WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES
SJIF Impact Factor 7.632
Volume 8, Issue 09, 1430-1438 Research Article ISSN 2278 – 4357

VITAMIN D3 AND CALCIUM RELATION: A MAJOR DILEMMA IN RECENT TIMES

Khaled Alhomsi*

Alsham Private University (ASPU), Damascus, Syria.

Article Received on
09 August 2019,

Revised on 29 August 2019,
Accepted on 19 Sept. 2019,

DOI: 10.20959/wjpps201909-14856

***Corresponding Author**
Khaled Alhomsi
Alsham Private University (ASPU), Damascus, Syria.
k.a.foph.LAT.aspu.edu.sy@outlook.com

ABSTRACT

Objective: This study was done to try to understand the correlation between Vitamin D3 and Calcium and to study how they affect each other. **Materials and Methods:** This is a cross sectional study of all patients who reviewed Alhomsi clinical laboratory to test for Vitamin D3 and Calcium levels based on the Physician evaluation and clinical presentation. This study was done on patients from July 2017 to October 2018. **Results:** At presentation, most of the patients' serum calcium values were in the low normal range. Vit D_3 values were deficient in most cases. After treatment with Vit D3 Most of the patients showed an improvement of vit D3 values from insufficient to sufficient. Most of the patients' serum calcium values reached the high normal range.

INTRODUCTION

Vitamin D insufficiency affects almost 50% of the population worldwide.[1] An estimated 1 billion people worldwide, across all ethnicities and age groups, have a vitamin D deficiency (VDD).[1,3] 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.[4] 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.[5] 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.[6] A meta-analysis

published in 2007 showed that vitamin D supplementation was associated with significantly reduced mortality.[7] Vitamin D receptor (VDR) is present in most tissues and cells in the body.[6,14] 1,25(OH)2D has a wide range of biological actions, such as inhibition of cellular proliferation and inducing terminal differentiation, inhibiting angiogenesis, stimulating insulin production, inhibiting renin production, and stimulating macrophage cathelicidin production.[6,14,16] The local production of 1,25(OH)2D may be responsible for regulating up to 200 genes[17] that may facilitate many of the pleiotropic health benefits that have been reported for vitamin D.[3,8,9,14] Children and young- and middle-aged adults are at equally high risk for VDD and insufficiency worldwide. VDD is common in Australia, the Middle East, India, Africa, and South America.[1,18,19] Pregnant and lactating women who take a prenatal vitamin and a calcium supplement with vitamin D remain at high risk for VDD.[20,22] The major source of vitamin D for children and adults is exposure to natural sunlight.[1,23,26] Thus, the major cause of VDD is inadequate exposure to sunlight.[23,27,29] Wearing a sunscreen with a sun protection factor of 30 reduces vitamin D synthesis in the skin by more than 95%.[30] People with a naturally dark skin tone have natural sun protection and require at least three to five times longer exposure to make the same amount of vitamin D as a person with a white skin tone.[31,32] There is an inverse association of serum 25(OH)D and body mass index (BMI) greater than 30 kg/m^2, and thus, obesity is associated with VDD.[33]

MATERIALS AND METHODS

This is a cross sectional study of all patients who reviewed AlHomsi Laboratory to test for Vitamin D3 and serum calcium levels based on the Physician evaluation and clinical presentation. This study was done on 450 patients from July 2017 to October 2018 whose tests included serum calcium and vit D3. It should be noted that all mentions for vitamin D3 lab values means 25 hydroxy vit D3, which is the substrate tested.

RESULTS

The mean age of patients in our study was 45 years old and most of the patients were females with 62% of all. In our laboratory, serum calcium normal range is 8.2-10.4 mg/dl and vitamin D3 levels are divided according the following: less than 19: Deficient vit D3, 20-29.9: Insufficient vit D3, 30-49.99: sufficient vit D3 and more than 50: Optimal (All in ng/ml) We divided the ranges to less than 8.2: low serum calcium, 8.2-8.99: low normal, 9-10.4: high normal and more than 10.4: high serum calcium. (All in mg/dl) Most of the patients' serum calcium values were in the low normal range with 77% (346 patients). 52 patients (11.5%)

www.wjpps.com Vol 8, Issue 10, 2019. Khaled World Journal of Pharmacy and Pharmaceutical Sciences were in the high normal range. 10.6% (48 patients) had low serum calcium levels, while only 4 patients (0.9%) had high serum calcium levels. (Table, Figure 1) Vit D3 values were insufficient in 31% of all patients, deficient in 56% which was the most common finding, sufficient were only found in 9% and optimal levels were the least common in only 4%. (Table, Figure 2) The patients continued with the doctors and were treated for their VDD according to their vit D3 and Serum calcium values and the clinical presentation. The patients were followed for three months and their lab tests showed the following changes after the treatment prescribed by physicians (Supplementary vit D3 of different doses). 68% showed an improvement of vit D3 values from insufficient to sufficient, 15% reached high sufficient and optimal vit D3 levels, while 17% did not show any changes in vit D3 levels. It is suspected that those who did not benefit from extra supplements and treatment were not taking the drugs as prescribed or had a medical condition affecting the process. Regarding serum calcium levels after 3 months of treatment, 80% of patients' serum calcium values reached the high normal range, while 20% had high serum calcium (more than 10.4 mg/dl). (Table, Figure 1, Figure 2)

Table: Levels of Ca and Vit D3 in our study.

At Presentation (Before Treatment)						**After Treatment**					
Ca Levels	N	%	Vit D3	N	%	Ca Levels	N	%	Vit D3	N	%
Low	48	10.6	Insufficient	140	31	Low	0	0	Insufficient	34	7.5
Low Normal	346	77	Deficient	252	56	Low Normal	0	0	Deficient	43	9.5
High Normal	52	11	Sufficient	40	9	High Normal	360	80	Sufficient	306	68
High	4	0.9	Optimal	18	4	High	90	20	Optimal	67	15

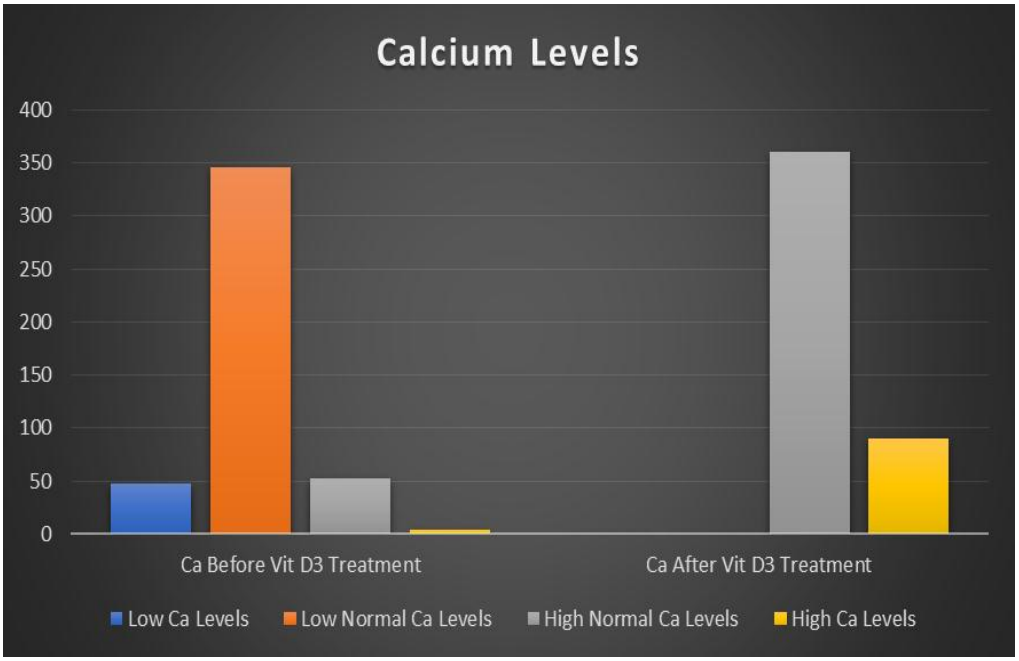

Figure 1: Serum calcium Levels before and after Vit D3 Treatment.

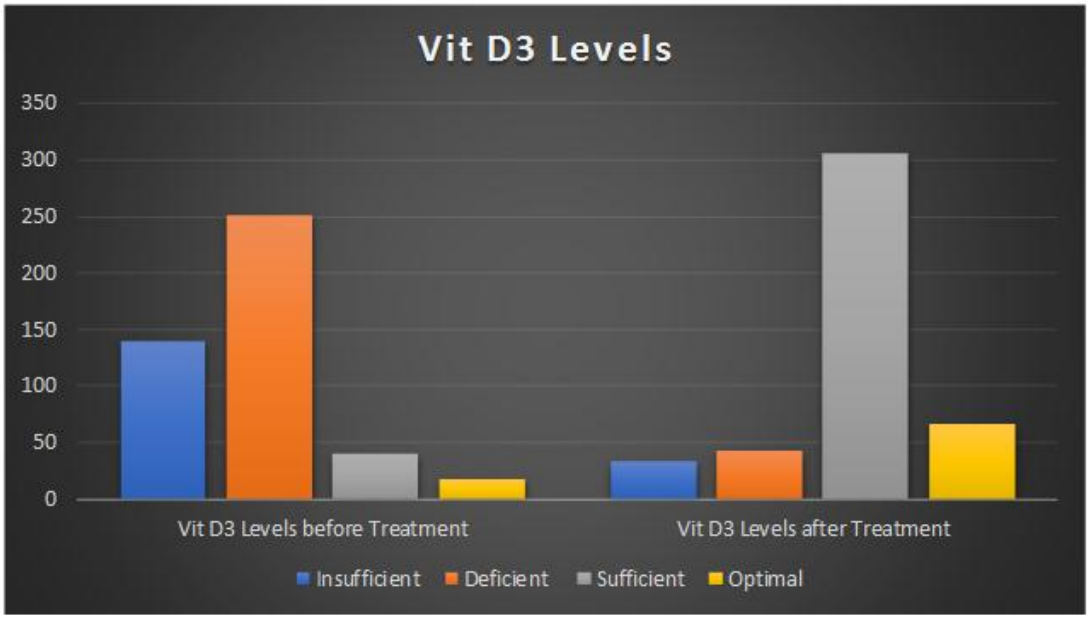

Figure 2: Vit D3 Levels before and after Vit D3 Treatment.

DISCUSSION

VDD results in abnormalities in calcium, phosphorus, and bone metabolism. VDD causes a decrease in the absorption of dietary calcium and phosphorus, resulting in an increase in PTH levels.[1,3,18,34] The PTH-mediated increase in osteoclastic activity creates local foci of bone weakness and causes a generalized decrease in bone mineral density (BMD), resulting in osteopenia and osteoporosis. An inadequate calcium–phosphorus product causes a mineralization defect in the skeleton.[1,35] In young children who have little mineral in their

skeleton, this defect results in a variety of skeletal deformities classically known as rickets.[36,37] VDD also causes muscle weakness; affected children have difficulty in standing and walking,[37,38] whereas the elderly have increasing sway and more frequent falls,[39,40] thereby increasing their risk of fractures. Obtaining sufficient vitamin D from natural food sources alone is difficult. Consumption of vitamin D-fortified foods and exposure to some sunlight are essential for maintaining a healthy vitamin D status. Dietary supplements might be required to meet the daily need for vitamin D in some group of people.[41] Vitamin D decreases cell proliferation and increases cell differentiation, stops the growth of new blood vessels, and has significant anti-inflammatory effects.[42,43] Many studies have suggested a link between low vitamin D levels and an increased risk of cancer, with the strongest evidence for colorectal cancer. In the Health Professionals Follow-up Study (HPFS), subjects with high vitamin D concentrations were half as likely to be diagnosed with colon cancer as those with low concentrations.[42] A definitive conclusion cannot yet be made about the association between vitamin D concentration and cancer risk, but results from many studies are promising. There is some evidence linking higher vitamin D intake to a lower risk for breast cancer.[43] The effect of menopausal status on this association is still unclear. The recommend screening for VDD in individuals at risk for deficiency and not for patients who are not at risk. Serum circulating 25-hydroxyvitamin D [25(OH) D] level should be measured to evaluate vitamin D status in patients who are at risk for VDD. VDD is defined as a 25(OH) D3 below 20 ng/mL (50 nmol/L).[44]

CONCLUSION

This study is to focus on the correlation between Serum calcium levels and Vitamin D_3 and the effect they cast on each other. In our country and as shown in this study, VDD is very common and is considered a major health issue especially for older patients because it has a major effect on osteoporosis and increased fractures. The results we found demonstrates the need for a bigger study and on a wider scale to further understand how vit D_3 and Serum calcium are related and the effect of PTH and different diseases on them.

REFERENCES

1. Holick MF. Vitamin D deficiency. N Engl J Med, 2007; 357: 266–81. [PubMed] [Google Scholar]

2. Gordon CM, DePeter KC, Feldman HA, Grace E, Emans SJ. Prevalence of vitamin D deficiency among healthy adolescents. Arch Pediatr Adolesc Med, 2004; 158: 531–7. [PubMed] [Google Scholar]
3. Lips P, Hosking D, Lippuner K, Norquist JM, Wehren L, Maalouf G, et al. The prevalence of vitamin D inadequacy amongst women with osteoporosis: An international epidemiological investigation. J Intern Med, 2006; 260: 245–54. [PubMed] [Google Scholar]
4. Rostand SG. Ultraviolet light may contribute to geographic and racial blood pressure differences. Hypertension, 1997; 30: 150–6. [PubMed] [Google Scholar]
5. Melamed ML, Michos ED, Post W, Astor B. 25-hydroxyvitamin D levels and the risk of mortality in the general population. Arch Intern Med, 2008; 168: 1629–37. [PMC free article] [PubMed] [Google Scholar]
6. Harvard School of Public Health Nutrition Source. Vitamin D and health. [Last accessed on 2010 Aug 30]. Available from: http://www.hsph.harvard.edu/nutritionsource/what-shouldyou-eat/vitamin-d/index.html .
7. Autier P, Gandini S. Vitamin D supplementation and total mortality: A meta-analysis of randomized controlled trials. Arch Intern Med, 2007; 167: 1730–7. [PubMed] [Google Scholar]
8. Standing Committee on the Scientific Evaluation of Dietary Reference Intakes Food and Nutrition Board, Institute of Medicine. Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. Chapter 7. Vitamin D. [Last accessed on 2010 Aug 02]. Available from:http://www.nal.usda.gov/fnic/DRI//DRI_Calcium/250–287.pdf .
9. NIH Office of Dietary Supplements. Dietary supplement fact sheet: Vitamin D. [Last accessed on Aug 04, 2010]. http://ods.od.nih.gov/factsheets/vitamind.asp .
10. Nair S. Symptoms of low vitamin D levels. [Last accessed on Sep 02, 2010]. Available from:http://www.buzzle.com/articles/symptoms-of-low-vitamin-d-levels.html .
11. MedlinePlus. 25-hydroxy vitamin D test. [Last accessed on Aug 04, 2010]. Available from:http://www.nlm.nih.gov/medlineplus/ency/article/003569.htm .
12. Moyad MA. Vitamin D: A rapid review: Side effects and toxicity. [Last accessed on Sep 02, 2010]. Available from: http://www.medscape.com/viewarticle/589256_10 .
13. Lappe JM, Travers-Gustafson D, Davies KM, Recker RR, Heaney RP. Vitamin D and calcium supplementation reduces cancer risk: Results of a randomized trial. Am J Clin Nutr, 2007; 85: 1586–91.[PubMed] [Google Scholar]

14. Chlebowski RT, Johnson KC, Kooperberg C, Pettinger M, Wactawski-Wende J, Rohan T, et al. J Natl Cancer Inst, 2008; 100: 1581–91. [PMC free article] [PubMed] [Google Scholar]
15. Stolzenberg-Solomon RZ, Vieth R, Azad A, Pietinen P, Taylor PR, Virtamo J, et al. A prospective nested case-control study of vitamin D status and pancreatic cancer risk in male smokers. Cancer Res, 2006; 66: 10213–9. [PubMed] [Google Scholar]
16. Stolzenberg-Solomon RZ, Hayes RB, Horst RL, Anderson KE, Hollis BW, Silverman DT. Serum vitamin D and risk of pancreatic cancer in the Prostate, Lung, Colorectal, and Ovarian Screening Trial. Cancer Res, 2009; 69: 1439–47. [PMC free article] [PubMed] [Google Scholar]
17. 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: 503–11. [PMC free article] [PubMed] [Google Scholar]
18. Marwaha RK, Tandon N, Reddy DR, Aggarwal R, Singh R, Sawhney RC, et al. Vitamin D and bone mineral density status of healthy schoolchildren in northern India. Am J Clin Nutr, 2005; 82: 477–82.[PubMed] [Google Scholar]
19. Thacher TD, Fischer PR, Strand MA, Pettifor JM. Nutritional rickets around the world: Causes and future directions. Ann Trop Paediatr, 2006; 26: 1–16. [PubMed] [Google Scholar]
20. Hollis BW, Wagner CL. Vitamin D requirements during lactation: High-dose maternal supplementation as therapy to prevent hypovitaminosis D for both the mother and the nursing infant. Am J Clin Nutr, 2004; 80: 1752S–8S. [PubMed] [Google Scholar]
21. Lee JM, Smith JR, Philipp BL, Chen TC, Mathieu J, Holick MF. Vitamin D deficiency in a healthy group of mothers and newborn infants. Clin Pediatr (Phila), 2007; 46: 42–4. [PubMed] [Google Scholar]
22. Bodnar LM, Simhan HN, Powers RW, Frank MP, Cooperstein E, Roberts JM. High prevalence of vitamin D insufficiency in black and white pregnant women residing in the northern United States and their neonates. J Nutr, 2007; 137: 447–52. [PMC free article] [PubMed] [Google Scholar]
23. Moan J, Porojnicu AC, Dahlback A, Setlow RB. Addressing the health benefits and risks, involving vitamin D or skin cancer, of increased sun exposure. Proc Natl Acad Sci USA, 2008; 105: 668–73.[PMC free article] [PubMed] [Google Scholar]

24. Hollis BW. Circulating 25-hydroxyvitaminDlevels indicative of vitamin D sufficiency: Implications for establishing a new effective dietary intake recommendation for vitamin D. J Nutr, 2005; 135: 317–22.[PubMed] [Google Scholar]
25. Maeda SS, Kunii IS, Hayashi L, Lazaretti-Castro M. The effect of sun exposure on 25-hydroxyvitamin D concentrations in young healthy subjects living in the city of Sao Paulo, Brazil. Braz J Med Biol Res, 2007; 40: 1653–9. [PubMed] [Google Scholar]
26. Brot C, Vestergaard P, Kolthoff N, Gram J, Hermann AP, Sorensen OH. Vitamin D status and its adequacy in healthy Danish peri-menopausal women: Relationships to dietary intake, sun exposure and serum parathyroid hormone. Br J Nutr, 2001; 86(Suppl 1): S97–103. [PubMed] [Google Scholar]
27. Holick MF, Chen TC. Vitamin D deficiency: A worldwide problem with health consequences. Am J Clin Nutr, 2008; 87: 1080S–6S. [PubMed] [Google Scholar]
28. Holick MF, Chen TC, Sauter ER. Vitamin D and skin physiology: A D-lightful story. J Bone Miner Res, 2007; 22(Suppl 2): V28–33. [PubMed] [Google Scholar]
29. Looker AC, Pfeiffer CM, Lacher DA, Schleicher RL, Picciano MF, Yetley EA. Serum 25-hydroxyvitaminDstatus of the US population: 1988–1994 compared to 2000–2004. Am J Clin Nutr, 2008; 88: 1519–27. [PMC free article] [PubMed] [Google Scholar]
30. Matsuoka LY, Ide L, Wortsman J, MacLaughlin JA, Holick MF. Sunscreens suppress cutaneous vitamin D3 synthesis. J Clin Endocrinol Metab, 1987; 64: 1165–8. [PubMed] [Google Scholar]
31. Clemens TL, Henderson SL, Adams JS, Holick MF. Increased skin pigment reduces the capacity of skin to synthesise vitamin D3. Lancet, 1982; 1: 74–6. [PubMed] [Google Scholar]
32. Hintzpeter B, Scheidt-Nave C, Müller MJ, Schenk L, Mensink GB. Higher prevalence of vitamin D deficiency is associated with immigrant background among children and adolescents in Germany. J Nutr, 2008; 138: 1482–90. [PubMed] [Google Scholar]
33. Wortsman J, Matsuoka LY, Chen TC, Lu Z, Holick MF. Decreased bioavailability of vitamin D in obesity. Am J Clin Nutr, 2000; 72: 690–3. [PubMed] [Google Scholar]
34. Holick MF, Siris ES, Binkley N, Beard MK, Khan A, Katzer JT, et al. Prevalence of vitamin D inadequacy among postmenopausal North American women receiving osteoporosis therapy. J Clin Endocrinol Metab, 2005; 90: 3215–24. [PubMed] [Google Scholar]

35. Aaron JE, Gallagher JC, Anderson J, Stasiak L, Longton EB, Nordin BE, et al. Frequency of osteomalacia and osteoporosis in fractures of the proximal femur. Lancet, 1974; 1: 229–33. [PubMed] [Google Scholar]
36. Holick MF. High prevalence of vitamin D inadequacy and implications for health. Mayo Clin Proc, 2006; 81: 353–73. [PubMed] [Google Scholar]
37. Gordon CM, Williams AL, Feldman HA, May J, Sinclair L, Vasquez A, et al. Treatment of hypovitaminosis D in infants and toddlers. J Clin Endocrinol Metab, 2008; 93: 2716–21. [PMC free article][PubMed] [Google Scholar]
38. Holick MF. Resurrection of vitamin D deficiency and rickets. J Clin Invest, 2006; 116: 2062–72.[PMC free article] [PubMed] [Google Scholar]
39. 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. JAMA, 2005; 293: 2257–64. [PubMed] [Google Scholar]
40. Bischoff-Ferrari HA, Dawson-Hughes B, Staehelin HB, Orav JE, Stuck AE, Theiler R, et al. Fall prevention with supplemental and active forms of vitamin D: A meta-analysis of randomised controlled trials. BMJ, 2009; 339: b3692. [PMC free article] [PubMed] [Google Scholar]
41. Dietary Supplement Fact Sheet: Vitamin D. Office of Dietary Supplements, National Institutes of Health, Jun 24, 2011. [Google Scholar]
42. Ahn J, Peters U, Albanes D, Purdue MP, Abnet CC, Chatterjee N, et al. Serum vitamin D concentration and prostate cancer risk: A nested case-control study. J Natl Cancer Inst, 2008; 100: 796–804.[PMC free article] [PubMed] [Google Scholar]
43. Anderson LN, Cotterchio M, Vieth R, Knight JA. Vitamin D and calcium intakes and breast cancer risk in pre- and postmenopausal women. Am J Clin Nutr, 2010; 91: 1699–707. [PubMed] [Google Scholar]
44. Holick MF, Binkley NC, Heike A, Bischoff-Ferrari, Gordon CM, Hanley DA, et al. Evaluation, Treatment, and Prevention of Vitamin D Deficiency: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab, 2011; 96: 1911–30. [PubMed] [Google Scholar]