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Dietary Toxicity of Heavy Metals; One Health Perspective

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INTRODUCTION

The term "heavy metals" (HMs) refers to a class of metallic elements with specific gravity larger than 4.0 and density greater than 5g/cm3 (Rehman et al. 2021) and an atomic number greater than 20 (El-Kady and Abdel 2018). Naturally, heavy metals are present everywhere but their concentration is different in many areas. Severe harmful effects occur due to the excessive use of heavy metals by living organisms (Rehman et al. 2019).

Heavy metal toxicity is a major concern fornutritional, ecological and evolutionary related reasons. The risk of heavy metals has been tremendously increased in the environment especially in agriculture setups because heavy metals remain in ground water and soil, which at certain levels leads to cause toxicity as heavy metals accumulate (Alengebawy et al. 2021; Balali-Mood et al. 2021).

Due to their widespread presence in the earth's crust, air, water, and food, heavy metal pollution poses a hazard to the ecosystem on a global scale. From coal burning facilities, smelters, and other industrial facilities, heavy metals emit airborne particles that penetrate the environment (Ali et al. 2019). Numerous human and natural activities have led to an increase in the amount of heavy metal contamination in the ecosystem. Waste disposal, unintended spills during processes, the application of agricultural pesticides and related chemicals, the transfer of contaminants into productive land through the inhalation of fumes, the movement of soil, the inhalation of dust, or the dispersion of sewage mire are just a few examples of these activities. The environment is contaminated by all of these sources (Alengebawyet al. 2021). The major source of pollution of heavy metals (HMs) in vegetables is the presence of heavy metals such as lead, nickel, cadmium, zinc, and mercury in pesticides (Zhong et al. 2018). Most of the metals e.g. copper, manganese, selenium and molybdenum have beneficial effects on human health (Ali et al. 2019).

On the basis of the importance of heavy metals in biological systems, they are classified into two categories such as essential and non-essential. Essential heavy metals are those which play an important role in biological metabolism processes while no3n-essential heavy metals don't have biological functions in living things and are non-essential to metabolic processes (Edelstein and Ben-Hur 2018; Rai et al. 2019). The toxicity of essential heavy metals depends on the concentration of exposure (Aliasgharpour2020) and includes the most important elements which are manganese, iron, zinc (Zn), nickel, chromium (Cr) and copper. Non-essential heavy metals include lead (Fe), cadmium (Cd), mercury (Hg), aluminum (Al) and arsenic (As) which even at low concentrations cause toxicity (Saleh and Koller 2018).

Food produced on tainted soil or irrigated with dirty water increase metal content and is a significant source of exposure to heavy metals in both animals and humans (Rai 2018). Application of sewage mud and sewage water to the soil over time gradually rise its harmful content of heavy metals, which are then increasingly absorbed by plants and vegetables and move up the food chain endangering the health of both animals and humans (Alengebawy et al. 2021).

Heavy metals present a serious risk in feed and diet and prolonged exposure might have toxicological repercussions for plants, animals, and people due to excessive exposure of metals including cadmium, lead, arsenic, chromium, and mercury (Ali et al. 2019). Both direct and indirect effects on human health are caused by these metals. The grazing animals deposit heavy metals on pasture grasses or forages because ofheavy metal contamination in rural areas caused by the dumping of industrial effluents and sewage sludge (Patel et al. 2019).

Sources of Environmental Contamination

Anthropogenic processes and natural sources contribute to the contamination of the environment due to heavy metals. The heavy metals are emitted naturallyby volcanism, wind erosion, wild fires, and biogenic sources. They are also found in nature as oxides, sulphates, phosphates, hydroxides, sulphidesand organic compounds (Masindiand Muedi 2018).

In agriculture industries, manufacturing of different chemicals like insecticides and pesticides are responsible for the release of arsenic and combustion of fossil fuels release nickel and mercury. Anthrogenic processes are also involved to release heavy metals into the environment through metallurgical processes, residuals of organic matter, and transportation. (Zaynab et al. 2022).

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Health Impact of Heavy Metals

Cadmium Toxicity

The most prevalentelement that occurs naturally is cadmium, which was identified in the early nineteen centuries (Gende and Schmeling 2022). Bivalent, bluish-white, soft, malleable, and ductile cadmium is highly hazardous to humans and other living things. It comes from the cadmium ore greenockite, where it may be found in nature in the form of a mineral (Vaid et al. 2022). Compounds containing cadmium are exceedingly harmful to humans, animals, and plants. The presence of cadmium is widespread in the air, soil, water, plants, and ultimately in animal tissues (Dad et al. 2021). The smelters are main sources where pollution of Cd occurs but burning fossil fuels like coal and burning municipal garbage like plastic and nickel-cadmium batteries are two additional possibilities (Balali-Mood et al. 2021).

Additionally, rain can drop cadmium on the ground, and changing the acidity of the water can make it more soluble in cadmium (Yaciuk et al. 2022). It can easily flow by water movement in the top layers of soil, from where it is absorbed by plants and collected in leafy vegetables, root crops, cereals and grains as a result of which it enters the food chain. In the human body, cadmium has been identified to perform not a single physiological task. Because of this, focus has been drawn to its potential for biohazards. As soon as cadmium is absorbed, it builds up in the body for the rest of one's life. Intoxication with cadmium can damage the kidneys, bones and lungs (Al-Lami et al. 2020). The liver, lung, testicles, and hematological system of animals are among the organs that cadmium poisoning is known to impact (Aliasgharpour2020).

High amounts of cadmium are known to irritate the stomach, which eventually leads to vomiting, pain in the abdomen and diarrhea. Abdominal and muscle cramps, headaches, fatigue, and shock are among the symptoms of acute cadmium consumption that often develop within 30 minutes (Al-Lami et al. 2020). The kidneys, liver and circulatory system are particularly affected, but reproductive tissues and growing embryos have seen the worst side effects (Mizoguchi et al. 2022).

Chromium Toxicity

Vaquelin made the discovery of chromium in 1798 and it is the 21st most common mineral on earth which is present in chromite ore, containing iron and oxygen. The threevalance states of chromium are chromium (0), chromium(III) and chromium (VI) (Majhi et al. 2021). Because chromium (VI) is the most poisonous and carcinogenic of all the metals and has negative effects on the health of people, animals and plants (Mushtaq et al. 2021). Industrial wastes and other sources such as plating, painting, cooling tower fluids and chromate manufacturing are found to have contaminated ground water in the United States (Yoshinagaet al. 2018). Due to the high volume of disposed residual tanning floats, chromium may be viewed as a source of pollution (Younas et al. 2022).

The metallurgical, chemical and refractory sectors are the three largest industries in the world which employ chromium. It is used to make different metal alloys and stainless steel and additionally it is utilized in the creation of joint prosthesis. Additionally, it is utilized in the purification of water, drilling mud, safety matches, copier toner, corrosion inhibitors and photographic chemicals, magnetic tapes and drilling (Laurenti et al. 2017). Cr (VI) is 1000 times more hazardous and 100 times more mutagenic than trivalent chromium (Mushtaq et al. 2022).

Water contamination through water leaching and industrial release is more critical than inhalation of chromium compounds via air emission spread by cigarette smoke, automobile emissions and others (Pavesi and Moreira 2020). Chromium plays an important role in boosting up of insulin for normal glucose metabolism and lipid metabolism and also helps in lowering triglycerides and cholesterol (Prasad 2016).

Chromium toxicity manifests similarly to other heavy metal toxicity in terms of signs and symptoms. Depression, diarrhea (dysentery), dyspnea, paralysis, inappetance, and mortality within a short period of time are some of these symptoms. The lungs, kidneys, and liver experience pathological alterations as a result of Cr poisoning. Chromium exposure severely damages the lungs, leading to mucosal erosion and inflammatory changes in the respiratory tract. Bronchial spasms or even an allergic reaction may occur as a result of chromium poisoning. Hexavalent chromium has also been linked to renal failure, acute renal tubular necrosis, and lung cancer (Deng et al. 2019).

Chromium exposure causes cellular toxicity by generating ROS and cause damage of DNA through activation of high levels of oxidative stress andepigenetic gene expression (DesMarias and Costa 2019). The toxicity and carcinogenicity of Cr depends on time, route and concentration of exposure (Aliasgharpour 2020; Balali-Mood et al.2021).

Nickel toxicity

Nickel occurs naturally in the environment but, in very small amounts. Australia, Canada, Cuba, Indonesia, New Caledonia and Russia are the main countries where nickel ores are found in deposits (Vahed et al. 2021). If nickel is volatile, it is extremely poisonous because it is lipid soluble and can pass through cell membrane. Humans have been discovered to be particularly poisonous to nickel carbonyl (Sule et al. 2020). It is used to create steels that are heat and corrosion resistant. Acute toxicity and immunological problems may result from its usage in the manufacture of

nickel salts,the fabrication of NI-CD batteries, the development of moulds for the hollow glass industry, the production of coins, jewelry and medical and dental implants (Al-Lami et al. 2020; Salimi et al. 2020). Animals and plants can become poisonous to nickel if they consume polluted water. Acid rain is by far the main cause of water pollution. Acid rain has the propensity to release nickel from the soil and raise the concentration of nickel in groundwater (Begum et al. 2022). Nickel contamination in water can have negative neurological consequences as well as gastrointestinal problems such as nausea, vomiting, and diarrhea (Pirhadi et al. 2021).

Nickel allergy"—an allergic dermatitis—can be brought on by occupational contact. Due to wearing nickel-plated jewellery, skin rash or allergic dermatitis may develop in cases of dermal contact. Women are more susceptible to the effects of nickel than men, particularly when pregnant women who work in the metallurgical industry have babies with structural defects (Aliasgharpour2020; Rehman et al. 2021).

At the cellular level, it can result in DNA strand breaks, cross-linking of DNA protection, DNA oxidation, nucleotide removal, gene mutations, changes of chromatids, binding to enzymes involved in DNA repair and protein degradation, formation of ROS, enhancement of lipid peroxidation, altering calcium, and sulfhydryl balance, and glutathione degradation (Das et al. 2019).

Lead toxicity

Lead is a bluish-grey metal that occurs naturally and is found in the earth's crust in small amounts (Khatun et al. 2022). It is found in rocks, soil, plants and animals. It is a ubiquitous element, which occurs at a pretty low level (Rahman and Singh 2019). Lead has been used in industry, household products, cigarettes, ceramic glazes, paint, smelters, televisions, pesticides, computer monitors, batteries, explosives, pipes and toys for centuries (Sanz et al. 2022).

Because it can result in significant environmental contamination and health issues, lead is the most significant toxic heavy metal in the environment (Aliasgharpour2020). Industrial processes like burning fossil fuels, mining, smelting, manufacturing, and recycling are the main causes of environmental contamination. (Marzilli 2019).

The chemical or heavy metal pollution which has caused toxic, mutagenic, or carcinogenic effects on human health has risen due to the combination of new chemical substances (Alengebawy et al. 2021). The noxiousness of lead was recognized in 200 B.C. The fact that lead causes anemia and colic in human beings was discovered in 250 B.C (Pereira et al. 2020).

The materials used in lead pipes, tin soldiers, and brass fixtures are the primary source of lead in drinking water (Chang et al. 2022). One of the sources of lead in the air, water and soil that ultimately enters the food chain is found in phosphate rocks (Kumar et al. 2019).

Lead produces lung disorders, anemia, liver damage, renal impairment and also affects nervous system by exposure to high concentration in adults and children (Singh et al. 2018). General symptoms of lead poisoning in children due to increase in lead levels in blood include abdominal pain, irritability, lethargy, anorexia, pallor body, ataxia and slurred speech (Rees and Fuller 2020). Encephalopathy and gastroenteritis are frequently seen in dairy cattle as a result of the animals grazing on contaminated forages caused by the application of sewage sludge to the pastures (Gupta et al. 2021).

High amounts of this heavy metal in the blood during pregnancy have been proven to allow it to breach the placental barrier, which can result in fetal abnormalities like low IQ, encephalopathy, neurological diseases, and disruptions in calcium levels in nerve cells. Lead exposure during pregnancy can cause miscarriage, early birth, low birth weight and stillbirth (Aliasgharpour 2020; Rehmanet al. 2021).

After ingestion, 99% of the lead is bound to hemoglobin and circulates through the circulatory system to soft tissues, bones, liver, kidneys, and hair, which is retained primarily in teeth and bones (where it is absorbed into the mineral in place of calcium). Particularly when a woman is pregnant, the bloodstream can be reintroduced with accumulated lead which exposes the foetus (Cioseket al. 2021).

Arsenic toxicity

Arsenic is among the most toxic metals found in the environment and is found in metallic, metalloid, inorganic, and organic form. Arsenic exist in three valence states: As (0), (III) and (VI). In general, the inorganic form of as is more toxic than organic form (Thakur et al. 2021; Genchi et al. 2022).

It is omnipresent metal found in air, land, ocean, lakes, and water (Rahamanet al. 2021). Arsine gas is a very poisonous substance. Mining, metallurgical and microelectronics sectors all produce arsine gas. Ground water contamination, which is a severe issue, is also discovered to contain arsenic. This is particularly true in the third world nations (Ali et al. 2019). More than 100 million people worldwide are at risk of mortality from arsenic poisoning from the food and drinking supplies (Nurchiet al. 2020).

Cancers of the kidney, liver, lungs, and bladder are brought on by prolonged exposure to arsenic (Aliasgharpour2020; Rehman et al. 2021). Abrupt arsenic exposure can result in a variety of symptoms, including tachycardia, acute encephalopathy, congestive heart failure, stupor, convulsions, paralysis, coma, and even death. Arsenic exposure causes peripheral neuropathy, cardiovascular discomfort, peripheral vascular disease, kidney and liver damage, hypertension, myocardial infarction, and leukopenia (Fakhar et al. 2022). Arsenic's long-term side effects include skin deformities, neurotoxicity effects, severe pulmonary illnesses, insanity, cognitive impairment, loss of hearing, and coronary heart disease (Singh et al. 2022).

Table 1: List of five key metal's effects on human health

Metals	Deficiency health effects	Toxicity health effects	References
Iron (Fe)	Anemia Mental retardation Brain damage	Cardiac toxicity Metabolic disorders Hepatotoxicity Neurodegenerative disorders Cancer	Engwa et al. 2019
Selenium (Se)	Kashin disease	Skin rash Loss of hair Neurologic disorders Fatigue Abdominal pain	Vinceti et al. 2018
Iodine (I)	Neutropenia Osteoporosis Impaired mental confusion Hypothyroidism	Hypothyroidism Goiter Hyperthyroidism	Niziński et al. 2021
Copper (Cu)	Neurological disorders Neutropenia Osteoporosis Hypopigmentation	Brain damage Necrosis Liver cell erosion Death	Rahman and Singh 2019
Zinc (Zn)	Abdominal disturbance Behavioral changes Growth retardation Immunological deficiencies	Nausea, vomiting and diarrhea Lethargy Fever Anemia	Chasapis et al. 2020

At the cellular level, arsenic compounds have the capacity to bind specific structures or substitute specific substances. They can also inhibit the mitochondrial enzymes involved in cellular respiration. It inactivate particular enzymes like thiolaseand dihydrolipoyl dehydrogenase and disrupt oxidative phosphorylation (Bahrami et al. 2020).

Mercury toxicity

Mercury is a metallic, shiny, odorless sliver white fluid, which upon heating converts into dull and colorless gas. Mercury is both extraordinarily deadly and bio-accumulative (Kumar and Kumar 2019). Mercury enters the climate through a typical breakdown of minerals present in rocks, which are moved to the soil via air and water. The centralization of mercury in the climate is expanding step by step, and this is exposed to human action. The majority of the mercury is delivered into the air through fossil fuel combustion, mining, refining, and strong waste burning (Charvát et al. 2020).

Mercury in all chemical forms has capability to cross the placental, and blood-brain barriers, and also secreted in milk (Pajewska-Szmytet al. 2019). Exposure of mercury causes the toxicity associated with fever, insomnia, tremors, weight loss, and excessive perspiration (Bharti and Sharma 2021). The reproductive system's ability to cause infertility in both men and women was proved by the research. The spermatogenesis of males is impacted, while progesterone and estrogen levels in females may be disturbed, resulting in ovaries that don't function normally, irregular menstruation, and a uterus that slopes (Balali-Mood et al. 2021).

Mercury genotoxicity was linked to DNA damage, conformational changes in DNA repaired proteins, genetic mutations, mitotic spindle, chromosomal segregation, and effects on nucleic acids (Gashi 2018). Moreover, for informative survey analysis, seafood is a core source of mercury contamination. Food products prepared from fishmeal for livestock and eventually for humans have great chances of septic conditions and ultimately cause toxicity (González-Montaña et al. 2019).

Other essential metals

The majority of necessary metals function as enzyme catalysts and can be hazardous in excessive concentrations. Metals frequently combine with organic substances including amino acids, proteins, and peptides in tissues and bodily fluids to produce complexes.

Table 1 shows the list of five key metals which show serious effects on the human health.

Conclusion

Heavy metal toxicity and its effects on the ecosystem are a global problem due to their transportation through the air, soil and water. The potential of ingesting heavy metals through food, air, and drinking water depends on a number of variables, including concentration and numerous primary sources. Humans need these metals in trace amounts for normal cellular, metabolic, and hormonal function; nevertheless, if the limit is exceeded, it can have serious negative health impacts. The toxicity of these metals has a significant negative impact on the soil by destroying microorganisms that are essential to improve soil fertility and nutrition.Much emphasis has been paid to their removal from aquatic and soil environments.

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