PREVALENCE OF VITAMIN D DEFICIENCY IN A POPULATION OF INDIAN WOMEN- A CALL FOR UNIVERSAL SUPPLEMENTATION?

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ABSTRACT

BACKGROUND

With improvement in serum vitamin D testing, there emerged an understanding that Vitamin D Deficiency (VDD) exists in sunny regions of the world where it was once thought to be a rare occurrence. In addition, new understanding on the deleterious effects of VDD on health has also grown over the last several years to include not only skeletal disorders, but cardiovascular disease, diabetes, cancer, infectious and autoimmune diseases.

The aim of the study was to examine the prevalence of Vitamin D Deficiency (VDD) among pregnant and non-pregnant women at a Multispecialty Hospital in Bengaluru, India.

MATERIALS AND METHODS

This is a retrospective chart review study. Charts belonging to all women who presented to Divakars Speciality Hospital from October 1, 2015, to November 1, 2016, were selected for initial review. Charts for all non-pregnant women who presented for a routine annual checkup and pregnant women in their 12th week of pregnancy were reviewed. All charts selected included serum 25 (OH) D levels that were obtained as part of routine care services. Charts of 213 pregnant women and 370 nonpregnant were reviewed. Serum 25 (OH) D levels for each patient were collected and entered into a Microsoft® Excel spreadsheet for analysis by physician researchers along with information regarding patient's age, employment status and education level. Serum 25 (OH) D level of 20.0 to <30.0 ng/mL was classified as vitamin D insufficiency and levels <20 ng/mL were classified as being vitamin D deficient. Data were compiled as percentages and means across population characteristics. Pearson's correlations were calculated to assess the correlation between 25 (OH) D levels and population parameters. A P value of <0.05 was considered statistically significant.

RESULTS

The mean age of the pregnant women and non-pregnant women was 29 and 43, respectively. Mean serum vitamin D level of pregnant women and non-pregnant women was 15.1 and 19.4, respectively. Ninety seven percent of pregnant women and 86% of non-pregnant women were vitamin deficient or insufficient. Vitamin D levels were not correlated to income or education in either pregnant women or non-pregnant women. Vitamin D levels were not correlated to age in pregnant women, but a correlation was found in non-pregnant women (r=0.223747; P=0.000014).

CONCLUSION

This study joins a significant number of previous studies in providing evidence of widespread VDD in south Asian populations. It underscores the need for vitamin D supplementation and fortification guidelines in India, especially considering the deleterious health effects of VDD.

KEYWORDS

Vitamin D Deficiency, India, Pregnant Women, Women, Income, Age, Education Level.

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BACKGROUND

The existence of vitamin D was deduced in 1922.¹ However, it was not until the 1930s that vitamin D was isolated and characterised.^{2,3} It was at this time that its role in the regulation of calcium and phosphate and thereby growth and bone development were being explored.⁴⁻⁶ For several decades, the focus of investigations into vitamin D's role in the body was that of growth and bone health. The prevailing wisdom during this time and up through the 1970s was that Vitamin D Deficiency (VDD) in south Asian populations was

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relatively rare. Researchers at this time inferred vitamin D status from the measurement of Alkaline Phosphatase (ALP).⁷ More recent evidence has demonstrated that serum vitamin D levels may not be correlated with increased ALP as previously thought.^{8,9}

With the introduction of commercial kit assays, the measuring of serum vitamin D levels became feasible, although initial work was hampered by a lack of reliability in testing. With improvement in serum vitamin D testing, there emerged an understanding that VDD exists in sunny regions of the world where it was once thought to be a rare occurrence.¹⁰⁻¹² Indeed, reports of widespread VDD in south Asian populations began to appear in the early 2000s.¹³⁻¹⁷ Included in this evidence were reports, now more than 10 vears old of widespread VDD in pregnant and postmenopausal women in India.^{15,18} In addition to this new understanding of the prevalence of VDD in populations once thought impervious, new understanding on the deleterious effects of VDD on health has also grown over the last several years to include not only skeletal disorders, but cardiovascular disease, diabetes, cancer and infectious and autoimmune diseases.¹⁹⁻²⁵ A multitude of studies that link VDD to adverse perinatal outcomes have been published in recent years.26-31

Current literature provides insight into subpopulations at risk for VDD. In addition to risks associated with dietary deficits of vitamin D rich foods, individuals with limitations to sun exposure have been identified as having an increased risk for VDD.^{12,32} Limitations to sun exposure in sunny regions have been linked to cultural clothing norms of extensive body covering and changes in lifestyle due to urbanisation resulting in fewer hours out-of-doors.^{12,32} The last few years have revealed that certain genetic variants in the Vitamin D Receptor (VDR) gene can influence vitamin D levels and disease in these populations as well.³³⁻³⁶

The aim of this study was to explore the prevalence of VDD among pregnant and non-pregnant women at a Multispecialty Hospital in Bengaluru, India. This study provides further evidence that VDD is widespread among Indian women and explores population-based remedies.

MATERIALS AND METHODS

The charts of women who presented to the Divakars Speciality Hospital, Bengaluru, India, from October 1, 2016, to November 1, 2016, were reviewed. All pregnant women who presented to the hospital for prenatal care in their 12th

week of pregnancy were considered. All non-pregnant women who presented for a routine annual checkup were selected. There were no criteria for exclusion, except if the women was already on vitamin D supplements, oral or injectable. Pregnant women's serum 25 (OH) D level was obtained during their 12th week of pregnancy as part of their routine prenatal care. Serum 25-hydroxy vitamin D (serum 25 (OH) D) was obtained for non-pregnant women that presented to the hospital clinic for an annual checkup as part of their routine care. All blood samples were processed at the Divakars Specialty Hospital. Serum 25 (OH) D was measured by chemiluminescent immunoassay. Serum 25 (OH) D level of 20.0 to <30.0 ng/mL was classified as Vitamin D Insufficiency (VDI) and levels <20 ng/mL were classified as Vitamin D Deficiency (VDD).

Patient's charts were retrospectively reviewed for serum 25 (OH) D test results that had been placed in each patient's permanent record. Serum 25 (OH) D levels for each patient were collected and entered into a Microsoft® Excel spreadsheet for analysis by physician researchers along with information regarding patient's age, employment status and education level. No patient identifiers were collected, thereby resulting in a de-identified dataset. The statistical analysis was carried out using Microsoft® Excel 2010. Data were compiled as percentages and means across population characteristics. Pearson's correlation was calculated to assess the correlation between 25 (OH) D levels and population parameters. A P value of <0.05 was considered statistically significant.

RESULTS

A total of 213 pregnant women and 370 non-pregnant women were enrolled in the study. The mean ages of the pregnant and non-pregnant women were 29 and 43, respectively. The mean serum vitamin D levels of the pregnant women and non-pregnant women were 15.1 ng/mL and 19.4 ng/mL, respectively (Table 1). Ninety-seven per cent of the pregnant women and 86% of non-pregnant women were vitamin deficient or insufficient (Table 1). Vitamin D levels were not correlated to income or education in either pregnant women or non-pregnant women (Table 2). Furthermore, they were not correlated to age in pregnant women, but a correlation was found in non-pregnant women (r=0.223747, P=0.000014) (Table 2).

| | Variab | le | Pregnant Women (n = 213) | | | Non-pregnant Women (n = 370) | | | | | | |
|---------------------------------|---------|-------------|--------------------------|------------|---------|------------------------------|--------------|--|--|--|--|--|
| Serum 25 (OH) D (ng/mL) Average | | | 15.1 | | | 19.4 | | | | | | |
| | | | | | | | | | | | | |
| | Pregi | nant Women | | | Non- | | | | | | | |
| Percentage | Total # | | | Percentage | Total # | | | | | | | |
| 3 | 7 | > 30 | sufficient | 14 | 53 | > 30 | sufficient | | | | | |
| 16 | 34 | 20-30 count | insufficient | 22 | 81 | 20-30 count | insufficient | | | | | |
| 81 | 172 | < 20 count | deficient | 64 | 236 | < 20 count | deficient | | | | | |

Table 1. Serum 25 (OH) D Values for Pregnant and Non-pregnant Women

| | Pregi | nant Wome | en (n=213) | Non-Pregnant Women (n=370) | | | | | | | |
|--|-------|-----------|--------------|----------------------------|----------|----------|--------------|--|--|--|--|
| Age category | <30 | 30<40 | | <30 | 30<40 | 40<50 | >50 | | | | |
| Total number by age category | 134 | 79 | | 37 | 89 | 154 | 90 | | | | |
| Percentage of age category in population | 63% | 37% | | 10% | 24% | 42% | 24% | | | | |
| Income category | High | Moderate | | High | Moderate | | | | | | |
| Total number by income category | 27 | 186 | | 117 | 253 | | | | | | |
| Percentage of income category in population | 13% | 87% | | 32% | 68% | | | | | | |
| Education category | Some | Graduate | Postgraduate | Nil | Some | Graduate | Postgraduate | | | | |
| Total number by education category | 40 | 166 | 7 | 3 | 130 | 255 | 180 | | | | |
| Percentage of education category in population | 19% | 78% | 3% | 1% | 35% | 69% | 49% | | | | |
| Table 2. Population Parameters | | | | | | | | | | | |

DISCUSSION

Several prior studies have shed light on the widespread VDD in south Asian populations.¹³⁻¹⁷ In India, the prevalence of VDD has been reported to fall between 70-100%. Among women, studies have reported a mean serum 25 (OH) D value of 9.28-23.4 ng/mL in pregnant women³⁷⁻³⁹ and 8.8-25.3 ng/mL in non-pregnant women.^{40,41} Among pregnant women, VDD has been found to be as high as 84%.¹⁵ Like these previous studies, we found high VDD and insufficiency among otherwise healthy pregnant and non-pregnant women presenting at a women's health centre in India. The mean serum 25 (OH) D values for pregnant and nonpregnant women reported in this study agree with those reported in the literature. Furthermore, the VDD prevalence of 97% reported in this study, although higher than those reported in the literature for pregnant women falls within the range for vitamin D prevalence reported in India.

Factors such as age, race (non-white), high BMI, low education level and low income status have been reported to be associated with VDD.⁴² Although, there are scarce data on the direct association between age, income category and education level and VDD in India, a study of healthy adults in Kashmir valley found no correlation between age and VDD.⁴³ In this study, we found that education level and income category were not predictors of VDD in pregnant and non-pregnant women; however, while age was not associated with VDD in pregnant women, we found that it was a predictor of VDD in non-pregnant women.

Vitamin D is synthesised on adequate exposure of skin to sunlight and can be obtained from dietary sources. In India, however, dietary habits and social, religious and cultural practices limit vitamin D synthesis and uptake. Cultural norms that dictate the covering of most body parts as well as limited outdoor activity preclude exposure to sunshine, while a diet low in calcium and vitamin D rich food sources reduces the ability of Indians to meet their dietary vitamin D needs.^{12,32} Fortification of food sources as well as supplementation offer a means to address the situation in India. However, it has been nearly 7 years since Babus called for a "concerted national effort to implement policies and auidelines for vitamin D fortification and/or supplementation."44 To many, such a lag in action has been frustrating. However, it is important to note that, while India lacks a vitamin D fortification food program, which could be a beneficial tool in combating widespread VDD, many

countries with such programs fail to reach vitamin D sufficiency levels within their populations through these Furthermore, consensus on vitamin D programs.³² supplementation guidelines have only been reached and published by the Endocrine Society of India within the last 18 months. Under these guidelines, The Endocrine Society of India recommends vitamin D supplementation of 400 International Units (IU) of vitamin D daily for infants, 600-1000 IU for children, 1000 IU for adolescents, 1000 IU for pregnant women after 12 weeks' gestation and 1000-2000 IU for adults.⁴⁵ When considering how to address the widespread VDD in Indian populations, it is important to deliberate on the cost associated with vitamin D supplementation. There are many appropriate formulations available on the Indian market today⁴⁶ and the yearly cost of a daily supplementation of 1000 IU would cost 120 rupees per year less than 2 US dollars.⁴⁷ In addition to the low cost, vitamin D supplementation is safe even in large doses.⁴⁷

These findings should be interpreted in light of the following acknowledged limitation. Parathyroid Hormone (PTH) levels have been used to determine the appropriate cutoff level of serum 25 (OH) D to define VDD in a particular population.^{48,49}

Limitation in this study was that the PTH levels of the study participants were not measured. This limitation notwithstanding the cutoff values we used in this study agree with those used in various studies of VDD in India.

CONCLUSION

Our study adds to the growing literature on the prevalence of VDD in India, especially in apparently healthy pregnant and non-pregnant women. Owing to the health effects of VDD and the high prevalence of VDD in India, we conclude that a state wide vitamin D supplementation initiative is required in India.

REFERENCES

- [1] Heaton TB. On the vitamin D. Biochem J 1922;16(6):800-808.
- [2] Ashford CA. The phosphorus distribution in blood and the calcium and phosphorus excretion during hypervitaminosis D. Biochem J 1930;24(3):661-668.
- [3] McGowan JP. Further investigations into the fundamental nature of vitamin D action. Biochem J 1933;27(3):943-950.

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- [4] Nicolaysen R. Studies upon the mode of action of vitamin D: the influence of vitamin D on the absorption of calcium and phosphorus in the rat. Biochem J 1937;31(1):122-129.
- [5] Liu SH, Su CC, Chou SK, et al. Calcium and phosphorus metabolism in osteomalacia. V. The effect of varying levels and ratios of calcium to phosphorus intake on their serum levels, paths of excretion and balances, in the presence of continuous vitamin D therapy. J Clin Invest 1937;16(4):603-611.
- [6] Albright F, Sulkowitch HW. The effect of vitamin D on calcium and phosphorus metabolism; studies on four patients. J Clin Invest 1938;17(3):305-315.
- [7] Hodgkin P, Hine PM, Kay GH, et al. Vitamin-D deficiency in Asians at home and in Britain. Lancet 1973;2(7822):167-171.
- [8] Smith GR, Collinson PO, Kiely PD. Diagnosing hypovitaminosis D: serum measurements of calcium, phosphate, and alkaline phosphatase are unreliable, even in the presence of secondary hyperparathyroidism. J Rheumatol 2005;32(4):684-689.
- [9] Shaheen S, Noor SS, Barakzai Q. Serum alkaline phosphatase screening for vitamin D deficiency states. J Coll Physicians Surg Pak 2012;22(7):424-427.
- [10] Gannagé-Yared MH Chemali R, Yaacoub N, et al. Hypovitaminosis D in a sunny country: relation to lifestyle and bone markers. J Bone Miner Res 2000;15(9):1856-1862.
- [11] van der Meer IM, MiddelKoop BJ, Boeke AJ, et al. Prevalence of vitamin D deficiency among Turkish, Moroccan, Indian and Sub-Sahara African populations in Europe and their countries of origin: an overview. Osteoporos Int 2011;22(4):1009-1021.
- [12] Wakayo T, Belachew T, Vatanparast H, et al. Vitamin D deficiency and its predictors in a country with thirteen months of sunshine: the case of school children in central ethiopia. PLoS One 2015;10(3):e0120963.
- [13] Goswami R, Gupta N, Goswami D, et al. Prevalence and significance of low 25-hydroxyvitamin D concentrations in healthy subjects in Delhi. Am J Clin Nutr 2000;72(2):472-475.
- [14] 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):359-364.
- [15] Sachan A, Gupta R, Das V, et al. High prevalence of vitamin D deficiency among pregnant women and their newborns in northern India. Am J Clin Nutr 2005;81(5):1060-1064.
- [16] Gulvady C, Pingle S, Shanbhag S. Incidence of vitamin B12/ D3 deficiency among company executives. Indian J Occup Environ Med 2007;11(2):83-85.
- [17] Goswami R, Mishra SK, Kochupillai N. Prevalence & potential significance of vitamin D deficiency in Asian Indians. Indian J Med Res 2008;127(3):229-238.

- [18] Harinarayan CV. Prevalence of vitamin D insufficiency in postmenopausal south Indian women. Osteoporos Int 2005;16(4):397-402.
- [19] Uitterlinden AG, Fang Y, Van Meurs JB, et al. Genetics and biology of vitamin D receptor polymorphisms. Gene 2004;338(2):143-156.
- [20] Agmon-Levin N, Theodor E, Segal RM, et al. Vitamin D in systemic and organ-specific autoimmune diseases. Clin Rev Allergy Immunol 2013;45(2):256-266.
- [21] van Schoor NM, Lips P. Worldwide vitamin D status. Best Pract Res Clin Endocrinol Metab 2011;25(4):671-680.
- [22] Al-Daghri NM. Vitamin D in Saudi Arabia: prevalence, distribution and disease associations. J Steroid Biochem Mol Biol 2016.
- [23] White JH. Vitamin D deficiency and the pathogenesis of Crohn's disease. J Steroid Biochem Mol Biol 2016.
- [24] Nelson SM, Batai K, Ahaghotu C, et al. Association between serum 25-hydroxy-vitamin D and aggressive prostate cancer in African American Men. Nutrients 2017;9(1):12.
- [25] Ombra MN, Paliogiannis P, Doneddu V, et al. Vitamin D status and risk for malignant cutaneous melanoma: recent advances. Eur J Cancer Prev 2017.
- [26] Yates N, Crew RC, Wyrwoll CS. Vitamin D deficiency and impaired placental function: potential regulation by glucocorticoids? Reproduction 2017;153(5):163-171.
- [27] Accortt EE, Mirocha J, Schetter DC, et al. Adverse perinatal outcomes and postpartum multi-systemic dysregulation: adding vitamin D deficiency to the allostatic load index. Matern Child Health J 2017;21(3):398-406.
- [28] Ercan M, Ozcetin M, Karaci M, et al. Relationship between newborn craniotabes and vitamin D status. North Clin Istanb 2016;3(1):15-21.
- [29] Wang LQ, Yan XT, Yan CF, et al. Women with recurrent miscarriage have decreased expression of 25hydroxyvitamin D3-1a-hydroxylase by the fetalmaternal interface. PLoS One 2016;11(12):e0165589.
- [30] Küçükler FK, Şimşek Y, Görkem Ü, et al. Relationship between gestational transient thyrotoxicosis and vitamin D. Turk J Med Sci 2016;46(5):1374-1378.
- [31] Yang L, Pan S, Zhou Y, et al. The Correlation between serum vitamin D deficiency and preterm birth. Med Sci Monit 2016;22:4401-4405.
- [32] Ritu G, Gupta A. Vitamin D deficiency in India: prevalence, causalities and interventions. Nutrients 2014;6(2):729-775.
- [33] Mackawy AM, Badawi ME. Association of vitamin D and vitamin D receptor gene polymorphisms with chronic inflammation, insulin resistance and metabolic syndrome components in type 2 diabetic Egyptian patients. Meta Gene 2014;2:540-556.

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- [34] Nissen J, Vogel U, Ravn-Haren G, et al. Real-life use of vitamin D3-fortified bread and milk during a winter season: the effects of CYP2R1 and GC genes on 25-hydroxyvitamin D concentrations in Danish families, the VitmaD study. Genes Nutr 2014;9(4):413.
- [35] Ou C, Zhao HL, Zhu B, et al. Association of vitamin D receptor gene polymorphism with the risk of renal cell carcinoma: a meta-analysis. J Recept Signal Transduct Res 2014;34(6):463-468.
- [36] Zumaraga MP, Medina PJ, Recto JM, et al. Targeted next generation sequencing of the entire vitamin D receptor gene reveals polymorphisms correlated with vitamin D deficiency among older Filipino women with and without fragility fracture. J Nutr Biochem 2017;41:98-108.
- [37] Farrant HJ, Krishnaveni GV, Hill JC, et al. Vitamin D insufficiency is common in Indian mothers but is not associated with gestational diabetes or variation in newborn size. Eur J Clin Nutr 2009;63(5):646-652.
- [38] Marwaha RK, Tandon N, Chopra S, et al. Vitamin D status in pregnant Indian women across trimesters and different seasons and its correlation with neonatal serum 25-hydroxyvitamin D levels. Br J Nutr 2011;106(9):1383-1389.
- [39] Sahu M, Bhatia V, Aggarwal A, et al. Vitamin D deficiency in rural girls and pregnant women despite abundant sunshine in northern India. Clin Endocrinol 2009;70(5):680-684.
- [40] Vupputuri MR, Goswami R, Gupta N, et al. Prevalence and functional significance of 25-hydroxyvitamin D deficiency and vitamin D receptor gene polymorphisms in Asian Indians. Am J Clin Nutr 2006;83(6):1411-1419.

- [41] Tandon N, Marwaha RK, Kalra S, et al. Bone mineral parameters in healthy young Indian adults with optimal vitamin D availability. Natl Med J India 2003;16(6):298-302.
- [42] Holick MF, Siris ES, Binkley N, et al Prevalence of vitamin D inadequacy among postmenopausal north American women receiving osteoporosis therapy. J Clin Endocrinol Metab 2005;90(6):3215-3224.
- [43] Zargar AH, Ahmad S, Masoodi SR, et al. Vitamin D status in apparently healthy adults in Kashmir valley of Indian subcontinent. Postgraduate Med J 2007;83(985):713-716.
- [44] Babu US, Calvo MS. Modern India and the vitamin D dilemma: evidence for the need of a national food fortification program. Mol Nutr Food Res 2010;54(8):1134-1147.
- [45] Mudur G. Indian endocrinologists set guidance to combat vitamin D deficiency. BMJ 2015;351:h5997.
- [46] Lhamo Y, Chugh PK, Tripathi CD. Vitamin D supplements in the Indian market. Indian J Pharm Sci 2016;78(1):41-47.
- [47] Vieth R. Vitamin D supplementation, 25hydroxyvitamin D concentrations, and safety. Am J Clin Nutr 1999;69(5)842-856.
- [48] Prentice A, Goldberg GR, Schoenmakers I. Vitamin D across the lifecycle: physiology and biomarkers. Am J Clin Nutr 2008;88(2):500S-506S.
- [49] Abrams SA, Griffin IJ, Hawthorne KM, et al. Relationships among vitamin D levels, parathyroid hormone, and calcium absorption in young adolescents. J Clin Endocrinol Metab 2005;90(10):5576-5581.