Editorial

Possible Causes of Vitamin D Deficiency (VDD) in Pakistani Population Residing in Pakistan

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For decades, adequate circulating Vitamin D (25OHD) concentration is considered essential for maintenance of bone health while inadequate levels of 25OHD have classically been associated with bone disorders, such as rickets, osteomalacia and osteoporosis. Recent literature identifies role of vitamin D in many other organ systems of the body and reports a pandemic of vitamin D deficiency/insufficiency globally, in a very diverse population around the world.[1-3] Population based studies from Norway, in immigrant Pakistanis in 2005 have shown VDD defined as secondary hyperparathyroidism to be more prevalent in Pakistani men and women than Norwegian men and women and highest prevalence of VDD in five different ethnic immigrant groups living in Oslo which included immigrants from Turkey, Srilanka, Iran, Pakistan and Vietnam.[4,5] Prevalence of 70% and 97 % of VDD has been identified in healthy asymptomatic volunteers in two different studies from our center.[6] Of more significance was the high PTH level seen in 30% of the healthy volunteers with negative correlation with 25OHD levels while their other biochemical parameters viz., calcium, phosphate and alkaline phosphatase remains normal (unpublished data). Prevalence of VDD of 92% and 81% in ambulatory patients has also been reported from centers in Karachi and Lahore recently.[7,8] Reports previously have also demonstrated VDD from various regions of Pakistan.[9-11]

The two main sources of vitamin D are food and sunlight. Generally natural food sources have low vitamin D content and therefore require fortification. Insufficient dietary supplies of vitamin D in countries where food stuffs are not fortified, leads to generally low dietary intake of vitamin D and calcium. Inadequate dietary intake of calcium associated with high phytate/calcium ratio also reduces the bioavailability of calcium in the gut. This then induces increased parathyroid hormone (PTH) level and increases bone turnover and catabolism of 25OHD.[1,12] In one of our study to assess the dietary calcium intake, we found the intake to be 433mg and 628 mg based on 24 hour dietary recall and food frequency questionnaire in contrast to the recommended intake of 1000-1200mg/day for adults (Romaina et al:unpublished data). Unlike many Western countries that have a VD food fortification policy, Pakistan does not have a mandatory VD fortification policy in place.

In this situation the major source of vitamin D is exposure to Ultra Violet B (UVB) rays in sunlight. Cutaneous synthesis of vitamin D, involves photo conversion of 7-dehydrocholestrol (7-DHC) present mainly in the stratum spinosus and basale of epidermis to pre-cholecalciferol (pre-D3), which subsequently undergoes isomerization to form cholecalciferol (D3). Subsequent hydroxylation in the liver produces 25OHD which further undergo 2nd hydroxylation in the kidney to form the active form of vitamin D; 1,25(OH)2 D.[1,3]

UVB rays in sunlight are the primary source of Vitamin D. It is most intense between 10:00 am and 3:00 pm when the sunlight is brightest. It is also more intense in the summer months accounting for 70% of a person's yearly UVB dose. Vitamin D3 is made in the skin when 7-DHC reacts with UVB at wavelengths between 270-300 nm. Optimal synthesis occurs in a narrow band of UVB spectra between 295-297nm while peak isomerization is found at 297 nm (which is thus known as D-UV). These wavelengths are present in sunlight when the UV index is greater than 3. Adequate amounts of vitamin D3 can be made in the skin after only 10 to 15 minutes of sun exposure at least two times per week to the face, arms, hands, or back without sunscreen. With longer exposure to UVB rays, equilibrium is achieved in the skin, and the vitamin simply degrades as fast as it is generated. Exposure to one minimal eryhthmal dose of UVB while wearing only a bathing suit is equivalent to ingestion of approx 20, 000 IU of Vitamin D while supplementation of 100 IU (2.5 microgram) vitamin D3 raises blood levels by 2.5 nmol/litre (1 ng/ml) only.[1,3]

Factors that govern the generation of pre-D3 are the quantity (intensity) and quality (appropriate wavelength) of the UVB irradiation reaching the 7-DHC deep in the stratum basale and stratum spinosum. A critical determinant of D3 production is the presence and concentration of melanin. The concentration of melanin in the skin is related to the ability of UVB light to penetrate the epidermal strata and reach the 7-DHC-containing stratum basale and stratum spinosum. Under normal

circumstances, ample quantities of 7-DHC (about 25-50 μg/cm² of skin) are available to meet the body's VD requirements, and melanin content does not alter the amount of vitamin D that can be produced. But individuals with higher skin melanin content will simply require more time in sunlight to produce the same amount of vitamin D as individuals with lower melanin content. The amount of time an individual requires to produce a given amount of Vitamin D may also depend upon the person's distance from the equator and on the season of the year.[1,3]

It is surprising to see so much of D deficiency in a country with ample sunshine where one would assume it to be non-existent. Increased pigmentation due to which more prolonged exposure to sun is required, use of sun block, purdah observation and possibly the reason that women in general do not go outside the home may be responsible for VDD. However, to note even this cannot explain the existence of vitamin D deficiency in many sun-drenched areas such as South America, where clothing style is such that sunlight activity may not be hindered, vitamin D deficiency is still becoming a major public health problem.[3]

The etiology of vitamin D deficiency could be multifactorial as further hydroxylation of vitamin D occurs first in liver followed by second hydroxylation in kidney to produce the biologically active 1, 25(OH)2D by 1-hydroxylase enzyme. In the kidney, another enzyme; 24-hydroxylase coverts 1, 25(OH)2D to 1, 24, 25(OH)2D limiting its availability and at the same time shunting available substrate 25OHD from 1-hydroxylase. 24 hydroxylase gene is under stringent transcriptional control by 1,25(OH)2D itself providing a robust means of proximate negative feedback regulation of the amount of 1,25(OH)2D made in and released from the kidney. Altered physiology of vitamin D endocrine system as indicated by increased activity of 24-hydroxylase in Indo-Asians of Southern United States may be an additional factor as shown by Awumey et al.[13] The decrease in serum 25OHD and urinary calcium with secondary hyperparathyroidism and increase in serum 1, 25(OH)2D resulting from deficiency of 25OHD may not be reversible due to life long stimulation produced by vitamin D depletion or deficiency.

The question remains that are we not getting enough sun exposure or are we breaking down this vitamin more rapidly? More detailed studies are required to unravel the cause of the vitamin D deficiency and calculation of population based prevalence rates requires large studies in community settings.[14] More active measures are needed to increase awareness to health care professionals and their clients about the importance of vitamin D for health, including the need for exposure to sunlight, adequate dietary intake of vitamin D and implementation of current recommendations to improve their vitamin D status.

References

1. Holick MF. Vitamin D Deficiency. N Engl J Med 2007; 357: 266-81.
2. Nagpal S, Na S, Rathnachalam R. Noncalcemic actions of vitamin D receptor ligands. Endocr Rev 2005; 26: 662-87.
3. Hollick MF, Chen TC. Vitamin D deficiency: a worldwide problem with health consequences. Am J Clin Nutr 2008; 87: 1080S-6S.
4. Meyer HE, Falch JA, Sogaard AJ, Haug E. Vitamin D deficiency and secondary hyperparathyroidism and the association with bone mineral density in persons with Pakistani and Norwegian background living in Oslo, Norway, The Oslo Health Study. Bone 2004; 35: 412-7.
5. Holvik K, Meyer HE, Hang E, Brunvand L. Prevalence and predictors of vitamin D deficiency in five immigrant groups living in Oslo, Norway. The Oslo immigrant health study. Eur J Clin Nutr 2005; 59: 57-63.
6. Zuberi LM, Habib A, Haque N, Jabbar A. Vitamin D deficiency in ambulatory patients. J Pak Med Assoc 2008; 58: 482-4.
7. Baig A, Anjum P, Khani MK, Islam N, Rahman A. Pattern of serum Vitamin D in OPD patients. Pak J Surg 2007; 23: 145-9.
8. Masud F. Vitamin D levels for optimum bone health. Singapore Med J 2007; 48: 207-12.
9. Rab SM. Occult osteomalacia amongst health and pregnant women in Pakistan. Lancet 1976; 2: 1211-3.
10. Atiq M, Suria A, Nizami SQ, Ahmed I. Maternal Vitamin D deficiency in Pakistan. Acta Obstet Gynaecol Scand 1998; 77, 970-3.
11. Sahibzada AS, Khan MS, Javed M. Presentation of osteomalacia in Kohistani women. J Ayub Med Coll Abottabad 2004; 16: 63-5.
12. Calvo MS, Whiting SJ, Barton CN. Vitamin D Intake: A Global Perspective of Current Status. Jr Nutr 2007; 135: 310-7.
13. Awumey EMK, Mitra DA, Hollis BW, Kumar R, Bell NH. Vitamin-D Metabolism is altered in Asian Indians in Southern United States: A clinical research center study. JCE & M 1998; 83: 169-73.
14. Khan AH, Jabbar A, Baig P. Vitamin D deficiency osteomalacia: the continuing challenge. J Coll Phys Surg Pak 2008; 18: 664-6.