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Vitamin D Deficiency: Beyond Sunshine!

In the current issue of the *Journal*, Beshyah *et al*. review the literature on vitamin D deficiency (VDD) in the United Arab Emirates (UAE) and demonstrate that local and expatriate population have generally low serum 25-hydroxyvitamin D (25OHD) levels.[1] The article is a narrative non-systematic review of the literature on the epidemiological and clinical aspects of vitamin D status in the UAE. It mainly focuses on epidemiology, disease burden and impact of culture and lifestyle factors among UAE population on vitamin D status. The article also emphasizes how levels of vitamin D may affect pregnancy, neonates and children. The article briefly describes the different clinical management guidelines, interventional trials and clinical practices currently used for VDD.

VDD is a widely recognized health problem among the UAE population and may have serious skeletal and non-skeletal health implications. The medical literature from the Middle East and North Africa region also shows that approximately 50% of the studied populations have moderately severe VDD with 25OHD levels below 25 nmol/L.[2,3] Such low levels can result in rickets and osteomalacia. Studies also show that moderately severe VDD is common in pregnant women and their infants in the UAE as well as many Arab and Asian countries, especially in exclusively breast-fed infants.[4-6] VDD is mainly attributed to low vitamin D intake and insufficient sunlight exposure, mainly due to the hot climate and conservative dress style especially in dark-skinned individuals.[7,8] Although genetic variants in key proteins of vitamin D metabolism including cholesterol synthesis, 25 hydroxylation, vitamin D transport and vitamin D receptor polymorphisms have been shown to be associated with significantly lower vitamin D levels, the median 25OHD levels remain low irrespective of the genetic variant (25OHD of 26-30 nmol/L vs. 36 nmol/L) and doesn't explain the high prevalence of moderately severe VDD in the Arab world.[9]

Measures to prevent vitamin D deficiency include increased skin exposure to sunlight, increased fortification of food items with vitamin D, and vitamin D supplementation. Vitamin D fortification of food in the UAE and many other Arab countries is not mandatory or well-regulated to meet the international standard.[7] Vitamin D supplementation currently remains the most appropriate mode for improving vitamin D status in this high-risk population.

Recent studies however have cast doubt on the benefits of routine vitamin D supplements on skeletal and non-skeletal health. The clear exception to this is for the prevention or treatment of rickets and osteomalacia, which can occur after a prolonged lack of exposure to sunshine that leads to 25OHD concentrations lower than 25 nmol/L.[10] In VITAL (Vitamin D and Omega-3 Trial), researchers randomized nearly 26,000 middle-aged and older adults with no history of cardiovascular (CV) disease, cancer, or other serious disorders to receive vitamin D3 (2000 IU daily) or placebo. Mean serum 25OHD level increased in vitamin D3 recipients only. During median follow-up of 5 years, major adverse CV events and invasive cancer occurred with equal frequencies in the two groups.[11] The effect of vitamin D supplementation on incident bone fractures has not yet been reported. In a recent metanalysis, vitamin D supplementation alone was not associated with all-cause mortality in adults compared with placebo or no treatment. Vitamin D supplementation reduced the risk of cancer death however by 16%.[12] In the bone ancillary study of VITAL trial, daily supplementation with vitamin D3 2000 IU vs. placebo didn't increase areal bone mineral density (aBMD) or reduce bone loss at the spine, femoral neck total hip, or whole body.[13] Although most of the subjects had normal vitamin D levels at baseline there were no differences in the changes in BMD in the group with baseline vitamin D levels below 30nmol/L. Admittedly the study was not designed to test the benefits in those who were vitamin d deficient. It was interesting however that among participants with baseline free 25OHD levels below the median (5.7 pg/ml) vitamin D3 supplementation had a slight benefit on spine and total hip aBMD respectively, $P = 0.04$. Whether baseline free vitamin D levels help to identify those more likely to benefit from supplementation warrants further study.[13] Free 25OHD measurement may prove useful when there is alteration of vitamin D binding proteins such as pregnancy, cirrhosis, acute illness, hypoalbuminemia, sex hormone use, or genetic polymorphisms.[14]

It is noteworthy that most of the above studies showing lack of benefit of vitamin D supplementation were conducted in subjects who were vitamin D sufficient at baseline, emphasizing the need to do more research in our population. There may be a threshold effect in which a certain amount of vitamin D benefits bone, but at higher levels there is no further benefit to nutrient supplementation.[15] It remains therefore reasonable to consider vitamin D supplementation (800-1000 IU/day or more) for patients with VDD, and those at increased risk for osteoporosis and falls.[16] This is consistent with recommendations of the Endocrine Society and National Osteoporosis Foundation.

Hussein F. Saadi, Juma M. Alkaabi[1]

Medical Subspecialties Institute, Cleveland Clinic Abu Dhabi, [1]Department of Medicine, College of Medicine and Health Sciences Al Ain United Arab Emirates University, Abu Dhabi, United Arab Emirates

Address for correspondence: Prof. Hussein F. Saadi, Medical Subspecialties Institute, Cleveland Clinic Abu Dhabi, Abu Dhabi, United Arab Emirates.
E-mail: SaadiH@ClevelandClinicAbuDhabi.ae

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References

1. Beshyah SA, Hafidh K, Abdelmannan DK, Jabbar A, Wafa WS, Khalil AB. Paradoxical Vitamin D deficiency in a sunny country: A narrative review of the literature from the United Arab Emirates (1992–2018). Ibnosina J Med Biomed Sci 2019;11(3):97-109.
2. Arabi A, El Rassi R, El-Hajj Fuleihan G. Hypovitaminosis D in developing countries-prevalence, risk factors and outcomes. Nat Rev Endocrinol. 2010 Oct; 6:550-61.
3. Ardawi MS[1], Sibiany AM, Bakhsh TM, Qari MH, Maimani AA. High prevalence of vitamin D deficiency among healthy Saudi Arabian men: Relationship to bone mineral density, parathyroid hormone, bone turnover markers, and lifestyle factors. Osteoporosis International 2012; 23:675-86.
4. Dawodu A, Saadi HF, Bekdache G, Javed Y, Altaye M, Hollis BW. Randomized controlled trial (RCT) of vitamin D supplementation in pregnancy in a population with endemic vitamin D deficiency. J Clin Endocrinol Metab 2013;98(6):2337-46.
5. Saadi HF, Dawodu A, Afandi B, Zayed R, Benedict S, Nagelkerke N, *et al*. Effect of combined maternal and infant vitamin D supplementation on vitamin D status of exclusively breastfed infants. Matern Child Nutr 2009;5(1):25-32.
6. Dawodu A, Agarwal M, Moshaddeque H, Kochiyil J, Zayed R. Hypovitaminosis D and vitamin D deficiency in exclusively breast-feeding infants and their mothers in summer: A justification for vitamin D supplementation of breast-feeding infants. The Journal of Pediatrics 2003;142:169-73.
7. Saadi HF, Nagelkerke N, Benedict S, Qazaq HS, Zilahi E, Mohamadiyeh MK, *et al*. Predictors and relationships of serum 25 hydroxyvitamin D concentration with bone turnover markers, bone mineral density, and vitamin D receptor genotype in Emirati women. Bone. 2006;39(5):1136-43.
8. Al-Daghri NM, Al-Saleh Y, Khan N, Sabico S, Aljohani N, Alfawaz H, Alsulaimani M, Al-Othman AM, Alokail MS. Sun exposure, skin color and vitamin D status in Arab children and adults. J Steroid Biochem Mol Biol 2016;164:235-8.
9. Elkum N, Alkayal F, Noronha F, Ali MM, Melhem M, *et al*. Vitamin D Insufficiency in Arabs and South Asians Positively Associates with Polymorphisms in GC and CYP2R1 Genes. PLoS ONE 2014;9(11):e113102.
10. Bolland MJ, Grey A, Avenell A. Effects of vitamin D supplementation on musculoskeletal health: A systematic review, meta-analysis, and trial sequential analysis. Lancet Diabetes Endocrinol 2018;6(11):847-58.
11. Manson JE, Cook NR, Lee IM, Christen W, Bassuk SS, Mora S, *et al*. VITAL Research Group. Vitamin D Supplements and Prevention of Cancer and Cardiovascular Disease. N Engl J Med 2019;380(1):33-44.
12. Zhang Y, Fang F, Tang J, Jia L, Feng Y, Xu P, Faramand A. Association between vitamin D supplementation and mortality: Systematic review and meta-analysis. BMJ 2019;366:l4673.
13. LeBoff M, Chou S, Murata E, Cook N, Mora S, Lee I-M, *et al*. Vitamin D and omega-3 trial (VITAL): Effects of vitamin D on bone density, turnover, and structure. American Society for Bone and Mineral Research 2019; Abstract 1046.
14. Aloia J, Dhaliwal R, Mikhail M, Shieh A, Stolberg A, Ragolia L, Fazzari M, Abrams SA. Free 25(OH)D and Calcium Absorption, PTH, and Markers of Bone Turnover. J Clin Endocrinol Metab. 2015;100(11):4140-5.
15. Heaney RP. Toward a physiological referent for the vitamin D requirement. J Endocrinol Invest 2014;37:1127-30.
16. Bischoff-Ferrari HA, Bhasin S, Manson JE. Preventing Fractures and Falls: A Limited Role for Calcium and Vitamin D Supplements? JAMA 2018;319(15):1552-3.

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