

## VITAMIN D; AN EVIDENCE-BASED MEDICINE

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Vitamin D (25-dihydroxy Vitamin D [25(OH)D]) is both a nutrient and hormone which provides a wide variety of health benefits to human health; hence, makes it unique. Vitamin D deficiency prevails all over Indian subcontinent including both urban and rural population with a prevalence rate 70-100% in general Indian population [1]. Vitamin D deficiency leads to rickets, osteomalacia, and osteoporosis. Vitamin D also plays an important role in cardiovascular diseases, diabetes, cancer, and infectious disease such as tuberculosis.

The health benefits of Vitamin D are beyond bone metabolism confirmed from various studies. Vitamin D not only regulate calcium metabolism but also regulates insulin production, reduces the risk of diabetes and cancer, rennin production, helps in the destruction of infectious agents, regulates cell growth, enhances immunity, maintenance of vascular tone of the body, myocardial function and helps in many more complex diseases [2]. Recently, Vitamin D has received enormous attention worldwide and referred as the drug of the decade.

The advocacy for Vitamin D supplementation would not have been done only for populations who are at risk for developing Vitamin D deficiency; sensible sun exposure is an inexpensive and enjoyable way to maintain Vitamin D stores. Unfortunately, it seems a paradox where the majority of the population is Vitamin D deficient living in the sunny country. Reasons to this problem are many including higher melanin content, environmental (latitude and altitude), clothing pattern, food habits, and genetic factors [3].

Although, randomized controlled trials provide some low-quality evidence to support Vitamin D supplementation for the reduction of asthma exacerbations in children is either limited or inconclusive with limitations such as high degree of clinical diversity (interventions and outcomes) and methodological heterogeneity (sample size and risk of bias) in included trials are challenges [4]. Results of recent trials assessing the effect of Vitamin D supplementation on the prevention of childhood acute respiratory infections have been also inconsistent [5] and have no beneficial effect of Vitamin D in improving insulin resistance was identified as well Poolsup *et al.* [6]. In addition, Vitamin D supplementation (1400 IU/week) to low birth weight infants did not decrease the incidence of severe morbidity and mortality [7].

On the other hand, results of various studies support the Vitamin D supplementation including improvement in handgrip strength [8] increased newborn's length [9] reduces the risk of maternal co-morbidities and helps improve neonatal outcomes [10]. Vitamin D requirements are probably greater in pregnancy, as evidenced by physiologically higher 1, 25(OH)D levels seen in the second and third trimesters. Studies recommended that Vitamin D should continue to supplement in all pregnant women from the 12<sup>th</sup> week of gestation onwards [11].

Whether Vitamin D supplementation in pre-diabetes subjects prevents the development of diabetes is a matter of debate, and the results are inconsistent from available studies. Short-term Vitamin D

supplementation was found helpful in the decline of residual beta cell function in children with type 1 diabetes [12]. A study in subjects with pre-diabetes evaluated the effect of 12 months of Vitamin D supplementation on glycemic parameters and progression of pre-diabetes to diabetes in an ethnically homogeneous Kashmiri population, found that Vitamin D supplementation helps significantly in lowering fasting plasma glucose, 2 hrs plasma glucose, and A1C levels [13]. On the other hand, Vitamin D supplementation (200 IU/day) did not affect plasma C-reactive protein and whole blood cytokine production of low birth weight infants [14]. Study on healthy subjects also shown the beneficial effect that was supplemented with cholecalciferol at a dose of 60,000IU/week for 12weeks resulted in improvement in the skeletal muscle energy metabolism [15].

An oral dose of Vitamin D can be easily distributed among populations. However, 1000 IU of Vitamin D/day has shown better results than 60,000 IU/week in populations, but it will be difficult to feed 1000 IU/day to populations due to logistics issues. So, 60,000 IU/week up to 8 weeks then once a month may be chosen as a dose schedule in populations [16]. Moreover, the usual calcium pill contains 200 IU of Vitamin D and 2 pills a day equals 400 IU/day which is grossly inadequate. To achieve optimal serum 25(OH)D levels, i.e., 30 ng/ml in population; 2000 IU of Vitamin D/day is required [17], and thus at present, it may be safest to adhere to 2000 IU/day as a standard practice in India. Indian studies regarding Vitamin D supplementation including pregnant women [18], Young women [19], and Asian Indians [20] already shown a beneficial effect.

Studies in animal models show plausible evidence in favor of Vitamin D as an anti-inflammatory agent and a viable option for treatment of anti-inflammatory disease, i.e., Crohn's disease (CD). Epidemiological and cross-sectional studies indicate that Vitamin D may have a potential of treating CD in humans [21]. Recent findings from various studies provide evidence of a possible beneficial effect of Vitamin D supplementation in patients with early Parkinson's disease [22], respiratory tract infections [23] chronic heart disease [24] and also helps in strengthening femoral neck in a dose-dependent manner, especially in women [25]. In a recent study, we have shown improvement in bone health after Vitamin D supplementation in patients with hyperthyroidism [26].

Hence, we propose that Vitamin D may be used as evidence-based medicine in clinical practice. This will also helpful in mitigating the growing burden of communicable and non-communicable diseases in India.

### REFERENCES

1. Ritu G, Gupta A. Vitamin D deficiency in India: Prevalence, causalities and interventions. *Nutrients* 2014;6(2):729-75.
2. Hossein-nezhad A, Holick MF. Vitamin D for health: A global perspective. *Mayo Clin Proc* 2013;88(7):720-55.
3. Mithal A, Wahl DA, Bonjour JP, Burckhardt P, Dawson-Hughes B,

- Eisman JA, *et al.* Global vitamin D status and determinants of hypovitaminosis D. *Osteoporos Int* 2009;20(11):1807-20.
4. Riverin BD, Maguire JL, Li P. Vitamin D supplementation for childhood asthma: A systematic review and meta-analysis. *PLoS One* 2015;10(8):e0136841.
  5. Xiao L, Xing C, Yang Z, Xu S, Wang M, Du H, *et al.* Vitamin D supplementation on insulin resistance and glycaemic control in prediabetes: A systematic review and meta-analysis. *Diabet Med* 2016;33(3):290-9.
  6. Poolsup N, Suksomboon N, Plordplong N. Effect of Vitamin D supplementation on insulin resistance and glycaemic control in prediabetes: A systematic review and meta-analysis. *Diabet Med* 2016;33(3):290-9.
  7. Kumar GT, Sachdev HS, Chellani H, Rehman AM, Singh V, Arora H, *et al.* Effect of weekly vitamin D supplements on mortality, morbidity, and growth of low birthweight term infants in India up to age 6 months: Randomised controlled trial. *BMJ* 2011;342:d2975.
  8. Cavalcante R, Maia J, Mesquita P, Henrique R, Griz L, Bandeira MP, *et al.* The effects of intermittent vitamin D3 supplementation on muscle strength and metabolic parameters in postmenopausal women with type 2 diabetes: A randomized controlled study. *Ther Adv Endocrinol Metab* 2015;6(4):149-54.
  9. Asemi Z, Esmailzadeh A. The effect of multi mineral-Vitamin D supplementation on pregnancy outcomes in pregnant women at risk for pre-eclampsia. *Int J Prev Med* 2015;6:62.
  10. Sablok A, Batra A, Thariani K, Batra A, Bharti R, Aggarwal AR, *et al.* Supplementation of vitamin D in pregnancy and its correlation with foeto-maternal outcome. *Clin Endocrinol (Oxf)* 2015;83(4):536-41.
  11. Mithal A, Kalra S. Vitamin D supplementation in pregnancy. *Indian J Endocrinol Metab* 2014;18(5):593-6.
  12. Mishra A, Dayal D, Sachdeva N, Attri SV. Effect of 6-months' C Vitamin D supplementation on residual beta cell function in children with type 1 diabetes: A case control interventional study. *J Pediatr Endocrinol Metab* 2015.
  13. Kuchay MS, Laway BA, Bashir MI, Wani AI, Misgar RA, Shah ZA. Effect of Vitamin D supplementation on glycemic parameters and progression of prediabetes to diabetes: A 1-year, open-label randomized study. *Indian J Endocrinol Metab* 2015;19(3):387-92.
  14. Trilok-Kumar G, Arora H, Rajput M, Chellani H, Singh V, Raynes J, *et al.* Effect of vitamin D supplementation of low birth weight term Indian infants from birth on cytokine production at 6 months. *Eur J Clin Nutr* 2012;66(6):746-50.
  15. Rana P, Marwaha RK, Kumar P, Narang A, Devi MM, Tripathi RP, *et al.* Effect of vitamin D supplementation on muscle energy phospho-metabolites: A <sup>31</sup>P magnetic resonance spectroscopy-based pilot study. *Endocr Res* 2014;39(4):152-6.
  16. Haines ST, Park SK. Vitamin D supplementation: What's known, what to do, and what's needed. *Pharmacotherapy* 2012;32(4):354-82.
  17. Aloia JF. African Americans, 25-hydroxyvitamin D, and osteoporosis: A paradox. *Am J Clin Nutr* 2008;88(2):545S-50.
  18. Sahu M, Das V, Aggarwal A, Rawat V, Saxena P, Bhatia V. Vitamin D replacement in pregnant women in rural north India: A pilot study. *Eur J Clin Nutr* 2009;63(9):1157-9.
  19. Malhotra N, Mithal A, Gupta S, Shukla M, Godbole M. Effect of vitamin D supplementation on bone health parameters of healthy young Indian women. *Arch Osteoporos* 2009;4(1-2):47-53.
  20. Goswami R, Gupta N, Ray D, Singh N, Tomar N. Pattern of 25-hydroxy vitamin D response at short (2 month) and long (1 year) interval after 8 weeks of oral supplementation with cholecalciferol in Asian Indians with chronic hypovitaminosis D. *Br J Nutr* 2008;100(3):526-9.
  21. O'Sullivan M. Is vitamin D supplementation a viable treatment for Crohn's disease? *Expert Rev Gastroenterol Hepatol* 2016;10(1):1-4.
  22. Yoon JH, Park DK, Yong SW, Hong JM. Vitamin D deficiency and its relationship with endothelial dysfunction in patients with early Parkinson's disease. *J Neural Transm (Vienna)* 2015;122(12):1685-91.
  23. Ali SR, McDevitt H. Question 1: Does vitamin D supplementation prevent acute lower respiratory tract infections in children? *Arch Dis Child* 2015;100(9):892-5.
  24. Heidari B, Nargesi AA, Hafezi-Nejad N, Sheikhbahaei S, Pajouhi A, Nakhjavani M, *et al.* Assessment of serum 25-hydroxy Vitamin D improves coronary heart disease risk stratification in patients with type 2 diabetes. *Am Heart J* 2015;170(3):573-9.e5.
  25. Kim H, Lee SH, Kim J, Lim KH, Ahn SH, Kim BJ, *et al.* The association of Vitamin D With femoral neck strength: An additional evidence of vitamin D on bone health. *J Clin Endocrinol Metab* 2015;100(8):3118-25.
  26. Dixit V, Singh V, Marwaha RK, Dhanwal DK. Vitamin D supplementation improves bone mineral density in patients with hyperthyroidism. *J Adv Res Med* 2015;2(2):16-22.