Vitamin D: D-Lightful And D-Ficient Health Perspective

Radhika Bandaroo
Lecturer (Home Science)
Sarvodaya VidyalayaVasant Vihar, New Delhi-57

Abstract- *Vitamin D is derived from skin production through exposure to ultraviolet light and from oral intake of natural foods, fortified foods and supplements. While the principal source of vitamin D is skin production, oral intake has primacy over sunlight exposure in both the correction and prevention of privational vitamin D deficiency. Vitamin D deficiency is associated causally with rickets in childhood and osteomalacia in adulthood, but the evidence is inconsistent and inconclusive for a causal association with cancer, infections, autoimmune diseases and cardiovascular disease. Measurement of serum 25-hydroxyvitamin D (25OHD) is the best marker of vitamin D supply. It is not a clinical outcome, but is a measure of risk of skeletal disease. Adequate supply corresponds to a 25OHD level ranging from 30–50 nmol/L (12–20 ng/ml). A value below 30 nmol/L (12 ng/ml) constitutes an increase in risk of skeletal disease. In those at risk, the clinician must decide whether it is necessary to advise empirically about ensuring adequate intake according to the dietary reference intakes of the 2011 Institute of Medicine (IOM) Report, or to proceed with initial biochemical tests such as serum calcium, phosphorus, total alkaline phosphatase and parathyroid hormone (PTH). Additional tests include bone turnover markers, bone densitometry, bone imaging and rarely dynamic bone histomorphometry. Patients who are diagnosed with vitamin D deficiency should be divided into those who are sun-deprived (privational vitamin deficiency) and those who are disease-related such as those with intestinal, liver or kidney disorders. The principal differential diagnosis for vitamin D-related bone disease is hypophosphataemic bone disease, especially that mediated by excessive fibroblast growth factor 23 (FGF23). Regarding treatment, those with privational vitamin D deficiency should be managed according to IOM recommendations with respect to vitamin D and calcium requirements. Patients with disease-specific causes may require higher intakes of calcium and vitamin D. High dose vitamin D therapy should be avoided; instead, 1α,25-dihydroxyvitamin D is preferable in refractory cases with close metabolic supervision. Patients with severe hyperparathyroidism secondary to chronic malabsorption may need parathyroid surgery.*

Keywords- Vitamin D Metabolites, Vitamin D Metabolism, Vitamin D and Bone Cells, VitaminD and Sun Exposure

I. INTRODUCTION

Vitamin D insufficiency affects almost 50% of the population worldwide. An estimated 1 billion people worldwide, across all ethnicities and age groups, have a vitamin D deficiency (VDD). This pandemic of hypovitaminosis D can mainly be attributed to lifestyle and environmental factors that reduce exposure to sunlight, which is required for ultraviolet-B (UVB)-induced vitamin D production in the skin. Black people absorb more UVB in the melanin of their skin than do white people and, therefore, require more sun exposure to produce the same amount of vitamin D.

The high prevalence of vitamin D insufficiency is a particularly important public health issue because hypovitaminosis D is an independent risk factor for total mortality in the general population. Emerging research supports the possible role of vitamin D against cancer, heart disease, fractures and falls, autoimmune diseases, influenza, type-2 diabetes, and depression. Many health care providers have increased their recommendations for vitamin D supplementation to at least 1000 IU. A meta-analysis published in 2007 showed that vitamin D supplementation was associated with significantly reduced mortality. In this review, we will focus on the biology of vitamin D and summarize the mechanisms that are presumed to underlie the relationship between vitamin D and its clinical implications.

II. OBJECTIVES OF THE STUDY

- To study the main sources of Vitamin D and people are having higher risk
- To assess complications of deficiency of Vitamin D
- To examine the impact of Vitamin D in immune function
- To evaluate the future challenges to prevent deficiency of Vitamin D

III. RESEARCH METHODOLOGY

Vitamin D Deficiency: A Global Concern

If you live north of the line connecting San Francisco to Philadelphia and Athens to Beijing, odds are that you don't get enough vitamin D. The same holds true if you don't get outside for at least a 15-minute daily walk in the sun. African-Americans and others with dark skin, as well as older individuals, tend to have much lower levels of vitamin D, as do people who are overweight or obese.

Worldwide, an estimated 1 billion people have inadequate levels of vitamin D in their blood, and deficiencies can be found in all ethnicities and age groups. Indeed, in industrialized countries, doctors are even seeing the resurgence of rickets, the bone-weakening disease that had been largely eradicated through vitamin D fortification.

Why are these widespread vitamin D deficiencies of such great concern? Because research conducted over the past decade suggests that vitamin D plays a much broader disease-fighting role than once thought. Being "D-ficient" may increase the risk of a host of chronic diseases, such as osteoporosis, heart disease, some cancers, and multiple sclerosis, as well as infectious diseases, such as tuberculosis and even the seasonal flu.

Currently, there's scientific debate about how much vitamin D people need each day. The Institute of Medicine, in a long-awaited report released on November 30, 2010 recommends tripling the daily vitamin D intake for children and adults in the U.S. and Canada, to 600 IU per day. The report also recognized the safety of vitamin D by increasing the upper limit from 2,000 to 4,000 IU per day, and acknowledged that even at 4,000 IU per day, there was no good evidence of harm. The new guidelines, however, are overly conservative about the recommended intake, and they do not give enough weight to some of the latest science on vitamin D and health. For bone health and chronic disease prevention, many people are likely to need more vitamin D than even these new government guidelines recommend.

IV. VITAMIN D SOURCES AND FUNCTION

Vitamin D is both a nutrient we eat and a hormone our bodies make. Few foods are naturally rich in vitamin D, so the biggest dietary sources of vitamin D are fortified foods and vitamin supplements. Good sources include dairy products and breakfast cereals (both of which are fortified with vitamin D), and fatty fish such as salmon and tuna.

For most people, the best way to get enough vitamin D is taking a supplement, but the level in most multivitamins (400 IU) is too low. Encouragingly, some manufacturers have begun adding 800 or 1,000 IU of vitamin D to their standard multivitamin preparations. If the multivitamin you take does not have 1,000 IU of vitamin D, you may want to consider adding a separate vitamin D supplement, especially if you don't spend much time in the sun. Talk to your healthcare provider.

Two forms of vitamin D are used in supplements: vitamin D2 ("ergocalciferol," or pre-vitamin D) and vitamin D3 ("cholecalciferol"). Vitamin D3 is chemically indistinguishable from the form of vitamin D produced in the body.

The body also manufactures vitamin D from cholesterol, through a process triggered by the action of sunlight on skin, hence its nickname, "the sunshine vitamin." Yet some people do not make enough vitamin D from the sun, among them, people who have a darker skin tone, who are overweight, who are older, and who cover up when they are in the sun.

Correctly applied sunscreen reduces our ability to absorb vitamin D by more than 90 percent. And not all sunlight is created equal: The sun's ultraviolet B (UVB) rays—the so-called "tanning" rays, and the rays that trigger the skin to produce vitamin D—are stronger near the equator and weaker at higher latitudes. So in the fall and winter, people who live at higher latitudes (in the northern U.S. and Europe, for example) can't make much if any vitamin D from the sun.

Vitamin D helps ensure that the body absorbs and retains calcium and phosphorus, both critical for building bone. Laboratory studies show that vitamin D can reduce cancer cell growth and plays a critical role in controlling infections. Many of the body's organs and tissues have receptors for vitamin D, and scientists are still teasing out its other possible functions.

Food sources of vitamin D

Food	Vitamin D content in IU
Milk	3 - 40/L
Butter	35/100 grams
Yogurt	99/100 grams
Cheeses	12 - 45/100 grams
Shitaki fresh mushrooms	100/100 grams
Shitaki dried mushrooms	1660/100 grams
Egg yolk	20 - 25/yolk
Shrimps	150/100 grams
Beef liver	15 - 50/100 grams
Tuna, sardines, salmon, canned mackerel	225 - 335/100 grams
Canned pink salmon with bones	625/100 grams
Salmon, cooked mackerel	345 - 360/100 grams
Raw Atlantic mackerel	360/100 grams
Raw Atlantic herring	1600/100 grams
Bloater	120/100 grams
Pickled herring	700/100 grams
Cod	45/100 grams
Cod liver oil	175grams - 1350/spoon

WHO ARE THE PEOPLE AT HIGHER VD DEFICIENCY RISK (OR WHEN IT SHOULD BE SUSPECTED)?

- ELDERS (>65 years), (often underestimated in the deficiency of males)
- OBESE
- WITH LIMITED EXPOSURE TO THE SUN
- WITH DARK SKIN (e.g. African Americans)
- WITH FATS malabsorption (e.g. Inflammatory bowel disease, celiac disease, liver disease, gastrointestinal bypass, etc.)
- WITH SEVERE THINNESS and/or food intake disorders (ex. Anorexia)
- WITH INCREASE OF VD REQUIREMENTS (pregnancy, lactation)
- IN TREATMENT WITH DRUGS THAT INTERFERE WITH ITS METABOLISM (anticonvulsants, long-term glucocorticoids, antifungals, HIV + drugs, immunosuppressive drugs)
- WITH DISEASES THAT INCREASE ITS METABOLISM (lymphomas, granulomatosis, primary hyperparathyroidism)
- WITH EXTENDED DERMATOLOGICAL DISEASES (e.g. psoriasis, atopic dermatitis, vitiligo)
- WITH DECREASED SYNTHESIS OF ACTIVE VD (chronic renal failure, liver failure)
- WITH OSTEOPOROSIS OR NOTES OF OSTEOMALACIA, or with frequent spontaneous fractures
- WITH FAMILY HISTORY OF BONE FRAGILITY FRACTURE

New Vitamin D Research: Beyond Building Bones

Several promising areas of vitamin D research look far beyond vitamin D's role in building bones. And, as you might expect, the news media release a flurry of reports every time another study links vitamin D to some new ailment. These reports can be confusing, however, because some studies are stronger than others, and any report needs to be interpreted in the light of all other evidence. More answers may come from randomized trials, such as the VITamin D and OmegA-3 TriaL (VITAL), which will enroll 20,000 healthy men and women to see if taking 2,000 IU of vitamin D or 1,000 mg of fish oil daily lowers the risk of cancer, heart disease, and stroke. Here, we provide an overview of some of the more promising areas of vitamin D research, highlighting the complex role of vitamin D in disease prevention—and the many unanswered questions that remain.

Vitamin D and Bone and Muscle Strength

Several studies link low vitamin D levels with an increased risk of fractures in older adults, and they suggest that vitamin D supplementation may prevent such fractures—as long as it is taken in a high enough dose.

A summary of the evidence comes from a combined analysis of 12 fracture prevention trials that included more than 40,000 elderly people, most of them women. Researchers found that high intakes of vitamin D supplements—of about 800 IU per day—reduced hip and non-spine fractures by 20 percent, while lower intakes (400 IU or less) failed to offer any fracture prevention benefit.

Vitamin D may also help increase muscle strength, which in turn helps to prevent falls, a common problem that leads to substantial disability and death in older people. Once again, vitamin D dose matters: A combined analysis of multiple studies found that taking 700 to 1,000 IU of vitamin D per day lowered the risk of falls by 19 percent, but taking 200 to 600 IU per day did not offer any such protection.

A recent vitamin D trial drew headlines for its unexpected finding that a *very* high dose of vitamin D *increased* fracture and fall risk in older women. The trial's vitamin D dose—500,000 IU taken in a once-a-year pill—was much higher than previously tested in an annual regimen. After up to 5 years of treatment, women in the vitamin D group had a 15 percent higher fall risk and a 26 percent higher fracture risk than women who received the placebo.

It's possible that giving the vitamin D in one large dose, rather than in several doses spread throughout the year, led to the increased risk. The study authors note that only one other study—also a high-dose, once-a-year regimen—found vitamin D to increase fracture risk; no other studies have found vitamin D to increase the risk of falls. Furthermore, there's strong evidence that more moderate doses of vitamin D taken daily or weekly protect against fractures and falls—and are safe.

So what is the significance of this study for people who want to take vitamin D supplements? A reasonable conclusion would be to continue taking moderate doses of vitamin D regularly, since these have a strong safety record, but to avoid extremely high single doses. This recent finding does present a challenge to scientists who will work to

understand why the extreme single dose appears to have adverse effects.

Vitamin D and Heart Disease

The heart is basically a large muscle, and like skeletal muscle, it has receptors for vitamin D. So perhaps it's no surprise that studies are finding vitamin D deficiency may be linked to heart disease. The Health Professional Follow-Up Study checked the vitamin D blood levels in nearly 50,000 men who were healthy, and then followed them for 10 years. They found that men who were deficient in vitamin D were twice as likely to have a heart attack as men who had adequate levels of vitamin D. Other studies have found that low vitamin D levels were associated with higher risk of heart failure, sudden cardiac death, stroke, overall cardiovascular disease, and cardiovascular death. How exactly might vitamin D help prevent heart disease? There's evidence that vitamin D plays a role in controlling blood pressure and preventing artery damage, and this may explain these findings. Still, more research is needed before we can be confident of these benefits.

Vitamin D and Cancer

Nearly 30 years ago, researchers noticed an intriguing relationship between colon cancer deaths and geographic location: People who lived at higher latitudes, such as in the northern U.S., had higher rates of death from colon cancer than people who live closer to the equator. Many scientific hypotheses about vitamin D and disease stem from studies that have compared solar radiation and disease rates in different countries. These can be a good starting point for other research but don't provide the most definitive information. The sun's UVB rays are weaker at higher latitudes, and in turn, people's vitamin D levels in these high latitude locales tend to be lower. This led to the hypothesis that low vitamin D levels might somehow increase colon cancer risk.

Since then, dozens of studies suggest an association between low vitamin D levels and increased risks of colon and other cancers. The evidence is strongest for colorectal cancer, with most (but not all) observational studies finding that the lower the vitamin D levels, the higher the risk of these diseases. Vitamin D levels may also predict cancer survival, but evidence for this is still limited. Yet finding such associations does not necessarily mean that taking vitamin D supplements will lower cancer risk.

The VITAL trial will look specifically at whether vitamin D supplements lower cancer risk. It will be years, though, before it releases any results. It could also fail to detect a real benefit of vitamin D, for several reasons: If people in the placebo group decide on their own to take vitamin D supplements, that could minimize any differences between the placebo group and the supplement group; the study may not follow participants for a long enough time to show a cancer prevention benefit; or study participants may be starting supplements too late in life to lower their cancer risk. In the meantime, based on the evidence to date, 16 scientists have circulated a "call for action" on vitamin D and cancer prevention: Given the high rates of vitamin D deficiency in North America, the strong evidence for reduction of osteoporosis and fractures, the potential cancer-fighting benefits of vitamin D, and the low risk of vitamin D supplementation, they recommend widespread vitamin D supplementation of 2000 IU per day.

Vitamin D and Immune Function

Vitamin D's role in regulating the immune system has led scientists to explore two parallel research paths: Does vitamin D deficiency contribute to the development of multiple sclerosis, type 1 diabetes, and other so-called "autoimmune" diseases, where the body's immune system attacks its own organs and tissues? And could vitamin D supplements help boost our body's defenses to fight infectious disease, such as tuberculosis and seasonal flu? This is a hot research area and more findings will be emerging.

Vitamin D and Multiple Sclerosis:

Multiple sclerosis (MS) rates are much higher far north (or far south) of the equator than in sunnier climes, and researchers suspect that chronic vitamin D deficiencies may be one reason why. One prospective study to look at this question found that among white men and women, those with the highest vitamin D blood levels had a 62 percent lower risk of developing MS than those with the lowest vitamin D levels. The study didn't find this effect among black men and women, most likely because there were fewer black study participants and most of them had low vitamin D levels, making it harder to find any link between vitamin D and MS if one exists.

***Vitamin D and Type 1 Diabetes*:**

Type 1 diabetes is another disease that varies with geography—a child in Finland is about 400 times more likely to develop it than a child in Venezuela. Evidence that vitamin D may play a role in preventing type 1 diabetes comes from a 30-year study that followed more than 10,000 Finnish children from birth: Children who regularly received vitamin D supplements during infancy had a nearly 90 percent lower risk of developing type 1 diabetes than those who did not receive supplements. Other European case-control studies, when analyzed together, also suggest that vitamin D may help protect against type 1 diabetes. No randomized controlled trials have tested this notion, and it is not clear that they would be possible to conduct.

Vitamin D,* the *Flu, and the Common Cold:

The flu virus wreaks the most havoc in the winter, abating in the summer months. This seasonality led a British doctor to hypothesize that a sunlight-related "seasonal stimulus" triggered influenza outbreaks. More than 20 years after this initial hypothesis, several scientists published a paper suggesting that vitamin D may be the seasonal stimulus. Among the evidence they cite:

- Vitamin D levels are lowest in the winter months.
- The active form of vitamin D tempers the damaging inflammatory response of some white blood cells, while it also boosts immune cells' production of microbe-fighting proteins.
- Children who have vitamin D-deficiency rickets are more likely to get respiratory infections, while children exposed to sunlight seem to have fewer respiratory infections.
- Adults who have low vitamin D levels are more likely to report having had a recent cough, cold, or upper respiratory tract infection.

A recent randomized controlled trial in Japanese school children tested whether taking daily vitamin D supplements would prevent seasonal flu. The trial followed nearly 340 children for four months during the height of the winter flu season. Half of the study participants received pills that contained 1,200 IU of vitamin D; the other half received placebo pills. Researchers found that type A influenza rates in the vitamin D group were about 40 percent lower than in the placebo group; there was no significant difference in type B influenza rates. This was a small but promising study, and more research is needed before we can definitively say that vitamin D protects against the flu. But don't skip your flu shot, even if vitamin D has some benefit.

Vitamin D and Tuberculosis:

Before the advent of antibiotics, sunlight and sun lamps were part of the standard treatment for tuberculosis (TB). More recent research suggests that the "sunshine vitamin" may be linked to TB risk. Several case-control studies, when analyzed together, suggest that people diagnosed with tuberculosis have lower vitamin D levels than healthy people of similar age and other characteristics. Such studies do not follow individuals over time, so they cannot tell us whether vitamin D deficiency led to the increased TB risk or whether taking vitamin D supplements would prevent TB. There are also genetic differences in the receptor that binds vitamin D, and these differences may influence TB risk. Again, more research is needed.

Vitamin D and Risk of Premature Death

A promising report in the *Archives of Internal Medicine* suggests that taking vitamin D supplements may even reduce overall mortality rates: A combined analysis of multiple studies found that taking modest levels of vitamin D supplements was associated with a statistically significant 7 percent reduction in mortality from any cause. The analysis looked at the findings from 18 randomized controlled trials that enrolled a total of nearly 60,000 study participants; most of the study participants took between 400 and 800 IU of vitamin D per day for an average of five years. Keep in mind that this analysis has several limitations, chief among them the fact that the studies it included were not designed to explore mortality in general, or explore specific causes of death. More research is needed before any broad claims can be made about vitamin D and mortality.

V. CONCLUSION

Numbers of people with VDD are continuously increasing; the importance of this hormone in overall health and the prevention of chronic diseases are at the forefront of research. VDD is very common in all age groups. Very few foods contain vitamin D therefore guidelines recommended supplementation of vitamin D at tolerable UL levels. It is also suggested to measure the serum 25-hydroxyvitamin D level as the initial diagnostic test in patients at risk for deficiency. Treatment with either vitamin D2 or vitamin D3 is recommended for the deficient patients. More research is required to recommend screening individuals who are not at risk for deficiency or to prescribe vitamin D to attain the noncalcemic benefit for cardiovascular protection

REFERENCES

[1] Holick MF. Vitamin D deficiency. 2007; 357:266-81.
[2] Gordon CM, DePeter KC, Feldman HA, Grace E, Emans SJ. Prevalence of vitamin D deficiency among healthy adolescents. 2004; 158:531-7.
[3] Lips P. Worldwide status of vitamin D nutrition. 2010; 121:297-300.
[4] Robinson PD, Hogler W, Craig ME, et al. The re-emerging burden of rickets: a decade of experience from Sydney. 2006; 91:564-8.
[5] Kreiter SR, Schwartz RP, Kirkman HN, Jr., Charlton PA, Calikoglu AS, Davenport ML. Nutritional rickets in African American breast-fed infants. 2000; 137:153-7.
[6] Misra M, Pacaud D, Petryk A, Collett-Solberg PF, Kappy M. Vitamin D deficiency in children and its management: review of current knowledge and recommendations. 2008; 122:398-417.
[7] Institute of Medicine. Dietary Reference Intakes for Calcium and Vitamin D. Washington, D.C.: National Academies Press, 2010.
[8] Holick MF. Vitamin D: importance in the prevention of cancers, type 1 diabetes, heart disease, and osteoporosis. 2004; 79:362-71.
[9] Boonen S, Lips P, Bouillon R, Bischoff-Ferrari HA, Vanderschueren D, Haentjens P. Need for additional calcium to reduce the risk of hip fracture with vitamin d supplementation: evidence from a comparative metaanalysis of randomized controlled trials. 2007; 92:1415-23.
[10] Bischoff-Ferrari HA, Willett WC, Wong JB, Giovannucci E, Dietrich T, Dawson-Hughes B. Fracture prevention with vitamin D supplementation: a meta-analysis of randomized controlled trials. 2005; 293:2257-64.
[11] Cauley JA, Lacroix AZ, Wu L, et al. Serum 25-hydroxyvitamin D concentrations and risk for hip fractures. 2008; 149:242-50.
[12] Cauley JA, Parimi N, Ensrud KE, et al. Serum 25 HydroxyVitamin D and the Risk of Hip and Non-spine Fractures in Older Men. 2009.

[13] Bischoff-Ferrari HA, Willett WC, Wong JB, et al. Prevention of nonvertebral fractures with oral vitamin D and dose dependency: a meta-analysis of randomized controlled trials. 2009; 169:551-61.
[14] Bischoff-Ferrari HA, Dawson-Hughes B, Willett WC, et al. Effect of Vitamin D on falls: a meta-analysis. 2004; 291:1999-2006.
[15] Broe KE, Chen TC, Weinberg J, Bischoff-Ferrari HA, Holick MF, Kiel DP. A higher dose of vitamin D reduces the risk of falls in nursing home residents: a randomized, multiple-dose study. 2007; 55:234-9.
[16] Bischoff-Ferrari HA, Orav EJ, Dawson-Hughes B. Effect of cholecalciferol plus calcium on falling in ambulatory older men and women: a 3-year randomized controlled trial. 2006; 166:424-30.
[17] Bischoff-Ferrari HA, Dawson-Hughes B, Staehelin HB, et al. Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomised controlled trials. 2009; 339:b3692.
[18] Sanders KM, Stuart AL, Williamson EJ; et al. Annual high-dose oral vitamin D and falls and fractures in older women: a randomized controlled trial. 2010;303:1815-1822.
[19] Giovannucci E, Liu Y, Hollis BW, Rimm EB. 25-hydroxyvitamin D and risk of myocardial infarction in men: a prospective study. 2008; 168:1174-80.
[20] Pilz S, Marz W, Wellnitz B, et al. Association of vitamin D deficiency with heart failure and sudden cardiac death in a large cross-sectional study of patients referred for coronary angiography. 2008; 93:3927-35.
[21] Pilz S, Dobnig H, Fischer JE, et al. Low vitamin D levels predict stroke in patients referred to coronary angiography. 2008; 39:2611-3.