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Review article

EMERGING ROLE OF VITAMIN D IN HEALTH

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ABSTRACT

Vit. D is a steroid prohormone. It is synthesized in the skin under ultra-violet light exposure. Traditionally, Vit.D3, cholecalciferol and calcitriol were known to have a role only in calcium and bone mineral metabolism. This article takes an account of the current view on the impact of Vit D deficiency on human health. Research has now shown the indisputable role of Vit D in prevention/treatment of some cancers, osteoporosis, rheumatoid arthritis, multiple sclerosis, tuberculosis, hypertension, and diabetes mellitus. In addition lower maternal Vit. D levels are associated with Pregnancy Induced Hypertension (PIH), suggesting that Vit. D deficiency may be a modifiable risk factor for PIH. Greater awareness of the problem of a high prevalence of vitamin D inadequacy is required among researchers, clinicians, and patients. Special efforts on the medical and social fronts are necessary to combat this preventable epidemic of vitamin D deficiency.

Keywords: Vitamin D, 25-Hydroxyvitamin D, PIH, Pregnancy, Hypervitaminosis D, Cholecalciferol, Calcitriol.

INTRODUCTION

Vitamin D is more important nutrient for health. Vitamin D is actually a hormone rather than a vitamin. Despite its discovery 100 years ago, Vit D has emerged as one of the most controversial nutrients and prohormones of the 21st century, and a lot of research has been in place on this molecule. Traditionally, Vitamin D was viewed as a permissive factor in calcium and bone mineral metabolism. It works with the Parathyroid hormone (PTH), acts on the kidneys, bone & intestine and influences gene expression. The research leads us to newer therapies with newer concepts.¹ Research has now shown Vit D's indisputable role in both inherent and adaptive immunity. Vit D is a Steroid prohormone and it is synthesized in the skin under ultra-violet light exposure. 7-Dehydrocholesterol present in the skin absorbs UV light over wavelengths of 290-300 nm [UVB] to synthesize Vit D3. Synthesis in the skin epidermis takes place over several days; the quantity (intensity)

and quality (appropriate wavelength) of sunlight are both important this biosynthesis can be inadequate due to poor dietary intake, absorption, or poor exposure to sunlight [UVB]. The deficiency can occur because of fat malabsorption, anticonvulsant use, chronic kidney disease and obesity and is seen in high-risk groups like elderly women, dark-skinned people, people from areas with a thick layer of ozone, women using sunscreen lotions, and people from urban areas.² In urban and polluted areas, the UV light of 290-300-nm wave length gets filtered out; hence, skin may not get enough of this light. Therefore, there is a high rate of Vit D deficiency even among the urban population. Hence, foods and dietary supplements are necessary. Cod liver oil, salmon and sardines, fortified milk, egg, fortified yogurt, mushrooms, fortified soy products, oysters, and fortified cereals are rich sources of Vit D. **Activation of Vitamin D:** It takes place in the following manner:¹

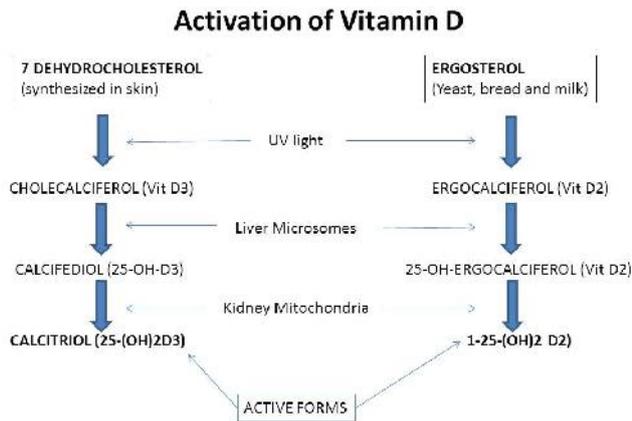


Fig 1: Activation of Vitamin D

Under situations of minimal exposure to sunlight, a specific recommendation of a daily supplement of 400 IU (10 µg) is retained for the Indian population. RDA for pregnant women is 200 IU per day and the maximum safe daily dose is 2,000 IU. Due to increased deficiency screening for vitamin D levels is important for most individuals. A serum concentration of 25 (OH) D is the best indicator of vitamin D.

The Emerging Roles of Vit D: It is now considered important in cell differentiation, proliferation, and immune function. It is an important factor in prevention/treatment of some forms of cancer, osteoporosis, rheumatoid arthritis, multiple sclerosis, hypertension, cardiovascular disease, obesity, psoriasis, and psychiatric diseases. The role of vitamin D in pregnancy is also taking new dimensions.

Vit. D and Pregnancy: Maternal Vit.D deficiency is common during pregnancy and throughout gestation. If a women is Vit. D deficiency, it leads to a number of serious health problems likes poor bone mineralization in infants, low birth weight baby and other adverse pregnancy outcomes.³⁻⁵ There are different deficiency levels. The risk of rickets increases significantly when the total circulating 25(OH)D falls below 10 ng/mL (25 nmol/L), whereas cathelicidin mRNA expression as a marker of immune function continues to be suppressed until 25(OH)D circulating levels reach at least 20 ng/mL (50 nmol/L).⁶

The recently revised Institute of Medicine's (IOM) 2010 criterion for Vit D deficiency of total circulating 25(OH) D is <20 ng/mL (50 nmol/L), Optimal serum concentrations of 25(OH) D3 are at or above 30 ng/mL (>75 nmol/L), and Vit D toxicity is present when levels are at or above 150 ng/mL (374 nmol/L).⁷

Rates of deficiency of Vit D are more with women who have darker pigmentation and women who have limited access to sunlight, through limited outdoor activity.⁸ Vit D deficiency exists in a higher percentage in obese women. Women including pregnant women, with a BMI >30, are at increased risk of Vit D deficiency.⁸ The adipose tissue serves as a repository for Vit D that does not get into the circulation.

As per recent guidelines Recommended Daily Allowance (RDA) of Vit. D during pregnancy is 200-400 IU/day and more than 2,000 IU/day has been toxic not just to the pregnant women but to the any one. As per recent research, higher dosages of Vit D are not just safe during pregnancy, but increased dosage may actually reduce the risk of complications.

In a study, 500 women who were at least 12 weeks pregnant took 400, 2000, or 4000 IU of Vit D per day. The women who took 4,000 IU were less prone for preterm labour or infections during pregnancy. Vit D intoxication is extremely rare and easy to treat. Pregnant women who get too little Vit D are more likely to develop PIH (Pregnancy induced hypertension) and are also more likely to require a Cesarean section. They concluded that giving 4,000 IU a day to pregnant women may not only improve birth outcomes but also does not cause toxicity.⁹

Pregnant women with a serum level of 25-OH Vit D <75 nmol/L are considered to be Vit D3 deficient.¹⁰

Until recently, it was thought that Vit D deficiency was common only in high-risk women (women with dark skin and those with minimal exposed skin), but it is quite high even in low-risk women.

All women therefore should be offered testing for Vit D status in early pregnancy and recommended supplementation if deficient.¹¹

Women with a 25-OH Vit D3 <75 nmol/L are considered Vit D deficient and should have a dietary assessment for calcium intake. They should receive a higher dose up to 1000 IU. They should be offered retesting at 28 weeks of pregnancy. If the higher dose of Vit D does not improve the serum Vit D levels, then malabsorption syndrome (such as celiac disease) should be ruled out or else the patient may be non-compliant.

Pregnant women should have enough Vit D at the time of delivery to insure sufficient Vit D levels in their baby for the first 4-6 months of life.

The transplacental passage of maternal 25-OH Vit D3 is the sole source of Vit D in the developing fetus.

Therefore, infants are wholly dependent on their mother for their Vit D status. Infants born to Vit D-deficient mothers will be Vit D deficient and hence will require supplementation in the form of cholecalciferol bolus (50,000 IU) dose orally. The obstetricians must understand the importance of vitamin D supplementation to pregnant and nursing mothers, which will go a long way in preventing rickets.

Emerging Role of Vitamin D in Other Diseases: The role of Vit D in osteoporosis and muscle weakness is indisputable. But, there is a recent trend to give a higher dose of Vit D to prevent the osteoporotic fracture.

In a placebo controlled study, oral Vit.D (700-800 IU/d) with or without calcium supplementation was given to elderly persons. The results show that there was statistically significant (23-43%) reduction in risk of a hip fracture and any non-vertebral fracture.¹²⁻¹⁵

Multiple sclerosis is an autoimmune disease which is more prevalent in temperate climates than the tropics and is also seen much more commonly in women. It is associated with lower serum vitamin D levels, and Vit D supplementation may have a preventive role in multiple sclerosis.

The protective role of optimal Vit.D status and lower risk of cancer has been reported in many studies. Seven decades ago, Pellers and et al first time reported that sunlight exposure may reduce the risk of cancer.¹⁶

In another study it has been reported that when the concentration of 25 OH Vit.D > 32 ng/ml, there was 50% reduction in breast and colorectal cancer.¹⁷⁻¹⁸ The higher the Vit D level, the lower the risk of cancer.

Vitamin D acts as an immunosuppressant in rheumatoid arthritis as well.

Vit.D has a preventive role in development of diabetes mellitus. Pittas AG and et al studied on high dosage of calcium and Vit.D over 2-4 years in 83779 women with no history of diabetes. In this study for group one calcium >1200 mg/day and Vit. D >800 IU/day was given. For group two calcium <600 mg/day and Vit. D <400 IU/day was given. The results show that in group one there was 33% lower risk of type 2 diabetes as compared to group two.¹⁹ In another study in Finland over 31 years Vit. D in a dose of 2000 IU/day was administered to 10366 children during their first year of life and result show that the risk of type 1 diabetes reduce by 80%.²⁰

Tuberculosis is associated with lower Vit D levels. Before the antikoch's treatment was available, high dosages of Vit D were given to patients. We see this disease in urban areas in women with a specific dressing style which prevents adequate sunlight exposure.

Adverse Effects of Vit D Therapy: The primary toxicity associated with Calcitriol is to increase intestinal calcium and phosphate absorption, along with the potential to mobilize osseous calcium and phosphorus concentrations.

Hypervitaminosis D is treated by immediate withdrawal of the vitamin, a low calcium diet, administration of glucocorticoids and vigorous fluid support. Forced saline diuresis with loop diuretics for hypercalcemia is useful. With this plasma Ca^{2+} concentration fall to normal and Ca^{2+} in soft tissue tends to mobilize. Conspicuous improvement in renal function occurs.¹

CONCLUSION

To summarize, Vit D deficiency is highly prevalent and contributes to women's health greatly. Getting too little vitamin D is worse than getting too much. Newer reports are changing our ideas about the optimal Vit D status and the role of Vit D in health, especially in relation to modern chronic diseases affecting women. It must be remembered that some populations are still very much under treated, and pregnancy-associated complications can be reduced with correction of the deficient state.

In spite of the close relation of vitamin D to human health, vitamin D deficiency is not widely recognized as a problem by doctors and patients. Greater awareness of the problem of a high prevalence of vitamin D inadequacy is required among researchers, clinicians and patients. Women in the underprivileged sections, both in urban and rural India, are battling inadequate resources, multiparty, imposed customs of clothing, and social vulnerability of the fairer sex which coupled with the urban environmental decay will continue to pose the threat of Vit D deficiency. Special efforts on the medical and social fronts are necessary to combat this preventable epidemic of vitamin D deficiency.

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