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Review Article

Is vitamin D deficiency contributing to high predisposition to non-communicable diseases in Indians? A review article

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ABSTRACT

Vitamin D deficiency is highly prevalent in Indians. The role of vitamin D in infectious diseases is a well-known fact. However, more recently, several studies have linked vitamin D deficiency with various non-communicable diseases like hypertension, cardiovascular diseases, diabetes, cancer and psychiatric illnesses amongst others. Indians are known to be prone to developing non-communicable diseases so a co-existing vitamin D deficiency will lead to a synergistic effect towards developing the same. Since vitamin D deficiency is completely preventable, opportunistic screening of people, screening the vulnerable population like the pregnant women and the elderly, patients with hepatic or renal failure, patients on retroviral or immunosuppressant therapy can be useful. Health education and promotion activities should be done to bring awareness in the community. This might as well reduce the growing burden of non-communicable diseases in India.

Keywords: Vitamin D, Non-communicable diseases, Diabetes, Hypertension, Cancer, Pregnancy

BACKGROUND

Vitamin D, a fat-soluble vitamin, is necessary in humans to maintain calcium and phosphorus homeostasis.[1] The chief source of vitamin D is exposure to ultraviolet B (UVB) from sunlight or artificial light. This makes dark-skinned people more vulnerable to Vitamin D deficiency (VDD) as skin pigment melanin renders action of sunlight in production of vitamin D less effective. This makes Indians very prone to develop this particular deficiency, which is largely diagnosed only when patients present with clinically overt symptoms like rickets and osteomalacia, which represent the tip of the iceberg. This may be further complemented by inadequate sun exposure and a vitamin D deficient diet. The main circulating storage form of vitamin D is 25-hydroxy-vitamin D [25(OH)D] and so vitamin D deficiency has been defined as a 25(OH) D level of <20 ng/ml (50 nmol/l), vitamin D insufficiency as 21 to 29 ng/ml severe vitamin D deficiency as <10 ng/ml and the optimal concentration of 25(OH) D is at least 30 ng/ml.[2] It has been observed that 25(OH) D is often as low as 30% to 50% in otherwise healthy middle-aged to elderly adults.[3-6] This is of serious concern as Vitamin D is not only crucial to maintaining musculoskeletal health but also has a role in cardiovascular diseases, cancers and even psychiatric morbidities.

PHYSIOLOGY

Vitamin D has two forms: vitamin D_2 (ergocalciferol) and vitamin D_3 (cholecalciferol). While vitamin D_2 is found in plants and is consumed as a supplement or used in fortified foods, vitamin D_3 is produced by action of UVB radiation on 7-dehydrocholesterol in the skin, which forms previtamin D_3.[7] Previtamin D_3 is rapidly converted to vitamin D_3 leading to its metabolization in the liver to form 25-hydroxyvitamin D_3. In the kidney, 25(OH)D is

converted by 1-hydroxylase to its active form, 1,25-dihydroxyvitamin D [1,25$(OH)_2$D], which is the hormonal form of vitamin D.[7] Vitamin D receptors are present in most tissues, including endothelium, vascular smooth muscle, and myocardium.[8] More than 200 genes are is believed to be regulated by 1,25$(OH)_2$D, including those involved in renin production in the kidney, insulin production in the pancreas, release of cytokines from lymphocytes, production of cathelicidin in macrophages, and growth and proliferation of both vascular smooth muscle cells and cardiomyocytes.[7] Though 1,25$(OH)_2$D circulates throughout the body depending on its serum levels for estimating overall vitamin D status can be misleading as they do not correlate well.[7]

RISK FACTORS OF VITAMIN D DEFICIENCY

Darkly pigmented skin, winter season, increased distance from the equator, time of day, aging, institutionalized patients, indoor lifestyles, covered-up clothing and sunscreen use reduces the cutaneous production of vitamin D_3.[2] Some medical risk factors are liver and kidney disease, obesity, use of anticonvulsants, glucocorticoids and antiretroviral medications.[2]

VITAMIN D DEFICIENCY IN PREGNANCY AND ITS OUTCOMES

The need for calcium increases in pregnancy and lactation. Vitamin D deficiency in pregnant women may affect the mother and the child and cause high bone turn over, bone loss, osteomalacia, and hypovitaminosis D myopathy in the mother.[9,10] If severe, vitamin D deficiency during pregnancy effects calcium homeostasis and skeletal mineralization of the fetus and may even lead to congenital rickets, craniotabes.[11,12] The predominant and often the only source of vitamin D for a baby during gestational period and exclusive breast-feeding period is the mother. So, maternal vitamin D deficiency during this time affect the functional characteristics of various tissues of the body, which, in later life makes the person more prone to develop various non-communicable diseases (NCDs) including mental health problems like schizophrenia.[13,14]

VITAMIN D AND CARDIOVASCULAR AND CEREBROVASCULAR DISEASES

There are several hypotheses to explain the role of vitamin D in cardiovascular diseases (CVDs). Firstly, 1,25$(OH)_2$D is a novel negative endocrine regulator of renin-angiotensin system and plays a central role in the regulation of blood pressure, electrolyte, and volume homeostasis thereby making vitamin D deficiency major risk factor for hypertension, heart attack, and stroke. [15] Also, vitamin D deficiency reduces intestinal calcium absorption by more than 50% which triggers PTH release.[7] And so, chronic vitamin D deficiency causes secondary hyperparathyroidism which may lead to poor cardiovascular health.

Though several studies hypothesized the role of vitamin D in morbidity and mortality from various cardiovascular diseases (CVDs) as early as the 1980s, it was not until the National Health and Nutritional Examination Surveys (NHANES) (1988–1994, 2000–2004) conducted in the United States that this hypothesis was seriously considered.[16,17] In NHANES, they observed that people with vitamin D deficiency [25(OH)D <20 ng/ml] had higher prevalence of self-reported angina, myocardial infarction, and heart failure compared with individuals with higher levels of vitamin D.[18] Several cardiovascular risk factors and CVDs have been associated with lower vitamin D status, including obesity (body mass index >30 kg/m^2), hypertension (HTN), diabetes mellitus (DM), coronary heart disease (CHD), heart failure (HF), peripheral vascular disease (PVD), elevated triglyceride (TG) level, and microalbuminuria.[19-21] In the Framingham offspring study, a cohort with no history of CVD was followed up for 5 years and it was observed that incidence of CVD in subjects with 25(OH)D <10 ng/ml was higher as compared with subjects with 25(OH)D >15 ng/ml. Those subjects with lower serum vitamin D levels elicited a hazard ratio of 1.80 for developing CVDs.[22] Severe vitamin D deficiency in patients undergoing coronary angiography has 3 to 5 times risk of dying from sudden cardiac death or heart failure and a 50% increase in fatal stroke compared to patients with no vitamin D deficiency.[23-24]

VITAMIN D AND DIABETES MELLITUS

Vitamin D plays an important role in the functional regulation of the endocrine pancreas, particularly the beta cells.[25] Several studies have suggested that vitamin D deficiency is associated with insulin resistance and impaired insulin secretion.[26,27] The prevalence of type 2 diabetes in individuals suffering from vitamin D deficiency is observed to be higher than in vitamin D-sufficient individuals. In the same study, it was elicited that administration of high doses of 1,25 $(OH)_2$ D_3 could prevent type 1 diabetes.[28] In a birth cohort study of 31 years of follow-up done in 10,366 children in Finland, it was observed that children who were administered 2,000 IU of vitamin D_3 per day throughout the first year of life experienced a 78% reduced risk of type 1 diabetes.[29]

VITAMIN D DEFICIENCY AND CANCER

Several studies suggest possible association between vitamin D and an increased risk of developing cancer. In studies conducted in rodents, vitamin D has been found to have several activities that might slow or prevent the development of cancer, including promoting cellular differentiation, decreasing cancer cell growth, stimulating apoptosis or cell death, and reducing angiogenesis or formation of blood vessel in malignant growth.[30-32] There are studies showing that higher vitamin D intake and adequate serum levels of vitamin D are associated with a reduced risk of colorectal cancer.[33-36] Breast cancer has been linked with low exposure to sun and low serum vitamin D levels.[37-39] It was elicited that

mice and rats with high intake of vitamin D and calcium-rich diet had markedly reduced incidence of breast cancer.[40,41] Vitamin D was attributed to reduced mortality resulting from ovarian cancer.[42,43] Similar associations have been found with prostate cancers too.[43-47]

CONCLUSION

Various sun-avoidance strategies like use of sunscreen, staying indoors increases the risk of vitamin D deficiency, which is otherwise completely preventable. Since, it has been shown in various studies that vitamin D has a wide and varied role in the body; vitamin D deficiency is destined to have serious consequences. The occurrence of several non-communicable diseases like hypertension, obesity, ischemic heart diseases, peripheral vascular diseases, multiple sclerosis, stroke, diabetes mellitus, cancers and also psychiatric illnesses can be reduced if adequate vitamin D levels are maintained in the body. As seen, Indians are predisposed to vitamin D deficiency as endowed owing to their darker skin tone. Unfortunately, Indians are also at an increased risk of having various NCDs, with or without vitamin D deficiency. However, unlike some Scandinavian countries amongst others, Indian climate favours vitamin D synthesis in the body. Maintaining optimum levels of vitamin D in the body does not need any costly intervention but a sensible exposure (neither over nor under) to the sun daily or for most days of the week would suffice provided the person is not wearing clothes baring face, arms and legs which are not smeared with sunscreen. However, if this exercise is not applicable, reasonable amount of vitamin D-enriched food like cod liver oil or mackerel and sardines can be taken. This can be supplemented by vitamin D-fortified foods. Monitoring serum 25-hydroxyvitamin D concentrations yearly should help reveal vitamin D deficiencies and if detected vitamin D analogues can be used after consulting the physicians. This is particularly important for persons who are at an increased risk of developing the deficiency like patients with liver and kidney disease, obesity or those on anticonvulsants, glucocorticoids, immunosupressants and anti-retroviral therapy amongst others. Also, some physiological conditions like pregnancy and aging warrant the same measure.

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REFERENCES

1. Norman W. Vitamin D: The Calcium Homeostatic Steroid Hormone, New York: Academic Press; 1979.
2. Lee JH, O'Keefe JH, Bell D, Hensrud DD, Holick MF. Vitamin D deficiency: an important, common, and easily treatable cardiovascular risk factor? J Am Coll Cardiol. 2008;52:1949–56.
3. Holick MF. High prevalence of vitamin D in adequacy and implications for health. Mayo Clin Proc. 2006;81:353–73.
4. Malabanan A, Veronikis IE, Holick MF. Redefining vitamin D insufficiency. Lancet.1998;351:805–6.
5. Chapuy MC, Preziosi P, Maamer M, Arnaud S, Galan P, Hercberg S, Meunier PJ. Prevalence of vitamin D insufficiency in an adult normal population. OsteoporosInt. 1997;7:439–43.
6. Nesby-O'Dell S, Scanlon KS, Cogswell ME, Gillespie C, Hollis BW, Looker AC, et al. Hypovitaminosis D prevalence and determinant samong African American and white women of reproductive age: third National Health and Nutrition Examination Survey,1988–1994. Am J Clin Nutr. 2002;76:187–92.
7. Holick MF. Vitamin D deficiency. N Engl J Med. 2007;357(3):266-81.
8. Zittermann A. Vitamin D and disease prevention with special reference to cardiovascular disease. Prog Biophys Mol Biol. 2006;92:39–48.
9. Glerup H, Mikkelsen K, Poulsen L, Hass E, Overbeck S, Andersen H, et al. Hypovitaminosis D myopathy without biochemical signs of osteomalacic bone involvement. Calcif Tissue Int. 2000;66(6):419-24.
10. Lips P. Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications. Endocr Rev. 2001;22:477–501.
11. Namgung R, Tsang RC. Bone in the pregnant mother and newborn at birth. Clin Chim Acta. 2003;333:1–11.
12. Specker BL. Do North American women need supplemental vitamin D during pregnancy or lactation? Am J Clin Nutr. 1994;59:484– 90.
13. McGrath JJ, Burne TH, Féron F, Mackay-Sim A, Eyles DW. Developmental Vitamin D Deficiency and Risk of Schizophrenia: A 10-Year Update. Schizophrenia Bulletin. 2010;36(6):1073-8.
14. Barker DJP. Mothers, babies and health in later life. 2nd ed. Edinburgh, United Kingdom: Churchill Livingstone; 1998.
15. Li YC, Kong J, Wei M, Chen ZF, Liu SQ, Cao LP. 1,25-Dihydroxyvitamin D(3) is a negative endocrine regulator of the renin-angiotensin system. J Clin Invest. 2002;110(2):229-38.
16. Fleck A. Latitude and ischaemic heart disease. Lancet. 1989;1:613.
17. Rostand SG. Ultraviolet light may contribute to geographic and racial blood pressure differences. Hypertension. 1997;30(2):150–6.
18. Kendrick J, Targher G, Smits G, Chonchol M. 25-Hydroxyvitamin D deficiency is independently associated with cardiovascular disease in the Third National Health and Nutrition Examination Survey. Atherosclerosis. 2009;205(1):255-60.
19. Scragg R, Sowers M, Bell C. Serum 25-hydroxyvitamin D, ethnicity, and blood pressure in the Third National Health and Nutrition Examination Survey. Am J Hypertens. 2007;20:713–9.
20. Martins D, Wolf M, Pan D, Zadshir A, Tareen N, Thadhani R, Felsenfeld A, et al. Prevalence of cardiovascular risk factors and the serum levels of

25-hydroxyvitamin D in the United States: data from the Third National Health and Nutrition Examination Survey. Arch Intern Med. 2007;167(11):1159-65.
21. Kim DH, Sabour S, Sagar UN, Adams S, Whellan DJ. Prevalence of hypovitaminosis D in cardiovascular diseases (from the National Health and Nutrition Examination Survey 2001 to 2004). Am J Cardiol. 2008;102(11):1540-4.
22. Wang TJ, Pencina MJ, Booth SL, Jacques PF, Ingelsson E, Lanier K, et al. Vitamin D deficiency and risk of cardiovascular disease. Circulation. 2008;117(4):503-11.
23. Pilz S, Dobnig H, Fischer JE, Wellnitz B, Seelhorst U, Boehm BO, März W. Low vitamin D levels predict stroke in patients referred to coronary angiography. Stroke. 2008;39(9):2611-3.
24. Pilz S, März W, Wellnitz B, Seelhorst U, Fahrleitner-Pammer A, Dimai HP. Association of vitamin D deficiency with heart failure and sudden cardiac death in a large cross-sectional study of patients referred for coronary angiography. J Clin Endocrinol Metab. 2008;93(10):3927-35.
25. Sooy K, Schermerhorn T, Noda M, Surana M, Rhoten WB, Meyer M, et al. Calbindin-D28k Controls [Ca2+] i and Insulin Release Evidence obtained from calbindin-d28k knockout mice and β cell lines. J Biological Chem. 1999;274(48):34343-9.
26. Norman AW, Frankel JB, Heldt AM, Grodsky GM. Vitamin D deficiency inhibits pancreatic secretion of insulin. Science. 1980;209(4458):823-5.
27. Liu E, Meigs JB, Pittas AG, McKeown NM, Economos CD, Booth SL, et al. Plasma 25-hydroxyvitamin d is associated with markers of the insulin resistant phenotype in nondiabetic adults. J Nutr. 2009;139(2):329-34.
28. Boucher BJ, Mannan N, Noonan K, Hales CN, Evans SJ. Glucose intolerance and impairment of insulin secretion in relation to vitamin D deficiency in east London Asians. Diabetologia. 1995;38(10):1239-45.
29. Hyppönen E, Läärä E, Reunanen A, Järvelin MR, Virtanen SM. Intake of vitamin D and risk of type 1 diabetes: a birth-cohort study. Lancet. 2001;358:1500–3.
30. Thorne J, Campbell MJ. The vitamin D receptor in cancer. Proceedings of the Nutrition Society. 2008;67(2):115-27.
31. Moreno J, Krishnan AV, Feldman D. Molecular mechanisms mediating the antiproliferative effects of vitamin D in prostate cancer. J Steroid Biochem Molecular Biol. 2005;97(1–2):31–6.
32. Holt PR, Arber N, Halmos B, Forde K, Kissileff H, McGlynn KA, et al. Colonic epithelial cell proliferation decreases with increasing levels of serum 25-hydroxy vitamin D. Cancer Epidemiol Biomarkers Prevention. 2002;11(1):113–9.
33. Ma Y, Zhang P, Wang F, Yang J, Liu Z, Qin H. Association between vitamin D and risk of colorectal cancer: a systematic review of prospective studies. J Clin Oncol. 2011;29(28):3775-82.
34. Gandini S1, Boniol M, Haukka J, Byrnes G, Cox B, Sneyd MJ, et al. Meta-analysis of observational studies of serum 25-hydroxyvitamin D levels and colorectal, breast and prostate cancer and colorectal adenoma. Int J Cancer. 2011;128(6):1414-24.
35. Woolcott CG, Wilkens LR, Nomura AM, Horst RL, Goodman MT, Murphy SP, et al. Plasma 25-hydroxyvitamin D levels and the risk of colorectal cancer: the multiethnic cohort study. Cancer Epidemiol Biomarkers Prevent. 2010;19(1):130-4.
36. Jenab M, Bueno-de-Mesquita HB, Ferrari P, van Duijnhoven FJ, Norat T, Pischon T, et al. Association between pre-diagnostic circulating vitamin D concentration and risk of colorectal cancer in European populations: a nested case-control study. BMJ. 2010;340:5500.
37. Gorham E, Garland C, Garland F. Acid haze air pollution and breast and colon cancer in 20 Canadian cities. Can J Public Health. 1989;80:96–100.
38. Garland F, Garland C, Gorham E, Young J Jr. Geographic variation in breast cancer mortality in the United States: a hypothesis involving exposure to solar radiation. Prev Med. 1990;19:614–22.
39. Shin MH, Holmes MD, Hankinson SE, Wu K, Colditz GA, Willett WC. Intake of dairy products, calcium, and vitamin D and risk of breast cancer. J Natl Cancer Inst. 2002;94(17):1301–1.
40. Lipkin M, Newmark HL. Vitamin D, calcium and prevention of breast cancer: a review. J Am Coll Nutr. 1999;18(5):392–7.
41. Newmark HL. Vitamin D adequacy: a possible relationship to breast cancer. Adv Exp Med Biol. 1994;364:109–14.
42. Lefkowitz ES, Garland CF. Sunlight, vitamin D, and ovarian cancer mortality rates in US women. Int J Epidemiol. 1994;23(6):1133–6.
43. Grant WB. An estimate of premature cancer mortality in the US because of inadequate doses of solar ultraviolet-B radiation. Cancer. 2002;94(6):1867–75.
44. Gorham ED, Garland FC, Garland CF. Sunlight and breast cancer incidence in the USSR. Int J Epidemiol. 1990;19(4):820–4.
45. Schwartz GG, Hulka BS. Is vitamin D deficiency a risk factor for prostate cancer? (Hypothesis). Anticancer Res. 1990;10(5):1307–11.
46. John EM, Dreon DM, Koo J, Schwartz GG. Residential sunlight exposure is associated with a decreased risk of prostate cancer. J Steroid Biochem Mol Biol. 2004;89–90(1–5):549–52.
47. Hanchette CL, Schwartz GG. Geographic patterns of prostate cancer mortality. Evidence for a protective effect of ultraviolet radiation. Cancer. 1992; 70(12):2861–9.

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