An Analysis of Effect of Zinc on Several Diseases

Dr Jyotirmaya Sahoo, Professor

Department of Health & Allied Science, Arka Jain University, Jamshedpur, Jharkhand, India

Email Id: dr.jyotirmaya@arkajainuniversity.ac.in

ABSTRACT: Zinc (Zn) is an important necessary nutrient with significant public health implications. It has a role in a variety of biological processes and is regarded as a versatile trace element because of its ability to bind to over 300 enzymes and over 2000 transcriptional factors. It plays a significant role in biochemical processes and physiological activities such as homeostasis, immunological responses, DNA replication, DNA damage repair, cell cycle progression, apoptosis, and aging. Zn is necessary for the production of protein and collagen, which aids wound healing and skin health. Metallothioneins are metal-binding proteins that are effective heavy metal scavengers, including Zn, and protect the body from stress. Zn deficiency affects almost 17 percent of the world's population and affects a variety of organ systems, causing both humoral and cell-mediated immunity to malfunction, and increasing infection susceptibility. This review delves into the most up-to-date research on the link between Zn biochemistry and human diseases, epigenetic processes, gut microbial composition, therapeutic targets, and nanomedicine.

KEYWORDS: Disease, Food, Metal, Proteins, Zinc.

1. INTRODUCTION

The human body contains 2–3 g of zinc, making it the second most abundant transition metal after Fe and the second most common divalent cation after calcium in humans and many other living creatures. Zn is a trace element that is required for all organisms' growth and development. It is an important antioxidant mineral for reducing the production and reactive reaction of free radicals, which are unstable atoms with one or more unpaired electrons that may harm cells and cause chronic and degenerative illnesses to proceed. Differentiation, cell division, cell growth, cellular transport, the endocrine and immunological systems, transcription, protein synthesis, RNA and DNA synthesis, and DNA replication are all dependent on Zn. It may be present in a variety of tissues, the majority of which are located in the testes, muscle, liver, bones, and brain. It is plentiful in synaptic vesicles and plays an important function in memory and learning. In addition, Zn serves as a cofactor in over 1000 enzymatic processes and over 2000 transcription factors[1].

Zinc finger proteins are one of the most common protein families, and they play a variety of molecular functions in both health and illness. The structural stability of Zn finger proteins is dependent on Zn (Zfp). Zn finger proteins are transcriptional factors that can change the way DNA, RNA, and other proteins are made. Signal transmission, cell differentiation or proliferation, cell adhesion, and transcription are all regulated by them. Furthermore, Zn preserves the enzymatic structure of CuZn-superoxide dismutase's active site (SOD). Class I Cys2His2 (C2H2) proteins, Class II Cys4 (C4) Zn fnger proteins, and Class III (C6) Zn fnger proteins, often known as Zn cluster proteins, are the three types. Zn has an important role in immune system function, wound healing, insulin production and secretion, and blood pressure control. It controls the expression of metallothioneins and is a biological regulator of gene expression and homeostasis. Zn homeostasis dysregulation plays a key role in the development of cardiovascular disorders, cancer, and the generation of reactive oxygen species. Zn is dispersed throughout the cytoplasm (50 percent), nucleus (30–40 percent), and cell membrane after absorption by cells (10 percent). Cellular Zn may bind firmly to metalloproteins/metalloenzymes and metallothioneins, be segregated into intracellular organelles and vesicles through Zn transporters for storage, or be kept in free form in the cytoplasm at extremely low concentrations.

Zn deficiency affects about 17 percent of the world's population, and it is responsible for 4% of all infant morbidity and death. Parenteral nutrition, undernourishment, malnutrition, and low Zn levels in breast milk are the most common causes of Zn deficiency in babies and children. Excessive Zn loss may also cause gastrointestinal and urinary tract problems, as well as chronic inflammatory bowel illnesses including Crohn's disease and ulcerative colitis. periorifcial dermatitis, alopecia, diarrohea, poor wound healing, gustatory abnormalities such as dysgeusia and dysosmia sensation, immunodeficiency, and an increased frequency of bacterial, fungal, and viral infections are all common clinical signs of Zn deficiency. This article tries to offer an overview of Zn biochemical participation in human diseases, epigenetic processes, gut microbial composition, and therapeutic targets, given Zn's diverse and important roles in the human body[2].

1.1 Biology and homeostasis:

After iron, zinc (Zn2+) is the body's second most essential trace element. Zn has three main biological functions as a structural, catalytic, and regulatory component in numerous metabolic processes. It is a cofactor for over 300 enzymes, including hydrolases, transferases, oxyreductases, ligases, isomerases, and lyases, and plays a role in the structure of over 2000 transcription factors. Zn is also involved in the control of gene expression and the correct functioning of the immune system. Because Zn is not stored in the body, it must be consumed on a regular basis to maintain necessary levels and support all of the body's activities. Zn2+ is absorbed in the stomach, mostly via the enterocytes of the jejunum, and any remaining Zn2+ is expelled. Zn is present in relatively high quantities in all bodily tissues and secretions, with an average quantity of 1.4–2.3 g in the adult body. Only a tiny quantity of Zn2+ is circulating in the blood, with the bulk of Zn2+ reserves being found in skeletal muscle and bones. Zn is mainly linked to proteins like albulin or 2-macroglobulin in the body, and only a tiny percentage of Zn2+ exists as a free labile form that may be taken up by cells such as blood cells, endothelial cells, and platelets through endocytosis or other transport processes[3].

1.2 Food sources and recommended daily doses:

Zn can be found in a broad variety of foods. Oysters are most abundant in Zn than any other food. However, the main sources of Zn intake are meat (beef, veal, pork and lamb) and meat products, cereals and grains, and milk and dairy products. Other good food sources such as fsh, vegetables, nuts, and ready-to-eat meals contain Zn but in smaller amounts. The recommended dietary allowance of Zn has been defned by the US Institute of Medicine/Food and Nutrition board in the 2001 Dietary Reference Intakes report to be 11 mg/day for men and 8 mg/day for women. The tolerable upper limit of intake is 40 mg/day in adult[4].

1.3 Zinc deficiency:

A number of studies have shown that trace element deficits are more common than previously thought. Because trace element deficits may affect any organ, doctors must keep an eye out for them while making a differential diagnosis. Zn is an essential trace element for human health, and a lack of it may cause stunted development, anorexia, loss of smell and taste, and other symptoms in humans. Zn insufficiency may be caused by a variety of factors. Poor Zn intake in babies and children may be caused by parenteral nutrition, malnutrition, or low Zn levels in breast milk. Furthermore, eating disorders like anorexia nervosa and bulimia, as well as alternative dietary patterns like veganism, may cause Zn insufficiency in both children and adults. Increased Zn loss may be caused by gastrointestinal issues such persistent diarrhoea or urinary tract issues like kidney illness or diabetes mellitus. Malabsorption problems are the most frequent cause of Zn deficiency. Inherited disorders including acrodermatitis enteropathica and cystic fibrosis, as well as chronic inflammatory bowel conditions like Crohn's disease and ulcerative colitis, may cause Zn deficiency. A high intake of copper, iron, or phytic acid, on the other hand, may cause dietary Zn malabsorption[5].

1.4 Zinc in oxidative stress and inflammation:

The state of imbalance between free radicals, which are any molecules with one or more unpaired electrons, and the capacity of the system to detoxify or prevent oxidative damage to DNA, proteins, and lipids is referred to as oxidative stress. The activation of phagocytes and/or the interaction of bacterial products with particular receptors may promote the assembly of NADPH oxidase, which catalyzes the generation of large quantities of superoxide anion radical during inflammatory events. Superoxide free radicals and H2O2 are produced by neutrophils and macrophages, which are necessary for defense against phagocytized or invading microorganisms. Antioxidants are required in stressful situations to control the processes that produce free radicals and to avoid free radical damage. Antioxidant substances such as vitamin E, vitamin C, b-carotene, and vital trace elements such as selenium, copper, iron, and zinc, which are all found in a healthy diet, boost immune function and protect against illnesses caused by bacteria, viruses, and parasites[6].

1.5 Zinc and apoptosis:

Apoptosis is a key method of planned cell death that plays a role in a variety of biological processes such as tissue formation, remodelling, and involution. In reaction to harmful substances, it is a regulated biological process that eliminates extraneous, mutant, or mildly damaged cells. In contrast to necrosis, which is cellular

'homicide,' apoptosis is a process of cellular 'suicide.' Cell death caused by lysosomal breakdown and/or necrosis varies morphologically from apoptosis. The biochemical signaling pathways commit a cell to apoptosis in the first phase, and the execution phase is defined by morphological changes leading to cell death in the second. Apoptosis may be triggered by a variety of external and intracellular triggers. Dysregulation of apoptosis has been linked to harmful processes in a variety of illnesses, including neurological disorders, autoimmune diseases, and malignancies[7].

Changes in intracellular and extracellular Zn concentrations control Zn's multi-directional function in the onset and prevention of apoptosis. Because it maintains caspase-3, caspase-8, and caspase-9 in the state of proenzyme, Zn serves as an inhibitor of these cysteine proteases with a fundamental role in apoptosis. When the apoptosis process is started, these enzymes exist as proenzymes in the cytoplasm and are converted into active forms. Caspases that are active may activate additional procaspases, resulting in a chain reaction. Proteases are enzymes that break down a variety of proteins, including poly (ADP-ribose) polymerase, which is involved in DNA repair, and transcription factors. MDM2, a protein that acts as a p53 negative regulator, is also inhibited. As a consequence, p53 may activate genes involved in cell repair or apoptosis, as well as activate members of the caspase family of proteases, causing the cell to die[8].

1.6 Zinc and immune system:

Because Zn is required for both cell-mediated and humoral immunity, it has a significant effect on the immune system. Innate immunity cellular mediators such as macrophages, neutrophils, and natural killer (NK) cell activity, cytokine synthesis, and complement activity may all be affected by a lack of zinc. Zn deficiency also affects phagocytosis and intracellular killing. Zn deficiency also has a detrimental effect on T and B cell development and function. Zn deficiency leads in a reduced number of peripheral and thymic T cells, poor proliferative response, and decreased activity of T helper and cytotoxic T cells because T-cell proliferation is linked to Zn. With addition, in Zn shortage, the Th1 response, which is essential for infection prevention, is reduced, while the Th2 response is increased. Increased vulnerability to infections may result from these immune system deficiencies[9].

1.7 Zinc and cardiovascular diseases (CVDs:

Zn deficiency has been linked to the onset of cardiovascular disorders, particularly atherosclerosis. 24 Zn transporters (ZIPs) were found in high abundance in human cardiac muscle regions, according to the Human Protein Atlas database, which hosts RNA-Seq transcriptomics and antibody-based proteomics. This suggests that Zn homeostasis is closely linked to CVDs. SOD1 deficiency results in oxidative stress and high amounts of oxygen (O2), which reacts with nitric oxide (NO) to produce peroxynitrite. RNS has the ability to oxidize eNOS and uncouple eNOS dimers, resulting in an increase in ROS generation and a reduction in NO synthesis.

NO is an essential regulator of vasodilation, and its decrease is linked to the pathophysiology of several CVDs, including hypertension. Nitric oxide may influence blood pressure both directly and indirectly, since it promotes arterial dilatation and is linked to the suppression of sympathetic nerve activity, which is implicated in vasoconstriction. Maintaining sufficient amounts of SOD and lowering O2 levels enhance Zn's protective effect against hypertension. Furthermore, a substantial increase of intracellular Zn levels in both pulmonary endothelium cells and vascular smooth muscle cells was observed in pulmonary artery hypertension, suggesting that loss of Zn homeostasis may be both a cause and a consequence of hypertension[10].

1.8 Zinc and diabetes:

Diabetes mellitus (DM) is a metabolic disease marked by a rise in blood sugar levels and a disruption in glucose metabolism, caused by either reduced insulin production or impaired insulin sensitivity in the body's cells. An imbalance between free radical generation and the body's diminished antioxidant defense systems may induce cellular and molecular damage, including the development of insulin resistance, according to many clinical and experimental evidence. Insulin secretion and action in peripheral tissues are thought to be influenced by zinc. Zn binding to insulin is necessary for the hormone's production, crystallization, and maturation. ZnT8 is primarily responsible for Zn transport into the insulin secretory granules of -cells.

1.9 Zinc and obesity:

Many studies believe that Zn deficiency is linked to the condition of adipose tissue in obesity and other diseases. A healthy adipogenic differentiation is required to maintain the essential activities of adipose tissue, such as insulin sensitivity. Zn finger proteins, which may control transcription, are implicated in these activities. Zinc-a2-glycoprotein (ZAG), for example, is a cytokine produced by adipose tissue that controls lipid metabolism. ZAG activity causes enhanced lipolysis and reduced lipogenesis in adipose tissue by affecting various enzymes, such as boosting hormone-sensitive lipase (HSL). Zn acts as a negative regulator by suppressing adipose tissue lipolysis and inactivating hormone-sensitive lipase via its insulin-mimetic characteristics.

1.10 Zinc and skin disorders:

Zn deficiency has been linked to a variety of skin conditions. Zn is needed for cell membrane repair, cell proliferation, growth, and immune system function as a cofactor for numerous metallo enzymes. Skin lesions, growth retardation, decreased immunological function, and slowed wound healing are all symptoms of zinc deficiency. Every step of the wound healing process, from coagulation through inflammation and immunological defense, angiogenesis, and scar formation, Zn plays a critical role.

1.11 Zinc and mental diseases:

Although not fully explained, a link between Zn dysregulation and neuropsychiatric diseases such as depression, Alzheimer's disease, and amyotrophic lateral sclerosis has been proposed. According to the World Health Organization (WHO), major depressive disorders affect about 35 million people globally, resulting in significant morbidity and death; therefore, the link to depression may account for the disease's greatest mental effect. Zn may have a role in the regulation of neurotransmission, endocrine, and neurogenesis pathways, according to research. Zn ions control numerous ligand- and voltage-gated ion channels and may influence synaptic transmission or function as neurotransmitters in the hippocampus and cortex. Zn is mainly found in glutamatergic neurons in the limbic system, where it acts as an NMDA receptor inhibitor.

1.12 Zinc and bone formation:

Growth, neural development, and immunology are all known to be regulated by zinc. This trace element supports anabolic activity by improving the strength, flexibility, and architecture of the skeleton in animals. Zn has a significant bone-protective impact at physiological doses, which is mediated via a variety of mechanisms. It works as a growth stimulant by activating enzymes involved in DNA, RNA, and protein synthesis, resulting in increased osteoblastic activity and collagen production. By shifting the turnover balance toward anabolism, Zn may also prevent osteoclastic bone resorption. Indirectly, a zinc deficit may affect bone health by reducing intestinal calcium absorption and raising the circulating parathyroid hormone (PTH), which promotes bone turnover.

2. DISCUSSION

Zinc insufficiency has been linked to poor mother health and poor pregnancy outcomes. Zinc supplementation trials and observational studies that evaluated maternal, foetal, and newborn health outcomes have documented these effects throughout the years. Pre-clinical research have revealed that zinc deficiency may alter biological processes involving epigenetic mechanisms in children due to its significance in the functioning of epigenetic enzymes. Zinc is a trace element that is essential for all living things. The significance of zinc in human nutrition and public health has only recently been recognized. A shortage of zinc has been recognized as a significant public health issue by a number of specialists, especially in developing countries. The prevalence of zinc deficiency and its clinical consequences for growth retardation, diarrhoea, pneumonia, decreased cognitive function, and prenatal development issues. Because zinc is such an essential mineral for human health, even a little deficiency may be deadly. This paper discusses effect of Zinc on several Diseases.

3. CONCLUSION

Zn seems to be a multifunctional element that is essential for human health and well-being. It is without a doubt one of the most important micronutrients, with roles in human physiology, cell-mediated immunological activities, oxidative stress, and as an intracellular signalling molecule. Zn biochemistry is involved in epigenetic processes, gut microbial composition, and therapeutic objectives, and it is an anti-inflammatory drug. Atherosclerosis, various malignancies, autoimmune illnesses, Alzheimer's disease and other neurological disorders, cancer, diabetes, depression, aging, and Wilson's disease are among the chronic diseases for which Zn has therapeutic advantages in humans. Experimental data in recent years has shown that Zn deficiency is linked to a slew of health issues, making it critical to address the problem. Zn supplementation has the potential to improve nutritional status as well as the treatment of certain illnesses, where Zn may be utilized as an additional therapy.

REFERENCES:

[1] A. S. Prasad, "Zinc in human health: Effect of zinc on immune cells," *Molecular Medicine*. 2008, doi: 10.2119/2008-00033.Prasad.

[2] L. M. Plum, L. Rink, and H. Hajo, "The essential toxin: Impact of zinc on human health," *International Journal of Environmental Research and Public Health*. 2010, doi: 10.3390/ijerph7041342.

[3] C. T. Walsh, H. H. Sandstead, A. S. Prasad, P. M. Newberne, and P. J. Fraker, "Zinc: Health effects and research priorities for the 1990s," *Environmental Health Perspectives*. 1994, doi: 10.1289/ehp.941025.

[4] D. van der Merwe, J. W. Carpenter, J. C. Nietfeld, and J. F. Miesner, "Adverse health effects in Canada geese (Branta canadensis) associated with waste from zinc and lead mines in the Tri-State Mining District (Kansas, Oklahoma, and Missouri, USA)," *J. Wildl. Dis.*, 2011, doi: 10.7589/0090-3558-47.3.650.

[5] C. H. Pan *et al.*, "Effects of size and surface of zinc oxide and aluminum-doped zinc oxide nanoparticles on cell viability inferred by proteomic analyses," *Int. J. Nanomedicine*, 2014, doi: 10.2147/IJN.S66651.

[6] A. K. Shukla, P. K. Tiwari, P. Abhijit, and P. Chandra, "Zinc and iron in soil, plant, animal and human health," *Indian J. Fertil.*, 2016.

[7] M. E. Penny, "Zinc supplementation in public health," *Ann. Nutr. Metab.*, 2013, doi: 10.1159/000348263.

[8] K. A. Lomagno *et al.*, "Increasing iron and zinc in pre-menopausal women and its effects on mood and cognition: A systematic review," *Nutrients*. 2014, doi: 10.3390/nu6115117.

[9] M. M. Almoudi, A. S. Hussein, M. I. Abu Hassan, and N. Mohamad Zain, "A systematic review on antibacterial activity of zinc against Streptococcus mutans," *Saudi Dental Journal*. 2018, doi: 10.1016/j.sdentj.2018.06.003.

[10] C. T. Chasapis, C. A. Spiliopoulou, A. C. Loutsidou, and M. E. Stefanidou, "Zinc and human health: An update," *Archives of Toxicology*. 2012, doi: 10.1007/s00204-011-0775-1.