Review Article

PREVALENCE OF VITAMIN D DEFICIENCY IN SOUTH ASIA

Syed Hassaan Masood[1], M. Perwaiz Iqbal[2]

ABSTRACT

Vitamin D, also described as 'the Sun Vitamin' is a steroid with hormone-like activity. It regulates the functions of over 200 genes and is essential for growth and development of the body. Vitamin D deficiency is quite prevalent throughout the world, but it appears to be much worse in the countries of sunny South Asia, especially among children, women and elderly. Poor diet, cultural practices of the region and poverty are some of the important reasons for vitamin D deficiency. Hypovitaminosis D (vitamin D deficiency) is considered responsible for rickets, birth defects, osteoporosis, osteoarthritis, osteomalacia, chronic pain and muscle pain. Recent research has associated vitamin D deficiency as a contributing factor in diseases, such as heart disease, hypertension, neurological disorders, autoimmune disease, depression and cancer.

This paper reviews the problem of vitamin D deficiency with special reference to South Asia and recommends that education regarding adequate exposure to sunlight, proper diet and fortification of selected foodstuff with vitamin D may be helpful in reducing vitamin D deficiency in this part of the world.

KEY WORDS: Vitamin D deficiency, South Asia.

Pak J Med Sci October - December 2008 (Part-II) Vol. 24 No. 6 891-897

How to cite this article:

Masood SH, Iqbal MP. Prevalence of vitamin D deficiency in South Asia. Pak J Med Sci 2008;24(6): 891-97.

1. Mr. Syed Hassaan Masood,
2. Prof. M. Perwaiz Iqbal,
Professor of Biochemistry,
1-2: Department of Biological & Biomedical Sciences,
Aga Khan University,
Karachi-74800,
Pakistan.

Correspondence

Dr. Mohammad Perwaiz Iqbal,
Professor of Biochemistry,
Department of Biological & Biomedical Sciences,
Aga Khan University,
Stadium Road,
P.O. Box-3500
Karachi-74800,
Pakistan.
Email: perwaiz.iqbal@aku.edu

* Received for Publication: Aril 4, 2008

* Revision Received: May 8, 2008

* 2nd Revision Received: September 13, 2008

* Final Revision Accepted: September 22, 2008

INTRODUCTION

Vitamin D deficiency is widespread throughout the world. It has been estimated that almost one billion people in the world suffer from vitamin D deficiency or insufficiency.[1] This estimate is based on serum level of 25-hydroxyvitamin D [25(OH)D] of 30 ng/ml.[2] Hypovitaminosis D, has been defined by Thomas et al as serum levels of 25(OH)D less than 15ng/ml (37nmol/l).[3] When the levels of 25(OH)D are between 8-15ng/ml (20-37 nmol/l), the condition is called "moderate hypovitaminosis D". When the levels of 25(OH) D become less than 8ng/ml (20nmol/l), the condition is regarded as "severe hypovitaminosis D".[3] However, investigators, in general, consider levels of 25(OH) D less than 20ng/ml (50nmol/l) as a vitamin D deficient state.[1,4] Vitamin D intoxication, however, occurs when

serum levels of 25(OH) D are greater than 150ng/ml.

In many of the Asian countries, vitamin D deficiency has been found to be rampant. Rickets, a consequence of vitamin D deficiency, is still widespread in regions, such as northern China where 42% of infants were found to suffer from this disease during the winter/spring period.[5] Sunlight exposure promotes vitamin D synthesis and given the number of days the sun shines in South Asia, one would expect the region to be free from vitamin D deficiency. Unfortunately, there is high prevalence of vitamin D deficiency due to lack of proper diet, poor calcium intake, social customs and remaining confined to the four walls of primitive housing that deprives the elderly, children and female population of the benefit of the sunshine.

Sachan et al,[6] investigated hypovitaminosis D in Lucknow, India and found that eighty-four percent of pregnant women had 25(OH) D values below 22 ng/ml (the cut-off point in their research). Siddiqui and Rai[7] found that in Northern Pakistan where sunlight was available in abundance, rickets was a common problem in infants and children. They attributed the hypovitaminosis D to malnutrition, lack of awareness and antenatal factors.

Atiq et al[8] investigated hypovitaminosis D in healthy breast-fed children and nursing mothers at a major teaching hospital in Karachi, Pakistan, and found that 55% of infants and 45% of mothers had very low serum 25(OH)D levels (<25 nmol/l or 10 ng/ml). This paper highlights the contribution of vitamin D to human growth, impact of vitamin D deficiency on human health and reviews the research work done on vitamin D deficiency in South Asian populations. Suggestions have also been made to overcome this problem which is acquiring epidemic proportions in this part of the world.

Biological functions of vitamin D: Before describing the prevalence of vitamin D deficiency, it is appropriate to understand the functional importance of this vitamin in our body. Vitamin D is actually a steroid that has a hormone-like function. It facilitates calcium and phosphorus absorption through the small intestine. Vitamin D from dietary sources and from sun exposure of skin is stored in fat cells and is brought into circulatory system by vitamin D binding protein. Vitamin D3 (cholecalciferol) is biologically inactive and must be metabolized to 25-(OH) D3 in the liver and then to its biologically active form 1,25-dihydroxycholecalciferol [1,25-di (OH)D3] in kidney.[9,10] In this form, vitamin D has been found to regulate functioning of over 200 genes, including the genes involved in cellular proliferation, apoptosis, differentiation and angiogenesis.[1,11,12] However, 25(OH)D3 [25(OH)D] is the predominant form of vitamin D in plasma and the major storage form as well.[10]

Vitamin D deficiency in South Asian population: The most important and freely available source of vitamin D is exposure to sunlight. Skin contains 7-dehydrocholesterol which on exposure to UV light in sunshine gets converted to cholecaliferol (Vitamin D3).[10] The dietary intake is also an important source of vitamin D but poverty, poor choice of diet and excessive cooking do not make this source as abundantly available as the sunlight.

South Asian population seems to be especially prone to vitamin D deficiency and its consequences. Table-I shows the serum/plasma levels of 25(OH) D in different South Asian populations. It is evident that as much as 69%-82% of the South Asian populations in India had 25(OH)D levels in plasma less than the minimum acceptable levels of 20 ng/ml.[13-15] This deficiency/insufficiency is not confined to the South Asians living in India and Pakistan,[8,13-15] but even the immigrants of South Asian origin in UK, Denmark and Norway have been found to be having very low serum/plasma levels of 25(OH)D.[16-21] This indicates that poverty alone can not be the major reason for hypovitaminosis D in South Asians. Therefore, other causes, such as use of unbalanced diet, excessive cooking of food and limited exposure to the sunshine must be taken into account.

Table-I: Serum/plasma levels of 25-hydroxyvitamin D [25(OH)D] in different South Asian populations

Area/Country/ Population	*Study Population*	*Age*	*Gender*			*Serum 25(OH) D Level Variations*	*Study Group & Reference*
			Not Specified	*Males*	*Females*		
South India women	Postmenopausal years	59 ± 8	-	-	164	52% had 25(OH)D insufficiency (10-20 ng/ml), & 30% had 25(OH)D deficiency (<10ng/ml)	Harinarayan [13]*
Lucknow, India	Healthy hospital staff	Working age adults	92	-	-	78.3% of the otherwise healthy individuals were found to be insufficient in 25(OH)D levels (<20 ng/ml). 20.6% had severe deficiency(< 5 ng/ml), and 27.2% had moderate deficiency (5-10 ng/ml) and 18.5% had mild deficiency [10-15 ng/ml]	Arya et al [14]*
South India	Rural & urban South Indian population of Tirpurti	Working age adults	407 rural & 125 urban subjects	-	-	54% had vitamin D insufficiency (10-20ng/ml) & 15% vitamin D deficiency (<10 ng/ml). Compared to urban subjects, rural subjects had a significantly higher 25(OH) D levels.	Harinarayan* et al [15]
South Asian immigrants in Manchester, United Kingdom	South Asian women	18-36 year	-	-	78	A majority of women in the sample (94%) had serum 25(OH)D levels ≤15ng/ml, while 26% had evidence of marked deficiency (≤5 ng/ml).	Roy et al [16]
Pakistani immigrant men in Denmark	Pakistani men	Mean age: 38.3 years (17.9-63.5 years)	-	95	-	Mean 25(OH)D level, 8.3 ng/ml.	Andersen et al [17]
Pakistani immigrant Women in Denmark	Pakistani Women	Mean age: 36.2 years (17.9-63.5 years)	-	-	115	Mean 25(OH)D level, 4.8 ng/ml.	Andersen et al [17]
Pakistani immigrant girls in Denmark	Pakistani girls	Mean age: 12.2 years (10.1-14.7 years)	-	-	37	Mean 25(OH)D level, 4 ng/ml.	Andersen et al [17]
Pakistan	Infants on breast milk	< 6 months	65	-	-	Mean 25(OH)D level, 13.96±5.58ng/ml; 25(OH)D level in 55% infants <10ng/ml	Atiq et al [8]
British Hindu Asians	Punjabi and Gujarati	Healthy adults (25-75 years)	-	60	60	57% of all subjects had 25(OH)D levels < 8 ng/ml.	Shaunak et al [18]
Oslo, Norway immigrants	Pakistani	31-60 years	-	94	97	52% of men and 65% of women had levels of 25(OH)D less than 10 ng/ml.	Holivk et al [19]
Oslo, Norway immigrants	Pakistani	Pre-menopausal women	-	-	26	Mean level of 25(OH)D being 9ng/ml (6-11 ng/ml)	Falch & Steihaug, [20]
Oslo, Norway immigrants	Pakistani	Adults	-	-	117	Mean level of 25(OH)D being 10±5.4 ng/ml	Meyer et al [21]

* Vitamin D insufficiency and deficiency ranges refer to those reported in these papers.

Powell and Greenberg[22] have pointed out some of the secondary causes. These include: decreased synthesis from skin due to dark skin pigmentation or excessive clothing, gastrointestinal problems leading to malabsorption, impaired hepatic 25 hydroxylation of vitamin D3 (due to anticonvulsant drugs, theophylline, isoniazid or severe liver disease), impaired

renal hydroxylation of 25-hydroxy vitamin D3 due to chronic renal failure or hypoparathroidism.[22] Major causes of vitamin D deficiency,[23] which could be specific to South Asian populations, must be highlighted.

Causes of vitamin D deficiency in South Asians:

Social and religious customs: The women folks largely stay at home which is almost closed to sunlight. The Muslim women of the region wear clothes which apart from face and hands cover all other parts of their bodies. Even if they go out, opportunity to expose their bodies in sunlight is not available in the all encompassing "Burqa" (a head to toe covering which only has small openings for the eyes). Infants dependent on their mothers also stay indoors and receive little or no exposure to sunlight. The old and weak also have no exposure to sunlight as they spend almost all of their time inside the tiny huts or houses. The middle class urban population is now increasingly living in densely populated apartment blocks with very little natural light.

Poverty and illiteracy: Poverty is one of the major reasons for most of the ills of the society including poor health. The governments' claims of only a third of the population being below the poverty line in this region are doubtful. Even those who actually live above this arbitrary line cannot afford to eat a proper diet due to the high cost of foods rich in vitamin D. A vast majority of people are illiterate and are not aware of the importance of balanced diet. Moreover, the dietary habits are also to blame as food is often overcooked destroying most of the vitamins and micronutrients in it.

Skin pigmentation of South Asian population: The color of skin of South Asian population varies from light brown to almost dark. Dark pigmentation has been found to decrease skin synthesis of vitamin D because UV light cannot reach the appropriate layer of the skin. Compared to the Caucasian population, healthy African Americans have also been found more likely to be vitamin D deficient regardless of age.[24]

Addictive Habits: A recent study on South Asian communities in UK by Ogunkolade et al has shown that chewing betel nut (Areca catechu), an addictive habit common among South Asians, contributes to hypovitaminosis D by modulating the enzymes which regulate circulating levels of 1,25di(OH)D.[25]

Impact of vitamin D deficiency on South Asian population

Vitamin D deficiency and bone mineral density: Vitamin D deficiency is associated with secondary hyperparathyroidism with consequent ill effects on bone mineral density.[26] Marwah et al,[27] studied vitamin D deficiency and its effects on bone mineral density in Indian adolescents of 10-18 years of age and concluded that metabolic bone disorders secondary to vitamin D deficiency continue to be prevalent in the Indian subcontinent and are more prevalent in lower socio economic population.

Vitamin D deficiency and osteoporosis: Postmenopausal women are known to be prone to vitamin D deficiency causing an early onset of osteoporosis. The tendency to the deficiency is universal as 28.4% post -menopausal women have been found to be deficient in vitamin D [25(OH)D, < 20 ng/ml] in most part of the world.[26] However, this percentage increased to 30% in a population from Southern India.[13]

Osteomalacia and rickets due to vitamin D deficiency: While rickets is a consequence of vitamin D deficiency in infants and children, older adults can suffer from osteomalacia due a loss of bone density causing pain and soft bones.[28] The problem of rickets among infants and children is widespread in cooler northern areas of South Asia.[7,8] Rickets remains one of the major causes of infant mortality in South Asia.[4]

Vitamin D deficiency in infants can often be traced to maternal nutritional status.[6] Neonatal concentrations are normally 60-70% of maternal vitamin D levels. In case of maternal deficiency, the neonate's low reserves of vitamin D can cause hypocalcaemic symptoms in the first six months of infant's life.[8,29,30] Pregnant women in South Asia are advised 400 IU (10μg) daily intake of vitamin D but compliance to this recommendation is often very

poor.[31] Experience with Indian and Pakistani populations in developed countries and in India and Pakistan suggests that for conventionally dressed pregnant women receiving insufficient sunlight, a 1000 IU (25 μg) daily intake of vitamin D is more appropriate.[32]

Due to low level of compliance to recommended daily intake of vitamin D, Lawson and Thomas[33] advocate an annual intramuscular booster of 150,000 IU for children of Asian origin up to the age of five years. In order to build vitamin D store of infants, it is now a standard practice in France is to give pregnant women a single large intramuscular dose of vitamin D of 100,000 to 150,000 IU during the 7th month of pregnancy.[34] A similar policy for children and pregnant women in India and Pakistan needs to be considered.

Roy et al[16] have reported that in South Asian women, a decrease in serum 25(OH)D level ≤15 ng/ml is associated with a progressive reduction in bone mass at the hip and wrist. Finch et al[35] claimed that osteomalacia was under-diagnosed in South Asians living in UK. They found that 22% of subjects in their study had varying degrees of osteomalacia.

Vitamin D deficiency and other diseases: Over 200 of human genes have receptors for vitamin D, making vitamin D deficiency a contributory factor to a wide variety of other human diseases. Johnson argues "that vitamin D is important for much more than just bones; the vitamin seems to have a role in preventing colorectal and other cancers, diabetes, arthritis and even multiple sclerosis (MS)".[36]

In vitro studies have shown that the active vitamin D metabolite - 1,25 di(OH))D3 may arrest the cell cycle progression, induce apoptosis as well as regulate T cells and antigen presenting cells function.[37] They point to the evidence that vitamin D deficiency accelerates development of autoimmune disease and cancers.

Recently, an inverse association between plasma 25(OH) D levels and risk of hypertension has been reported.[38] Richard and his associates have shown beneficial effects of vitamin D against aging and inflammation.[39] In a study at the Alzheimer's Disease Research Center, St Louis, USA, vitamin D deficiency was found to be associated with psychiatric and neurological disorders.[40] In another report, vitamin D deficiency was implicated in depression.[41]

Bottela-Carretero et al found an association between vitamin D deficiency and metabolic syndrome in obese patients.[42] Patients with vitamin D deficiency had significantly lower levels of HDL-cholesterol and hypertriglyceridemia compared to patients with normal levels of vitamin D.[42] Wang et al more recently, in a prospective study on 1739 participants and a mean follow-up of 5.4 years, showed vitamin D deficiency to be a risk factor for cardiovascular disease in participants with hypertension. [43] Cardiomyopathy due to vitamin D deficiency in infants is a rare but potentially fatal manifestation of hypovitaminosis D.[44]

Adequate intake of vitamin D: The mean serum concentration of 25(OH)D of 30 ng/ml is considered desirable for health.[1] A level of 20 ng/ml is considered as minimum acceptable.[1,4] The recommended daily intakes for vitamin D for infants, children and adults upto 50 years is 200 IU (5 μg) per day, and for adults between 50-70 years, it should be 400 IU (10 μg).[23,45] Several investigators have suggested that these values are insufficient especially for pregnant females, sick adults and older adults.[46] Perhaps all the adults need 800-1000 IU daily.[46]

Toxicity of Vitamin D: Excess of vitamin D can cause hypercalcemia and hypercalcuria.[23] However, these complications do not occur at the recommended intake amounts of vitamins D.[23,47] Toxicity is not likely to occur at doses less than 2400 IU (60μg) per day.[45] Studies have reported no observed adverse effects of vitamin D at an intake of 20μg/day.[23]

Conquering vitamin D deficiency: Vitamin D deficiency in South Asia has acquired epidemic proportions. It is surprising that in South Asia, where as much as 80% of the apparently healthy population is deficient in vitamin D (<20ng/ml) and up to 40% of the population is severely deficient (<9ng/ml),[14] no public awareness program or mandatory supplemen-

tation of common foodstuff with vitamin D is being implemented by the governments. It is incumbent on the Scientific Community to impress upon the policy makers to advocate for fortification of grains with vitamin D. The fears related to vitamin D toxicity have proved unfounded and the daily nutrient intakes recommended by Food and Nutrition Board of the Institute of Medicine, USA,[45,47] are too conservative even for the Western societies. In South Asia, where social factors, skin pigmentation and cold winters in northern parts have resulted in mild to severe deficiency in almost total population, these recommendations need to be revised upward in order to improve the vitamin D levels of the population. It had been suggested that approximately thirty minutes of skin exposure (without sunscreen) to sunlight could provide all the daily needs of vitamin D to the human body.[46] However, a recent study on Hawaian population revealed that even 11.1 hour total body exposure to sunlight per week was not enough to prevent the development of "low vitamin D status".[48] This shows that vitamin D synthesis by skin could be affected by a number of factors, yet unknown. Therefore, supplementation with vitamin D would, perhaps, be necessary in populations at risk of developing hypovitaminosis D.

CONCLUSION

Recommendation: Vitamin D deficiency is wide spread in South Asian population and is contributing to burden of disease in this region. It is suggested that the governments in South Asia should implement a mandatory vitamin D supplementation program of selected foodstuff, at least during the winter months. Vitamin D supplement and an annual intramuscular injection of a large single dose of vitamin D need to be considered for the special risk groups. The program needs to be reinforced through a mass awareness campaign over the electronic media of the importance of absorbing direct sunlight for at least 30 minutes a day. The adequate vitamin D daily intake for South Asians also needs to be set at least twice that of the above mentioned recommended intakes for Western populations.[23,45]

ACKNOWLEDGEMENT

Technical assistance provided by Mr. Irfanullah Baig is gratefully acknowledged.

REFERENCES

1. Holick MF. Vitamin D, Deficiency. N Engl J Med 2007;357:266-81.
2. Dawson-Hughes B, Heaney RP, Holick MF, Lips P, Meunier PJ, Vieth R. Estimates of optimal vitamin D status. Osteoporosis Int 2005;16:713-16.
3. Thomas MK, Lloyd-Jones DM, Thadhani RI, Shaw AC, Deraska DJ, Kitch BT, et al. Hypovitaminosis D in medical patients. N Engl J Med 1998;338:777-83.
4. 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.
5. Strand MA, Perry J, Jin M, Tracer DP, Fischer PR, Zhang P, et al. Diagnosis of rickets and reassessment of prevalence among rural children in northern China. Pediatr Int 2007;49:202-9.
6. Sachan A, Gupta R, Das V, Agarwal A, Pradeep K, Awasthi PK, et al. High prevalence of vitamin D deficiency among pregnant women and their newborns in northern India. Am J Clin Nutr 2005;81:1060-4.
7. Siddiqui TS, Rai MI. Presentation and predisposing factors of nutritional rickets in children of Hazara division. J Ayub Med Coll 2005;17(3):29-32.
8. Atiq M, Suria A, Nizami SQ, Ahmed I. Vitamin D status of breast-fed Pakistani infants. Acta Paediatr 1998;87(7):737-40.
9. DeLuca HF. Overview of general physiologic features and functions of vitamin D. Am J Clin Nutr 2004;80:1689S-1696S.
10. Champe PC, Harvery RA, Ferrier DR. Lippincotts' Illustrated Reviews: Biochemistry, 3rd edition, Philadelphia, Lippincott Williams & Wilkins, 2005;384-7.
11. Holick MF. Vitamin D. The under-appreciated D-lightful hormone that is important for skeletal and cellular health. Curr Opin Endocrinol Diabetes 2002;9:87-98.
12. Holick MF, Garabedian M. Vitamin D: photobiology, metabolism, mechanism of action and clinical applications. In: Favus MJ, editor. Primer on the metabolic bone diseases and disorders of mineral metabolism. 6th ed. Washington, DC: American Society for Bone and Mineral Research 2006;129-37.
13. Harinarayan CV. Prevalence of vitamin D insufficiency in postmenopausal south Indian women. Osteoporsis Int 2005;16(4):397-402.
14. Arya V, Bhambri R, Godbole MM, Mithal A. Vitamin D status and its relationship with bone mineral density in healthy Asian Indians. Osteoporsis Int 2004;15(1):56-61.
15. Harinarayan CV, Ramalakshmi T, Venkataprasad U. High prevalence of low dietary calcium and low vitamin D status in healthy south Indians. Asia Pac J Clin Nutr 2004;13(4):359-64.
16. Roy DK, Berry JL, Pye SR, Adams JE, Swarbrick CM, King Y. Vitamin D status and bone mass in UK South Asian women. Bone 2007;40(1):200-4.

17. Andersen R, Mølgaard C, Skovgaard LT, Brot C, Cashman KD, Jakobsen J, et al. Pakistani immigrant children and adults in Denmark has severely low vitamin D status. Eur J Clin Nutr 2007;April 18; doi:10.1038/sj.ejcn.1602753.
18. Shaunk S, Colston K, Ang L, Patel SP, Maxwell JD. Vitamin D deficiency in adult British Hindu Asians: a family disorder. BMJ 1985;291:1166-8.
19. Holvik K, Meyer HE, Haug E, Brunvand L. Prevalence and predictors of vitamin D deficiency in five immigrant groups living in Oslo, Nowway: the Oslo Immigrant Health Study. Eur J Clin Nutr 2005;59:57-63.
20. Falch JA, Steihaug S. Vitamin D deficiency in Pakistani premenopausal women living in Norway is not associated with evidence of reduced skeletal growth. Scand J Clin Lab Invest 2000;60:103-9.
21. Meyer HE, Falch JA, Søgaard AJ, Haug E. Vitamin D deficiency and secondary hyperparathyroidism and 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.
22. Powell HS, Greenberg D. Tackling vitamin D deficiency. Postgrad Med 2006;119(1):25-30.
23. Vitamins and minerals requirements in human nutrition. Second edition, World Health Organization and Food and Agriculture Organization of the United Nations-2004;45-58.
24. Bodnar LM, Simhan HN, Powers RW, Frank MP, Cooperstein E, Roberts JM. High prevalence of vitamin D deficiency in black and white pregnant women residing in the northern United States and their neonates. J Nutr 2007;137(2):447-52.
25. Ogunkolade WB, Boucher BJ, Bustin SA, Burrin JM, Noorian K, Mannan N, et al. Vitamin D metabolism in peripheral blood mononuclear cells is influenced by chewing "betel nut" (Areca catechu) in vitamin D status. J Clin Endocr Metab 2006;91(7):2612-7.
26. Lips P, Duong T, OleksikA, Black D, Cummings S, Cox D, et al. A global study of vitamin D status and parathyroid function in post-menopausal women with osteoporosis: Baseline data from the multiple outcomes of Raloxifene evaluation clinical trial. J Clin Endocr Metab 2001;86(3):1212-21.
27. Marwaha RK, Tandon N, Reddy D, Reddy HK, Aggarwal R, Singh R, et al. Vitamin D and bone mineral density status of healthy schoolchildren in northern India. Am J Clin Nutr 2005;82:477-82.
28. Ganong WF. Review of Medical Physiology. 22nd edition, New York, Mc Graw-Hill 2005;385-9.
29. Ahmed I, Atiq M, Iqbal J, Khurshid M, Whittaker P. Vitamin D deficiency rickets in breast-fed infants presenting with hypocalcaemic seizures. Acta Paediatr 1995;84:941-2.
30. Balasubramanian S, Shivbalan P. Saravana Kumar S. Hypocalcaemia due to vitamin D deficiency in exclusively breastfed infants. Indian Pediatric 2006;43:247-251.
31. Brunvald L, Henriken C, Haug E. Vitamin D deficiency among pregnant women in Pakistan. How best to prevent it? Tidsskr Nor Laegeforen 1996;116:1585-7.
32. Glerup H, Mikkelsen K, Poulsen L, Hass E, Overbeck S, Thomsen J, et al. Commonly recommended daily intake of vitamin D is not sufficient if sunlight exposure is limited. J Intern Med 2000;247:260-8.
33. Lawson M, Thomas M. Vitamin D concentrations in Asian children aged two years living in England: population survey. BMJ 1999;318:28.
34. Zeghoud F, Garabedian M, Jardel A, Bernard N, Melchior J. [Administration of a single dose of 100,000 IU of vitamin D3 in the pregnant woman in winter. The effect on blood calcium level of the newborn infant]. J Gynecol Obstet Biol Reprod (Paris) 1988;17(8):1099-105.
35. Finch PJ, Ang L, Eastwood JB, Maxwell JD. Clinical and histological spectrum of osteomalacia among Asians in south London. Q J Med 1992;83(302):439-48.
36. Johnson R. The New Vitamin D Debate, EatingWell.com, http://www.healthline.com/eatingwell/eth-the-new.vitamin-d-debate
37. Kuryowicz A, Bednarczuk T, Nauman J. The influence of vitamin D deficiency on cancers and autoimmune diseases development. Endokrynol Pol 2007;58(2):140-52.
38. Forman JP, Giovannucci E, Holmes MD, Bischoff-Ferrari HA, Tworoger SS, Willet WC, et al. Plasma 25-hydroxy vitamin D levels and risk of incident hypertension. Hypertension 2007;49:1063-9.
39. Richards JB, Valdes AM. Higher serum vitamin D concentrations are associated with longer leukocyte telomere length in women. Am J Clin Nutr 2007;85:1420-25.
40. Wilkins CH, Scheline YI, Roe CM, Birge SJ, Morris JC. Vitamin D deficiency is associated with low mood and worse cognitive performance in older adults. Am J Geriat Psychiat 2006;14(12):1032-40.
41. Berk M, Sanders KM, Pasco JA, Jacka FN, Williams LJ, Hayles AL, et al. Vitamin D deficiency may play a role in depression. Med Hypotheses 2007;69(6):1316-19.
42. Botella-Carretero JI, Alvarez-Blasco F, Villafruela JJ, Balsa JA, Vázquez C, Escobar-Morreale HF. Vitamin D deficiency is associated with the metabolic syndrome in morbid obesity. Clin Nutr 2007;26:573-80.
43. Wang TJ, Pencina MJ, Booth SL, Jacqwues PF, Ingelsson E, Lanier K, et al. Vitamin D deficiency and risk of cardiovascular disease. Circulation 2008; 29(117):503-11.
44. Maiya S, Allgrove J, Mok Q. Vitamin D deficiency and mortality and serious morbidity in infancy: time for action. Arch Dis Child 2006;91:A71.
45. Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, Institute of Medicine. Dietary reference intakes: calcium, phosphorus, magnesium, vitamin D and fluoride. Washington, D.C. National Academy Press, 1997.
46. Holick MF. Vitamin D-new horizons for the 21st century. McCollum Award Lecture. Am J Clin Nutr 1994;60:619-3.
47. Utiger RD. The need for more vitamin D. N Engl J Med 1998;338:828-9.
48. Binkley N, Novotny R, Krueger D, Kawahara T, Daida YG, Lensmeyer G, et al. Low vitamin D status despite abundant sun exposure. J Clin Endocr Metab 2007;92:2130-5.