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Role of Vitamin Supplements in Deep-Rooted Diseases

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ABSTRACT

Now-a-days the physicians prescribe vitamin supplements in most of the prescription so this review focus on the need of vitamin supplements are necessary to support the disease condition or worsen the condition. Many individuals use multivitamin/mineral supplements for disease-mitigating or prophylactic purposes, most of them using vitamin supplements for chronic diseases, especially for Cardiovascular disease and cancer and also used in obesity-related diseases such as type 2 diabetes, end-stage renal disease, and osteoarthritis. Many of them share common risk factors for chronic diseases is deficiency of vitamins results in pathological changes, Examples include reduction of Oxidative damage by antioxidants, DNA methylation regulated by folate and B vitamins, bone metabolism regulated by vitamin D and calcium, and cell differentiation, proliferation, and growth regulated by retinol, calcium, and vitamin D.

Key words: Vitamin deficiency, Vitamin supplements, cancer, diabetes, epilepsy, chronic kidney disease, psychiatric diseases.

1. INTRODUCTION

Most people use a daily multivitamin for treatment or prevention of chronic disease all over the world because of uncontrolled advertisements about the vitamins in addition to the wide availability of these agents result in the high prevalence of their consumption among people. But the effectiveness of multivitamins and minerals remains unclear, the prevalence of the use of multivitamin supplements in many developed countries is widened. The percentage of using any daily vitamin and mineral supplements in the adult age group has increased very rapidly in recent years. [1] 35 million people deaths occur due to chronic diseases worldwide, in this majority are Cardiovascular disease and cancer individuals in both developed and developing countries.4 Other than cardiovascular disease and cancer, obesity-related diseases such as end-stage renal disease, type 2 diabetes mellitus, osteoarthritis, and non-alcoholic steatorrhic hepatitis. [2]

2. Common Pathologic Mechanisms of Chronic Diseases

Many etiological factors responsible for the development of chronic diseases, major risk factors of several chronic diseases are:

- Cigarette smoking/tobacco use,
- Sedentary lifestyle,
- Unhealthy (high calorie, low fruit/vegetable intake) diet, and obesity.

2.1 Cigarette smoke : Oxidants (free radicals and reactive oxygen, nitrogen and chlorine species)leads to oxidative stress, a result of an imbalance between oxidative and reductive potential in favor of the former, may play an important role in the initiation, promotion, and progression of cardiovascular disease (in particular, ischemic heart disease and stroke), cancer, and several degenerative diseases/conditions, such as age-related cataract, age-related macular degeneration, and cognitive decline.

Oxidative damage to lipids by free radicals initiates and propagates chain reactions that may be intercepted by antioxidants or otherwise lead to the development of atherosclerosis and mutagenesis.

Oxidative damage to DNA causes the formation of DNA adducts, double-strand breaks, single-strand breaks, aberrations and instability of chromosomes, and genomic instability that may leads to mutagenesis and carcinogenesis.

Oxidative damage to proteins may affect enzyme expression and impair critical cellular signalling, leading to alterations in cell function.

2.2 Sedentary lifestyle, excessive caloric intake, and lack of physical activities: lead to obesity, and obese individuals have higher levels of inflammation, a key process of disease progress and leads to many cancers and chronic conditions. Inflammatory responses can induce the generation of free radicals and reactive oxygen species that cause oxidative stress and further exacerbate disease processes. In addition to oxidative damage and inflammation, one-carbon metabolism has been implicated to be important in several chronic diseases, particularly cardiovascular disease, renal failure, neurological dysfunction, and cancer. An important step in one-carbon metabolism is the synthesis/metabolism of methionine. Methionine is a precursor of S-adenosylmethionine (SAM), a universal methyl donor to DNA, RNA, protein, phospholipids, neurotransmitters, and hormones. Hyper methylation in the promoter regions of tumour suppressor genes and chromosome aberrations due to global hypo methylation may lead to ontogenesis. In methionine synthesis, an intermediate molecule is a homocysteine, which has been found to be associated with increased risk of coronary artery disease, stroke, peripheral vascular disease, cognitive impairment, dementia, depression, osteoporotic fractures, and functional decline [2].

3. Possible Mechanisms of Action of Vitamins and Minerals in Chronic Disease Prevention:

Multivitamin/mineral supplements often contain vitamin A, β-carotene, vitamin B1 (thiamine), vitamin B2 (riboflavin), vitamin B6 (pyridoxine), vitamin B12 (cyanocobalamin), vitamin C, vitamin D, vitamin E, folic acid, niacin, calcium, iron, zinc, magnesium, and selenium. These nutrients have numerous biological effects and have garnered considerable research interest in their potential as chemo-preventive agents for the prevention of chronic disease. As described previously, a common process of chronic disease is oxidative damage by free radicals or reactive species. There are multiple systems involved in the protection of the human body from oxidative damage. Endogenous enzymatic antioxidants, such as copper- and zinc-, or manganese-containing superoxide dismutase, selenium-dependent glutathione peroxidase, and Catalase, can catalyse radical- and peroxide-quenching reactions. Non-enzymatic antioxidants include but are not limited to vitamin C, vitamin E, bilirubin, urate, flavonoids, and certain carotenoids (e.g., β-carotene and lycopene).

3.1_Folate, vitamin B6, and vitamin B12 influence methylation by supplying methyl groups and are essential for nucleotide synthesis, DNA synthesis, and DNA repair. Folate and B vitamins maintain normal brain function through the methylation of neurotransmitters, phospholipids, and myelin. They are also essential in homocysteine metabolism because irreversible Tran's sulfuration and the remethylation of homocysteine rely on coenzymes derived from vitamin B6, vitamin B12, and folate. In addition to anti-oxidation and regulation of methylation, vitamins and minerals may have inhibitory effects on inflammation (γ-tocopherol, zinc, and vitamin A) and angiogenesis (α-tocopherol, vitamin A, vitamin C, vitamin D). Some may also regulate cell differentiation, proliferation, and apoptosis (vitamin A, α-tocopherol, vitamin D,

calcium) and enhance immunity (vitamin A, zinc, vitamin E, vitamin C, calcium)[2].

3.2 Calcium and Magnesium: play an important role in blood pressure regulation. Calcium also plays a major role in in the maintenance of cholesterol levels and body weight and may buckler the contact of carcinogens with bowel mucosa by forming insoluble chemical complexes with bile acid and fat [2].

4. Role of vitamins in cancer:

4.1 Vitamin D and cancer:

VDBP is a vitamin d binding protein act as a carrier and it combines with vitamin d and its metabolites to play a crucial role in transport to the cell. Deficiency of VDBP or low level of VDBP Leads to the development of many malignant tumours such as breast, prostate and colorectal cancers [3-5].

4.2 Vitamin C in cancer [6]:

- ✓ It plays a major role in the metabolism of tyrosine, folic acid, and tryptophan.
- ✓ Increases the elimination of cholesterol.
- ✓ Synthesis of catecholamine's.
- ✓ Helps the body to absorb and breakdown of histamine.
- ✓ Enhances the absorption of nonheme iron.
- ✓ Promotes the synthesis of collagen
- ✓ Neutralizes free radicals.
- ✓ Protects the DNA from damage due to free radicals and mutagens.
- ✓ Reduces the risk of premature death
- ✓ Fight against environmental pollutants.

5. Role of vitamin D in cardiovascular diseases:

Vitamin D receptors are present not only in the heart but also in the entire cardiovascular system. The 1, 25(OH) 2D3 active form of vitamin D combines with VDR and then regulates the expression of many genes. Vitamin D acts on many pathways such as the renin-angiotensin-aldosterone system, thrombosis, and inflammation and it also has anti-oxidant effects and prevents endothelial apoptosis. Vitamin D and its analogs consistently suppress pro-inflammatory cytokines and anti-inflammatory cytokines, by inhibition of NF-Kb and p38 pathways by VDRs and it also have anticoagulant activity through the regulation of the expression of procoagulant and ant fibrinolytic factors [7].

6. Role of Vitamin D in Chronic kidney disease:

Vitamin D receptors highly expressed in the kidney, vitamin D deficiency leads to activation of renin-angiotensin system results increased expression of renin and angiotensin-II production that leads to hypertension, cardiac hypertrophy, and increased water intake. In CKD patients active vitamin D supplements are administered, then active vitamin D binds to the VDR receptors results in a suppressed activation of the RAS system along along with concurrent attenuation of glomerular and tubulointerstitial destruction and improvement in blood pressure, underscoring the significance of this cascade in renal damage[8].

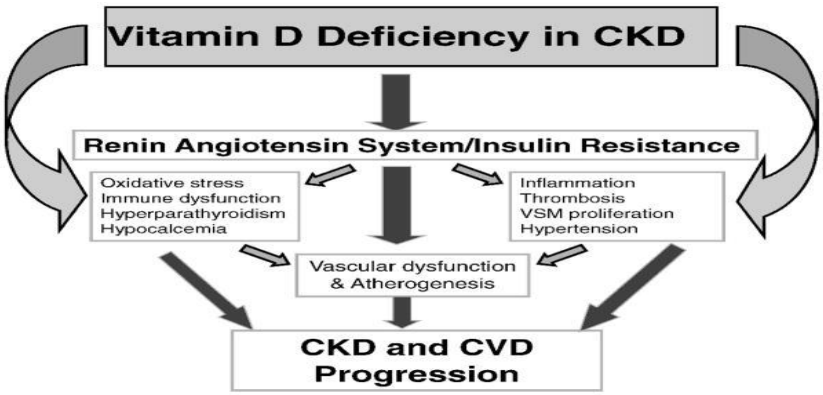

Fig 1 Conceptual model of major pathways through which vitamin deficiency in patients with chronic kidney disease (CKD) may lead to CKD progression and complications such as premature cardiovascular smooth muscle[8].

7. Role of vitamin D in Diabetes:

Active vitamin D is currently prescribed as the drug of choice for osteoporosis and hypocalcaemia, but it has been reported that vitamin D and active vitamin D might have additional metabolic effects on tissues other than bone and calcium metabolism because vitamin D receptors have been found in various tissues, such as the brain, pancreas, breast, kidney, colon, prostate and immune cells. One of the additional effects of vitamin D is expected on glucose metabolism. Vitamin D is regarded to have two mechanisms one is glucose metabolism in patients with glucose intolerance will be modulated, that is, a direct effect on pancreatic β-cells and an enhancing effect on insulin sensitivity in insulin-targeted organs. First, vitamin D receptors and 1-α-hydroxylase are activating the synthesis of active vitamin D (1, 25(OH) 2D3), are expressed in pancreaticβ- cells that result in active vitamin D is involved in insulin biosynthesis. Second, in insulin-targeted organs, such as adipose tissue and skeletal muscle, the expression of the insulin receptor is enhanced by active vitamin D in cultured cells. Also, it is reported that vitamin D modulates the activation of Peroxisome Proliferator-Activated Receptor δ (PPARδ), it is one of the transcription factors controlling lipid metabolism in adipocytes and skeletal muscle [9].

8. Vitamin D and neuropsychiatric disorders

Vitamin D is corresponding to the metabolism of CYP27B1. CYP27B1, these are highly expressed in neurons and glial cells, especially in the substantia nigra, supraoptic and hypothalamus paraventricular tissues in both foetus and adults. Additionally, VDR is highly present in the hypothalamus, pons, basal ganglia, hippocampus, as well as in developing brain tissues, so that Vitamin D participates in the process of neurotransmitter synthesis, inflammation, and calcium balance and Vitamin D can also protect nerve cells by its antioxidant effect [10, 11].

9. Role of vitamin D in immune system diseases:

Many immune cells in the human body such as monocytes, dendritic cells, B cells, macrophages, T cells express VDR. Vitamin D3 in combination with VDR in T cells can inhibit the activity of Th1 cells, thereby reducingCD4+ T cells to release IL-2, interferon-gamma, and tumour necrosis factor-alpha, beta and to delay the progression of chronic inflammatory autoimmune diseases. In addition, it can promote the differentiation of mononuclear cells into macrophages, and strengthen their chemokine production and ability to control infection [12, 13].

10. Chronic Obstructive Pulmonary Disease

In smokers with COPD, vitamin D deficiency occurred due to the alteration of the cutaneous synthesis of vitamin D due to age and the toxic effects of tobacco, low exposure to sunlight or increased catabolism of vitamin D by glucocorticoids, results in reduced intestinal absorption and poor hepatic and renal activation of vitamin D precursors, and some studies show that supplements of vitamin D in COPD individuals there is a significant improvement in inspiratory muscle strength and oxygen consumption[14-18].

11. Tuberculosis

Vitamin D plays an important role in the immune response against Mycobacterium tuberculosis infection through its immunomodulatory and anti-inflammatory mechanisms [19].

12. Interstitial Lung Disease

The vitamin D participates in fibro proliferation in response to inflammation and damage to the bronchial epithelium so that vitamin D deficiency leads to the development of interstitial lung disease [20].

13. Role of Vitamin D in Inflammatory bowel disease.

Vitamin D having both immune-modulatory and anti-inflammatory actions on cells from the innate and adaptive immune system that modulate the pathology

of gastrointestinal dysregulation and inflammation. Vitamin D also appears to play a major role in the maintenance of gastrointestinal barrier integrity by regulating proteins associated with epithelial cell gap junctions. vitamin D is having a barrier function so it linked to its impact on the gastrointestinal microbiota, therefore any changes in the serum vitamin D status in humans being corresponded with changes in gastrointestinal microbial flora results in inflammatory immune responses, because of vitamin D having the ability to both prevent the disease progression through the anti-inflammatory immune response and the onset of IBD via effects on barrier function and microbiota home [21-30].

14. Role of vitamins in epilepsy:

14.1 Thiamine:

Severe thiamine deficiency can cause seizures in both alcoholic and non-alcoholic patients; these seizures are reversible with thiamine supplementation. Low thiamine status was found in epileptic patients and consecutive neurological patients. Some studies show that supplementation of 50 mg thiamine daily for six months was associated with significant improvements in epileptic patients. Thiamine deficiency in individuals might be considered as one possible cause of late-onset epilepsy. So that supplementation of thiamine can prevent both thiamine deficiency and reverse the effects of low thiamine levels in epileptic individuals [31-33].

14.2 Pyridoxine, biotin, folic acid:

Deficiency of vitamins $B_{6,}B_{7,}B_{9}$ causes seizures because these three vitamins plays major role in neuronal functions, and using anti-epileptic drugs may also causes low levels of vitamins by accelerating their metabolism. So vitamin supplements are necessary to prevent reoccurrences of seizures [34-37].

14.3 Vitamin D:

Using antiepileptic drugs may promote the metabolism of hydroxyvitamin D (25-OHD) to less biologically active analog by inducing the hepatic cytochrome P450 system and show the negative effects on bone mineral density resulting in decreased bone mineralization, decreased intestinal calcium absorption, increased calcium mobilization from the skeleton to maintain eucalcemia, and decreased bone density. So, Vitamin D supplements are necessary for epileptic patients [38, 39].

15. Role of Vitamin D in HIV

vitamin D having immune-modulatory effects, deficiency of Vitamin D may influence the pathogenesis of HIV by modulation of innate and adaptive immune responses and Vitamin D also inhibits maturation of dendritic cells, thus preventing excessive inflammatory response to infectious diseases.so there is a link appears between vitamin D and its receptor and natural resistance to HIV-1 infection, possibly because of the upregulation of anti-inflammatory interleukin 10 and induction of anti-HIV-1 defences. Exogenous 1, 25(OH) 2D in monocytes has been reported to reduce HIV susceptibility by inhibiting viral entry, decreasing CD4 expression, and limiting monocyte proliferation. Toll-like receptor 8 ligand agonists in human macrophages have been shown to inhibit HIV infection via a vitamin D- and cyclic adenosine monophosphate-dependent autophagic mechanism. In HIV-positive patients, vitamin D deficiency has been linked to increased inflammation and activated monocyte phenotypes. Vitamin D also "affect T-cell responses indirectly via modulation of the dendritic cell phenotype and its stimulatory capacity toward T cells,"

Vitamin D alters T-cell phenotype and function via suppression of the Th1, Th17, and Th2 profile of cytokine production and Vitamin D may also upregulate the transcription of HIV RNA from latently infected CD4+ cells by reducing the capacity of tumour necrosis factor α [40].

16. Role of vitamin D in osteoarthritis:

Osteoarthritis (OA) is a chronic degenerative joint disease, occurs due to metabolic imbalance in bone, some

nutritional factors, particularly the vitamins are responsible for a metabolic imbalance in bones that results in the development and progression of OA. Vitamin D has the ability in the development and maintenance of the skeleton, as well as bone and cartilage metabolism, deficiency of Vitamin D leads to progress of Osteoarthritis. Vitamin E is responsible for enhancing chondrocyte growth and exhibits anti-inflammatory activity, as well as plays an important role in the prevention of cartilage degeneration. Deficiency of vitamin K produces abnormal growth plate calcification and inappropriate mineralization of cartilage. Thus fat-soluble vitamins are essential in the prevention of the onset of OA and progression of OA [41].

17. Role of Nicotinamide in Parkinson's diseases:

Nicotinamide participates in the biosynthesis of nicotinamide adenine dinucleotide (NAD; oxidized form: NAD+; reduced form: NADH) via various metabolic pathways [42]. NADH is an essential cofactor assisting the tetrahydrobiopterin functioning in tyrosine 2 Oxidative Medicine and Cellular Longevity hydroxylase, which can hydroxylate tyrosine and produce dopamine; NADH deficiency is common in PD [43].

18. Role of Vitamin D in Psoriasis:

The mechanism of action of calcitriol is thought to be inhibiting keratinocyte proliferation and stimulate keratinocyte differentiation In addition; calcitriol inhibits T cell proliferation and other inflammatory mediators [44].

CONCLUSION

Vitamins are essential micronutrients, they are not synthesized in the body and required in small amounts but play a major role in biological functions in the body. deficiency of vitamins predominantly affects the occurrence and development of many chronic diseases, especially deficiency of Vitamin D leads to development of Hypertension, Diabetes mellitus, chronic kidney disease, psoriasis, HIV-1 infection, chronic obstructive pulmonary disease, tuberculosis, multiple sclerosis because of vitamin D having both immunomodulatory and anti-inflammatory effects, so deficiency leads to progression of chronic diseases and deficiency of B vitamins (vitamin $B_{6,}$ $B_{3,}$ $B_{9,}$ $B_{1,}B_{7}$) leads to development of neurological diseases such as Parkinson's disease and epilepsy and some antiepileptic drugs also causes vitamin deficiency by improving its catabolism so, vitamin supplements are necessary in their prescription and vitamin D supplements are prescribed as supportive therapy in chronic diseases is necessary to prevent the progression and complications of diseases.

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