. In male, testosterone reduces vaccination response and depresses the cytokine response [36]. Study done by Johnson et al. [37] showed that cadmium also has potent estrogenlike activity in vivo. Zeng L. Study by et al [38] showed that Cd exposure promotes autophagosome formation, but blocks the fusion of autophagosomes and lysosomes, weakens the absorption of total cholesterol and triglycerides, and further exacerbates the disruption of testosterone synthesis. Overall, Cd induced ferroptosis through dysregulation of iron homeostasis mediated by overactivation of HMOX1. Destruction of autophagy flux contributed to Cd-induced testicular dysfunction and reduced testosterone synthesis. One of Saronia A et al. [39] Testosterone levels were found to be significantly lower in men with COVID 19.

Hemoglobin levels are reduced, especially in the elderly, and are negatively associated with COVID19 comorbidity and severity. In addition, consistently high levels of ferritin have been reported in COVID 19 between non-survivors and survivors [40]. Research by Kwon JA et al. [41] showed that the combination of abnormal serum ferritin levels and high Cd levels was significantly associated with high systolic blood

pressure. A study by Chen X et al. [42] showed that Cd and Pb could interact with Hb, and Hb levels were correlated with tubular dysfunction caused by exposure to Cd and Pb.

Gender variations in susceptibility at decrease publicity are uncertain, however current records suggest that cadmium has estrogenic outcomes and have an effect on lady offspring. Men usually have better blood lead degrees than women [43]. Study finished via way of means of Ebinger JE et al [44] confirmed that extra COVID-19 severity remains skilled amongst Hispanic/Latinx patients.

LaVangeL. Study by et al. [45] Dominica and Puerto Rico background non-smoking men and women without respiratory symptoms or illness were found to be significantly worse on spirometry tests. The results suggest that given the geographic background of Hispanic / Latino individuals, a more accurate diagnosis of pulmonary dysfunction may be obtained. The spirometer uses what is known as race-based correction, or ethnic adjustment. This assumes that black patients have 10-15% lower vital capacity and Asian patients have 4-6% lower vital capacity compared to white patients. Moitra S. Study by et al [46] show a marked loss of lung function and a strong response to Cd exposure. This is Skalny AV et al. Supported by the data reported by [47] supported that exposure to As, Cd, Hg, and Pb was associated with respiratory dysfunction and airway disease (COPD, bronchitis).

The Institute for Health Meterics Evaluation (IHME) estimates that in 2019, lead exposure will account for 62.5% of the global burden of unexplained intellectual developmental disorders and 8.2% of the global burden of hypertensive heart disease. , 7, 2% of these are the global burden of ischemic heart disease, which is 5.65% of the global burden of stroke [48].

Satarug S. One of them [49] showed that cd was associated with a significant increase in CKD risk and mortality from cardiovascular disease and cancer. Cd and Pb are associated with reduced cardiovascular morbidity and life expectancy, independent of CKD. Study by Molina Barragan AM et al. [50] showed that significant SARSCoV2 infection was associated with AKI, a risk factor for persistent endogenous renal injury and death. The setting of mechanical artificial respiration seems to be an important factor in renal dysfunction.

Study done by Zeng HL et al. [51], indicate that iron, arsenic, age, and gender are independent factors associated with disease severity, and that comorbidity with chromium, cadmium, and cardiovascular disease is an independent factor associated with mortality. discovered. Almost all known symptoms of COVID19 are similar to those of heavy metal toxicity, especially cadmium and lead overload. In addition, we observed that epidemiological risk factors for heavy metal poisoning were closely associated with the development of COVID 19, and Zhao, X et al. [18] had the highest exposure to Hg, Cd, As, and Pb in Wuhan. Suggested level. For vegetarians, this is a significantly higher plasma concentration of natural antioxidants. Sufficient antioxidant protection against the formation of cadmium-induced free radicals in vegetarians can suppress the harmful effects of increased cadmium intake from plant foods [52] but with ROS levels. Antioxidant levels increase under the influence of lead [17]. So I hypothesized that Lead increases concentration of cadmium and lead to coming out of delta variant of COVID.19, which was first detected in India in past due 2020, wherein vegetarians constitute 20-39% from the entire population [53].

Epsilon was first discovered in Southern California, USA in July 2020 [54]. This needs to be combined with information that the San Gabriel Block is one of the best areas to find gold in Southern California [55]. Von Behren J et al. [56] This study found that gold mining activities were carried out at the foot of the Sierra Nevada Mountains in California, leaving persistent toxic pollutants in soil, dust and water such as arsenic and cadmium. Shown. Their urine than the females in the national sample. Cadmium levels were similar to the national average, but increased in women over the age of 35 who had lived in the area for more than 10 years. Arsenic levels were higher in women who smoked, ate fish, ate homemade produce, and frequently hiked or hiked. California's national parks have also experienced some of the worst air pollution in the United States [57]. Studies conducted by Ngure V and Kinuthia G [58] at the Migori Gold Mine in Kenya show that soil concentrations of Pb, Cd, Zn and Ni exceed the maximum permissible concentrations (MAC) of agricultural soils.

Reactive oxygen species (ROS)-mediated oxidative harm is a not unusualplace denominator in arsenic pathogenesis, and this synergise cadmium effect [59]. So on basis of

this information I hypothesized that cadmium ,lead are responsible for mutation of influenza virus into COVID-19 [20] ,arsenic are responsible for appearance of epsilon variant of COVID-19 in southern California.

The Gamma variant, additionally referred to as lineage P.1, it changed into first sequenced in Itirapina, Brazil, and changed into already circulating in numerous municipalities within side the nation of São Paulo of the equal country [60].

The rapid expansion of sugar cane and land use in São Paulo (Brazil) have changed as a result of increased demand for ethanol [61], with heavy metals and radionuclides incorporated into phosphate fertilizers and additives each year during fertilization. In the process of harvesting sugar cane, you are transferred from the soil to sugar cane [62].

Da Silva FB et al. [63] assessed heavy metal sources in sugarcane Brazilian soils and found that the average concentration of accumulated Cd, Cr, Cu, Ni, Pb, and Zn were 1.9, 18.8, 6.4, 4.9, 11.2, and 16.2 mg kg(-1), respectively.

I hypothesized that cadmium ,lead are responsible for mutation of influenza virus into COVID-19 [20] and chromium are responsible for emergence of Gamma variant of COVID-19 in Brazil, because it presented in higher concentration and chemically stronger than Nickel and copper.

The Zeta variant, also known as the P.2 strain, is a variant of SARSCoV2. First detected in the state of Rio de Janeiro, Brazil [64]. Since the 2016 Olympics in Rio de Janeiro, many environmental troubles inside Rio de Janeiro had been introduced to light, specifically that of water pollution. Not handiest a terrible sewage device however additionally the commercial wastewater from 17,000 industries surrounding the Guanabara Bay is to be blamed for excessive ranges of water pollution [65].

Study done by Branquinho, C L, and Robinson [66] showed an elements of lead pollutants in in Rio de Janeiro Rio de Janeiro.

Study done by Junior RG et al. [67] examined Muscles, gonads, and liver tissues of fish stuck in Sepetiba and Ilha Grande Bay, Rio de Janeiro, Brazil and identified that Levels of Cr exceeded the most permissible awareness in muscle, observed with the aid of using Zn in a few species. Pb, Cu, and Cd provided concentrations above most permissible degrees in gonads and liver only. I hypothesized that cadmium, lead are responsible for mutation of influenza virus into COVID-19 [20] and copper is responsible for emergence of Zeta variant.

The alpha variant COVID was first identified in the United Kingdom in September 2020 [68]. After it was first detected in the United Kingdom in late 2020, Alpha spread rapidly around the world, suggesting it was significantly more transmissible than the original virus. But experiments in Towers` lab indicated that the new variant replicated no faster than its predecessor [69]. According to a study conducted in the United Kingdom, nickel, arsenic, cadmium, and, to a lesser extent, lead are the major heavy metal pollutants in the United Kingdom. As a result of this information, I assume that cadmium, lead is involved in the mutation of the influenza virus in COVID 19 **[**20], and nickel and arsenic are involved in the emergence of alpha variants of COVID. did. Low lead content in it. Alpha variants grow more slowly than other variants.

The beta variant was first identified in South Africa in late 2020 and caused a second wave of COVID 19 before it spread worldwide [70]. Among other chemical contaminants, the concentration and distribution of metals was determined by Greichus et al. (1977). At two lakes in South Africa. The Hartbeespoort Dam receives industrial and urban water mainly from Johannesburg and Voëlvlei Dams in agricultural areas. Water, sediments, aquatic plants and insects, fish, fish-eating birds and their eggs were analyzed for As, Cd, Cu, Mn, Pb, Zn, and Hg. The results showed that the levels of all metals in the Hartbeespoort dam deposits were higher than Voëlvlei [71]. Comparison of mechanisms of action reveals similar pathways by which cadmium, lead, mercury, and arsenic induce toxicity such as ROS formation, suppression of antioxidant defenses, enzyme inactivation, and oxidative stress [72]. As a result of this information I hypothesized that cadmium and lead are responsible for mutation of influenza virus into COVID-19 [20], Arsenic and Mercury are responsible for surfacing of Beta variant of COVID.

Cases of Eta variant Covid have been identified in Mangaluru, Karnataka, India [73]. The Kabini River in Karnataka, India, carries natural and anthropogenic pollutants, mainly containing

heavy metal concentrations Cr, Cu, Fe, Mn, Ni, and Pb, Zn. Emitted from industrial wastewater, agricultural wastewater and domestic wastewater.

Cu and Cr display the best pollutants intensity. The concentrations of Cr observed with the aid of using Zn and Ni are as an alternative better than the most historical past values withinside the Kabini River sediment [74]. Study done by Tejaswini M et al. [75] showed that the concentration of Cadmium and Chromium in vegetables that sold in local markets of Bangalore city, Karnataka state, India, were slightly exceeding the recommended maximum acceptable limits. Then based on the above mentioned information, I hypothesized that cadmium and lead are responsible for mutation of influenza virus into COVID-19 [20], Chromium and Nickel are responsible for surfacing of Eta variant of COVID.

The Lota variant is one of the variants of SARSCoV2, the virus that causes COVID19. It was first discovered in New York City in November 2020 [76]. Study done by Rebecca G. Mitchell et al. [77] in New York city showed that Barium (Ba) and Pb were most commonly found to exceed guide values and were strongly correlated with zinc (Zn) along with cadmium (Cd). Then based on the above mentioned information, I hypothesized that cadmium and lead are responsible for mutation of influenza virus into COVID-19 [20] , Barium (Ba) is responsible for appearance of Lota variant.

For the first time, five cases of `Kappa` variant of coronavirus have been detected in Gujarat [78]. Where, Highest uranium water content in Ahmedabad, widespread use of groundwater for agricultural and other purposes, elevated salt (TDL) levels, nitrite contamination due to widespread use of nitrogen fertilizers, and fluoride levels exacerbate the problem Only [79]. Nitrogen fertilizers have a low lead content [80].

A lower soil pH significantly increased the available Cu, Ni, and Zn concentrations and reduced Cd, Cu, Ni, and Zn accumulation [81]. The kappa mutant is called a "double mutant" because two mutations have been identified, E484Q and L452R [82].

In Gujarat, about 1.59 lakh were cultivated on tobacco [83] and farmers used phosphate fertilizers containing cadmium [84]. From the previous information I hypothesized that that cadmium and lead are responsible for mutation of influenza virus into COVID-19 [20], uranium reacts with Fluoride form uranium hexafluoride which is responsible for emergence of Kappa variant of COVID.

Lambda variants of COVID spread rapidly in Peru and are thought to be involved in 80% of cases there [68]. Peru is one of the top five producers of heavy metals such as copper, lead and zinc. The town of Cerro de Pasco at the top of the Andes in Peru is a mining town and is considered one of the most polluted places on the planet. In Peru, more than one million people are exposed to lead in the soil. The presence of higher concentrations of heavy metals in boys than girls exposed to the mine may be related to cultural practices (family roles and outdoor play) that make gender differences in exposure to environmental factors [85]. And Of the 150 Peruvians tested for heavy metals, 78% (117) have levels of metals and toxic substances above reference levels, more than 58% increase arsenic levels and more than 29% have manganese levels. More than 12% had elevated levels of cadmium, more than 4% had elevated levels of lead, and more than 3% had elevated levels of mercury in the body [86].

Study done by Ramírez-Soto MC et al. [87] showed that Men's mortality was twice that of women. As a result of this information I hypothesized that cadmium and lead are responsible for mutation of influenza virus into COVID-19 [20], Arsenic and manganese are responsible for developing of Lambda variant of COVID.

Theta (P.3) variant, additionally referred to as GR/1092K.V1 contains key spike mutations (141-143 deletion E484K; N501Y; and P681H) and changed into first detected withinside the Philippines and Japan in February 2021 [88]. Study done by Diwa, R et al. [89] showed that heavy metal pollution in Manila Bay is due to several rivers flowing northeast of Manila Bay, especially the Marilao Meycauayan Obando River System. It is ranked as one of the 30 dirtiest river systems in the world. Ecological risks associated with heavy metals in sediments have revealed high rates of toxicity in the northern and central parts of Manila Bay. Cu and Cr have shown a higher risk of toxicity than any other heavy metal. Study done by Judilynn N. Solidum [90] showed that all rice varieties and

fish samples involved in the study showed the presence of lead. Study done by Solidum JM et al [91] showed the presence of lead, cadmium and chromium in all fish samples included. Study dony by Bakshi A and Panigrahi AK [92] showed that Chromium is concentrated in the muscles of the fish. Theta COVID signs appear to be minimal, making the Theta coronavirus stress much less dangerous [68]. Study done by Diez-Quijada L et al. [93] showed that after freezing for a month, fish muscle toxins were most reduced. As a result of this information I hypothesized that cadmium and lead are responsible for mutation of influenza virus into COVID-19 [20], chromium and copper is responsible for appearance of Theta variant of COVID and the mildness of this variant is due to the deposition of chromium on fish muscle, freezing reduces its concentration, and the presence of reactive oxygen species leads to the indirect reduction of hexavalent chromium by copper [94].

Mu variant of COVID was first discovered in Colombia in January 2021 [95]. It has a "mutation constellation" that suggests that it can cause some problems with the COVID19 vaccine and treatment [96]. Study done by Lizarazo MF et al. [97] examined Cu, As, Pb, Cr, Zn, Co, Cd, Ni contained in the vegetables contained in a typical Colombian diet showed that Cd, Cr, As, Co, and Ni showed high transfer coefficients in Cynarascolymus. In addition, Petroselinum crispum had high Pb, Cu, and Zn transfer factors. Fig. 1 shows interaction between plant and heavy metals.

Study done by Akbar M et al. [98] suggested that Co-Cr lodges modified immune system function. As a result of this information I hypothesized that cadmium and lead are responsible for mutation of influenza virus into COVID-19 [20], cobalt and chromium are responsible for surfacing of Mu variant of COVID.

The first sequenced case of Omicron was reported by Botswana on November 11, 2021, and a few days later another sequenced case from Hong Kong was reported by a traveler from South Africa [99]. Study done by Manyiwa T et al. [100] revealed that the environmental impact of the BCL-CuNi mine indicates high levels of heavy metal contamination in soil and some plant species, with a higher exchangeable metal fraction than in normal soil, which is on the soil. This is due to the high solubility of the sediment. surface. Estimates of daily intake indicate potential risks associated with Pb and Cu contamination in grazing animals in the study area. Furthermore study done by Arshad H et al. [101] examined heavy metals` infection in beauty merchandise is take a look at located excessive awareness of Ni, Pb and Cr sunblock lotions and while lipsticks had expanded degrees of Fe and Cd became most in lotions. Women are extra susceptible to the newly-emerged Covid-19

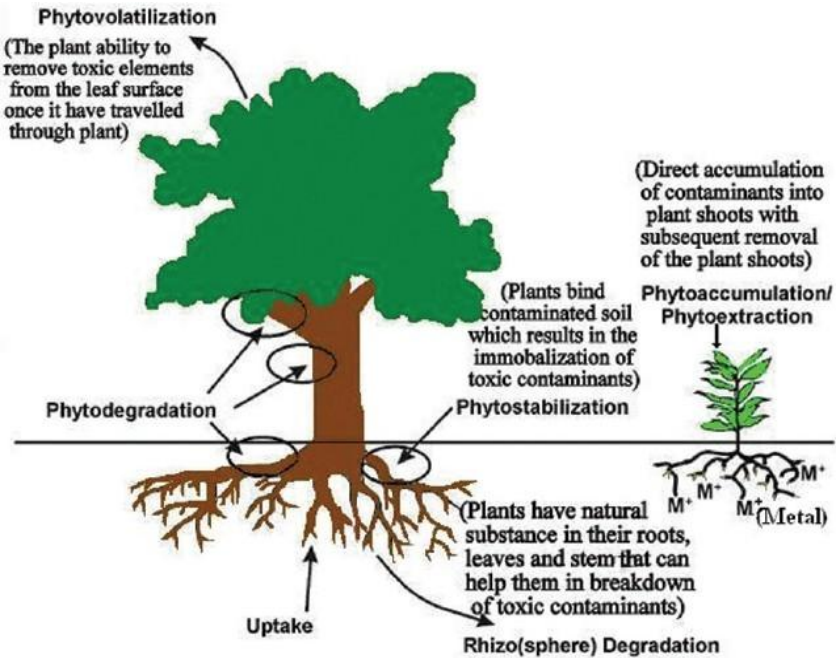

Fig. 1. Shows interaction between plant and heavy metals

version Omicron throughout the globe than men, information discovered in South Africa in which the version become detected first is displaying a unique trend, women, kids and teenagers are being inflamed extra [102]. Study done by Gomez-Berrada MP et al. [103] showed that Babies were always most exposed to family cosmetics, followed by children and adults. South Africa the first known point of OMICRON variant of COVID dominates the African cosmeceutical market [104]. As a result of this information I hypothesized that cadmium and lead are responsible for mutation of influenza virus into COVID-19 [20], and Nickel, chromium are responsible for emergence of omicron.

Study done by Wijngaard RR et al. [105] indicated that Cd and Zn loads in surface waters, and average flux-weighted concentrations in runoff, increase towards the end of the 21st century as a result of Cd and Zn invasion into the soil system, and future climate change will be in winter runoff. Expected to bring about an increase. Reduced summer emissions. Study done by Yang XD et al. [106] identified that temperature and relative humidity were the main contributors to COVID 19 infection. In the summer, higher relative humidity and lower maximum temperatures promote COVID19 infection in dry inland cities, where lower relative humidity is suitable for the spread of COVID19 in coastal cities. Study done by Netz RR, Eaton WA et al. [107] showed that Estimates of aerial virion release support the suggestion that mouth coverings may help contain the COVID 19 pandemic. From the previous mentioned studies I hypothesized that the main mode of COVID-19 is 19 transmission is speaking and metals behaviour of COVID-19 and its strains due to its heavy metals contents.

The clinical manifestations of COVID-19 and its new strains resembles toxicity of heavy metals particularly cadmium and Lead , and that support the above mentioned hypothesises. Furthermore Cadmium, Lead, Arsenic, Chromium, uranium are known mutagens where other metals. While barium showed mutagenic activity on Salmonella typhimurium [108] and nickel and copper also showed mutagenic behaviour [109,110].

Cadmium metals and their oxides are insoluble in water [111], lead is insoluble in water under normal conditions, the compound is generally soluble in soft, weakly acidic water [112], and the elemental nickel is in water. Insoluble nickel sulfide and tetracarbonyl nickel, such as nickel compounds, nickel oxide, are insoluble in water [113], so elemental chromium does not react with water at room temperature. Many chromium compounds are relatively water-insoluble [114]. Pure cobalt is insoluble in water, the water-insoluble compounds are cobalt carbonate and cobalt oxide [115], because oxygen in the water is trapped in water. Copper does not react with water, one part oxygen and two parts compound hydrogen [116], and uranium metal usually dissolves slowly and incompletely in water [117]. So, due to complete or partial insolubility of these metals, it makes their way into plants, vegetables and sea creatures and by this route it contaminates the human food chain. Unfortunately, medicinal plants are listed as a potential cause of heavy metal toxicity to humans and animals. The most common heavy metals involved in human toxicity include lead, mercury, arsenic and cadmium, but aluminum and cobalt can also cause toxicity [118].

Luckily, I observed that six out of twelve top countries publish research on medicinal plants are the known first point of COVID-19 (China) and almost (India, USA, Brazil, Japan and United Kingdom) and that is a strong indicator of the extensive use of these herbal medicines among inhabitants of these countries [119]. And that supports the hypothesis about the probable responsibility of heavy meals in the current pandemic.

Study done by Stickl HA. Schädigung [120] showed that Low concentrations of Pb and Cd in foods lead to diminished cellular and humoral immune responses after months of application. After induction by various infectious pathogens, mortality was higher in mice in the experimental group. Finally, I hypothesized that influenza virus utilized cadmium and lead to reduce immune response, but they changed its genetic structure into COVID-19 and this mutation extended in the presence of other mutagenic metals like arsenic, chromium, cobalt, uranium nickel and even copper and viral variants acquired the characteristics of heavy metals it contained.

I hypothesized that Aryl hydrocarbon receptor explains the relation between COVID-19 and malaria as it decreases concentrations of proinflammatory cytokines by influencing the number of Th17 cells and maintenance of a tight balance between proinflammatory and anti-inflammatory cytokines [121] and one of the prominent features of severe malaria is an imbalance between inflammatory and regulatory

cytokines , study done by Darwish WS [122] showed that Pb concentrations induced oxidative stress in terms of production of reactive oxygen species (ROS). Micronutrients, like β-carotene or ascorbic acid , significantly reduced the levels of ROS production and recovered AhR mRNA expression to normal levels, and the above supports the hypothesized role of lead in the developing pandemic. Furthermore study done by Kluxen FM et al. [123] showed that cadmium alters expression of aryl hydrocarbon receptor associated genes by interaction with estrogen receptor.

3. CONCLUSION

We conclude that viral strains may show metals behaviour and the route of metal administration determines how metals act on viruses. Furthermore the importance of first detection point of the disease identification in understanding etiologies. High cadmium content of soil in Asia, North America, and Europe explained the heavy infections of COVID in this contents in comparison to other continents. OMICRION spread in Africa because the source of this strain in heavy metals in cosmetic products which are used excessively in it, particularly in South Africa. The COVID-19 and its strains mostly resulted from soil and water pollution with heavy metals either from industrial sources or inorganic fertilizers. The main mode of transmission of viral strains is speaking without a mask and Aryl hydrocarbon receptor clarifies the relationship between COVID-19 and malaria, via regulating cellular immunity. This pandemic represents how human activities harmfully affected the global health. Experimental studies recommended.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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