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## Prevalence of Hypovitaminosis D and its association with lifestyle factors and chronic disorders

Monika Kapoor<sup>1</sup>, Jagminder Kaur Bajaj<sup>2</sup>

<sup>1</sup> Department of Pharmacy Practice, Indo Soviet Friendship (ISF) College of Pharmacy, Moga- 142001, Punjab, India  
<sup>2</sup> Professor and Head, Department of Pharmacology, Punjab Institute of Medical Sciences, Jalandhar-144006, Punjab, India

### Abstract

Vitamin D is one of the essential fat-soluble vitamins, playing a crucial role in the regulation of physiological activities. Deficiency of vitamin D is a global public health issue observed in all the age groups. Vitamin D deficiency has been correlated with Diabetes mellitus, hypertension, autoimmune diseases, thyroid dysfunction, obesity, CVS disorders, neuropsychiatric disorders and infectious diseases. Vitamin D is obtained by conversion of 7-dehydrocholesterol into vitamin D3 (cholecalciferol) on the exposure of ultraviolet B radiations or by oral ingestion of vitamin D2 (ergocalciferol) and D3 (cholecalciferol). Lowered consumption of vitamin D due to vitamin D deficient diet, modified lifestyle and avoiding sun exposures completely or by using sunscreens leads to the deficiency of vitamin D and its increasing prevalence around the globe. This paper reviews the prevalence of hypovitaminosis D and its association with lifestyle and other chronic disorders.

**Keywords:** Vitamin D deficiency, Prevalence, Chronic disorder, Skeletal effects, Extraskelatal effects, Clinical manifestations.

### INTRODUCTION

Vitamin D deficiency is a pervasive and the most underdiagnosed condition. Hypovitaminosis D can occur in all, regardless of gender, age, race and geography. The prevalence of vitamin D deficiency is reported to be between 40-99 % in previous studies which makes it essential to study the risks associated with its deficiency [1]. Serum levels of calcifediol or 25(OH)D above 30-32 ng/mL are required for ideal health. Serum level of calcifediol  $\geq 30$  ng/mL is known as vitamin D sufficiency, serum levels between 20-29 ng/mL are defined as vitamin D insufficiency and Serum levels of calcifediol  $< 20$  ng/mL indicates vitamin D deficiency [2]. Vitamin D is essential for the maintenance of the normal levels of calcium and phosphate in the blood which is important for mineralization of bone, contraction of muscles, neuronal conduction, the functioning of the immune system, cell proliferation and other cellular functions of the body. Its active form known as calcitriol prompts the absorption of calcium in the duodenum [3].

Prevalence of Hypovitaminosis D is reported to be 70-100% of the population of India [4]. The rising prevalence is commonly linked to the lifestyle pattern of people like wearing burkhas, purdah, completely covering the body parts to avoid sun exposure, application of high SPF sunscreens, indoor jobs, skin pigmentation, fairer complexion, high socioeconomic status. Phytate and phosphorus-rich diets are blamed to cause depletion of vitamin D stores and thereby increasing the requirement of calcium in the body. Traditional cooking style, high intake of caffeine and completely vegetarian diets are also implicated in the causation of vitamin D deficiency [5-8]. Lactose intolerance, smoking, obesity and some severe chronic disorders like, cardiovascular disorder, diabetes mellitus type 2, depression, infectious disease, Parkinson, autoimmune disease and cancer also increases the risk of deficiency of vitamin D [9-10]. Its deficiency also shows complications in pregnancy like anemia, gestational diabetes mellitus (GDM), iron deficiency and preeclampsia [11-12]. Since it is known for the regulation of calcium and phosphorus and mineralization of bones, its deficiency also contributes to the decreased bone density and causes rickets, osteomalacia, fractures, and osteoporosis [13].

\*Corresponding author:

Monika Kapoor

Department of Pharmacy Practice, Indo Soviet Friendship (ISF) College of Pharmacy, Moga- 142001, Punjab, India  
Email:

[monikakapoor01.mk@gmail.com](mailto:monikakapoor01.mk@gmail.com)

### Hypovitaminosis: Manifestations and consequences

Vitamin D deficiency manifests as skeletal and extraskelatal disorders. Hypovitaminosis D causes rickets in children, osteomalacia, and osteoporosis in adults. Rickets and external skeletal deformities arise due to mineralization of bones and imbalance between calcium and phosphorus in the bones which in turn also results in muscles infirmity and bone pain. Serum calcium beyond its normal range results in increased parathyroid hormone concentration that leads to an increase in the tubular recoupment of calcium in kidneys and reabsorption from the skeleton which results in a lowered density of the bones. Therefore, bones become weak and brittle and cause osteoporosis and osteomalacia in adults. Previous studies show an association between low vitamin D status and the risk of falls in adults which occurs as a result of depletion of the fast twitch (type II) fibers which are needed to prevent falling [13-18].

Vitamin D receptors are present in abundance not only in bones but also in other body tissues which results in the association of hypovitaminosis D with other chronic conditions also. Some of the diseases associated with its deficiency have been reviewed.

**Cardiovascular disease:-** Previous studies suggest that there is a link between vitamin D and renin production which regulates the blood pressure. Hence, deficiency of Vitamin D contributes to the occurrence of hypertension and other cardiovascular diseases [18]. Vitamin D acts on endothelial cells, stimulates the production of nitric oxide, prevents oxidative stress and endothelial apoptosis by the genomic as well as a non-genomic pathway. Cholecalciferol also exhibits anticoagulant effects via expression of antifibrinolytic and pro-coagulant factors. Vitamin D deficiency leads to the activation and release of pro-inflammatory cytokines which in turn potentiates the risk of cardiovascular disease by arbitrating endothelial dysfunctioning and stiffness of arterial wall [19-21].

**Type 1 and Type 2 Diabetes Mellitus:-** Many studies reveal the association of type 1 DM and deficiency of vitamin D. The elimination of vitamin D receptor in macrophage triggers insulin resistance and hence its deficiency has also been linked with risk of DM type 2, resistance to insulin and reduced insulin production. Also, vitamin D dependent calcium-binding protein is present on islet  $\beta$ -cells, PP cells, and D cells and abundantly on  $\alpha$  cells. The intracellular concentration of calcium is regulated by vitamin D dependent calcium binding protein thereby it affects the endocrine and metabolic processes pancreatic cells. Apart, from suppressing insulin secretion by incapacitating the islet  $\beta$ -cell functions, it also elevates the blood sugar levels via enhancement of functions of islet  $\alpha$  cell. Various evidence suggests that the risk of development of type 2 DM is reduced by adequate vitamin D levels [21-25].

**Obesity:-** 25(OH)D levels have an inverse association with body mass index, waist circumference and body fat has a direct association with age, lean body weight and vitamin D intake. In 2012, Christy B et.al., reported the prevalence of vitamin D deficiency in healthy-weight, overweight, obese, and severely obese children to be 21% (20%–22%), 29% (27%–31%), 34% (32%–36%) and 49% (45%–53%), respectively. Thus the prevalence of Vitamin D deficiency is more in overweight and obese children than nonobese [26-27].

**Autoimmune disease:-** Vitamin D is an essential modulator of the immune system and is involved in cell differentiation and proliferation. Its deficiency may worsen the immune tolerance and lead to the induction of autoimmune disease like type 1 DM, type 2 DM and rheumatoid arthritis.

**Rheumatoid arthritis:-** Vitamin D is well-known for the induction of immunologic tolerance. Vitamin D deficiency is highly pervasive in patients with rheumatoid arthritis and may be linked with the severity

of disease in RA. Since vitamin D deficiency has been associated to spread musculoskeletal pain hence these consequences have therapeutic implications [28].

**Cancer:-** Vitamin D plays a defensive role in the case of particular tissues by inhibition of angiogenesis and stimulating apoptosis. It prevents the growth of new blood vessels and has remarkable anti-inflammatory effects. Deficiency of Vitamin D binding protein (VDBP) affects the functioning of vitamin D. Epidemiologic studies illustrate that levels of vitamin D below 20 ng/mL are associated with 30-50 % risk of various cancers targeting lung, breast, colorectal, prostate, ovary, pancreas and esophagus [29-31].

**Infectious diseases:-** Calcitriol inflates monocyte mycobacterial killing by increasing the production of cathelicidin, an antimicrobial protein. Infectious diseases like tuberculosis, upper respiratory tract infections, influenza, HIV are likely to be seen in vitamin D deficient people. Cells that line the lungs produce high levels of enzymes involved in the conversion of vitamin D into its active form i.e vitamin D3. Therefore, these cells may use vitamin D as part of their defensive system against various infections. Apart from this, many observational studies have found that HIV positive people have less than ideal levels of vitamin D in their blood and in a few cases its deficiency. By instigating the immune system, inflammation related cytokines chemical signals are overproduced which makes it possible for the HIV infection to indirectly speed up the enzymes which are responsible for conversion of vitamin D3 into its inactive form. [32 -33].

**Vitamin D and its association with neuropsychiatric disorders:-** vitamin D is known for the metabolism of CYP27B1. CYP27B1 is an enzyme which is expressed in the glial cells and neurons of both fetus and adults. Vitamin D receptor is expressed in the hypothalamus, pons, basal ganglia, hippocampus and the brain tissues which are developing, proposes that vitamin D is involved in the development and functioning of the brain. It is also involved in the process of synthesis of neurotransmitter, inflammation and calcium balance. Many studies also suggest that vitamin D exhibits antioxidant effects which in turn ensure the protection of nerve cells. Some of the neuropsychiatric disorders associated with its deficiency are as follows:

**Depression:-** People who are suffering from depression and are vitamin D deficient take a long time to recover in comparison to non-deficient people. Various evidence suggests that calcitriol increases the calcium binding protein and is also involved in increasing serotonin levels in the brain. Hence, treating hypovitaminosis D can help in the treatment of depression [34].

**Alzheimer's:-** Studies show evidence that calcitriol stimulates the phagocytosis of amyloid- $\beta$  and its clearance by macrophages in case of Alzheimer patients. Thus, it demonstrates that the increase in the prevalence of vitamin D deficiency is associated with neurocognitive decline and Alzheimer's [35].

**Parkinson's disease:-** Vitamin D receptor (VDR) is considered as a genetic risk factor for Parkinson's disease which emphasizes its importance in PD. Vitamin is a flexible factor, works as a therapeutic as well as a preventive approach for PD [36].

**Other diseases:-** Vitamin D is known to show antifibrotic effects and effects on the immune system. Hence it plays a role in the physiopathology of chronic liver diseases. People with hepatitis C viral infection have relevantly low levels of 25(OH)D. Studies also suggest that in adults with nonalcoholic fatty liver disease (NAFLD) the vitamin D levels have a significant effect on the development of hepatic steatosis and histological lesion. Vitamin D also plays a role in various other diseases like multiple sclerosis, psoriasis, osteoarthritis, chronic kidney disease, systemic lupus erythematosus, inflammatory bowel disease, etc. Vitamin D also targets helper type1 and type2 cells and causes a shift

towards anti-inflammatory process and regulates the production of inflammatory cytokines. Hence, lower levels of vitamin D affects various diseases [37].

## CONCLUSION

The increasing pervasiveness of hypovitaminosis D is due to low dietary intake of vitamin D fortified food, indoor jobs, fairer skin complexion and less exposure to sunlight which is the biggest natural source of vitamin D production. Therefore, its deficiency leads to increased risk for multiple other clinical conditions. The number of patients with rickets, osteoporosis, cardiovascular disorders, cancer, autoimmune diseases and other chronic diseases linked with hypovitaminosis D is increasing year by year which reduces the quality of life and increases the social and economic burden. Hence, attention must be paid to vitamin D deficiency and necessary actions must be taken to overcome the problem in order to improve the quality of life of the patients.

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## Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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