PREVALENCE OF VITAMIN D DEFICIENCY AND THE IMPACT OF ORAL SUPPLEMENTATION IN AN UNSELECTED PREGNANT INDIAN POPULATION

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ABSTRACT

BACKGROUND

There are many previous studies on vitamin D deficiency (VDD), 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.

The objectives of this study were

1. To explore the prevalence of VDD among pregnant women at a multi-specialty hospital in Bengaluru, India
2. To study the impact of daily oral vitamin D supplementation in pregnancy
3. To explore population-based remedies.

MATERIALS AND METHODS

This single center, open label clinical study was conducted at the Divakars Speciality Hospital, Bengaluru, India. Two hundred pregnant women were enrolled in the study in the 14th week of gestation. Serum vitamin D levels were measured at enrolment (baseline), and again on Day 3 postpartum. The vitamin D levels of the women were classified as follows: serum 25(OH) D levels <20 ng/ml = vitamin D deficiency (VDD); levels >20–<30 ng/ml = vitamin D insufficiency (VDI) and levels >30 ng/ml = vitamin D sufficient (VDS). All participants, regardless of their vitamin D status, were given an oral vitamin D supplementation regimen consisting of 1000 IU/day.

RESULTS

The mean age of the participants was 29±4 years. The mean serum vitamin D level at baseline was 11±93 ng/mL and on Day 3 postpartum it was 24.42±10.93 ng/mL, a statistically significant change ($p < 0.001$) at base line 86.3% (n = 173) women were vitamin D deficient (VDD), 12.5% (n = 25) were vitamin D insufficient (VDI), and 1% (n = 2) were vitamin D sufficient (VDS). The corresponding figures at the end of the study were 37% (n= 74) VDD, 32.5% (n = 65) VDI, and 30.5% (n = 61) VDS. Thus 30.3% (n = 60) of the participants had achieved vitamin D sufficiency by the end of the study period. There were no adverse effects reported as a result of taking the vitamin D supplements.

CONCLUSION

This study confirms previous reports of a high prevalence of VDD in pregnant Indian women**.** Oral vitamin D supplementation at a dose of 1000 IU/day significantly improved serum 25(OH)D levels in pregnant women, with a significant proportion attaining vitamin D sufficiency status. Further research is required to explore the potential clinical benefits of routine screening for VDD and supplementation as a part of routine prenatal services in India.

KEYWORDS

Vitamin D Deficiency, India; Pregnancy; Vitamin D Supplementation, Maternal Mortality.

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BACKGROUND

It is estimated that more than 1 billion people worldwide have vitamin D deficiency (VDD) or insufficiency.[1] India has a high VDD burden, with a prevalence of 70–100% in the general population,[2] despite its tropical climate with abundant overhead sunshine, which was historically thought to be associated with low VDD rates. This high prevalence has been attributed to cultural clothing norms of extensive body covering, changes in lifestyle due to urbanization, resulting in fewer hours out-of-doors, and diets that are poor

in vitamin D rich foods, such as fatty fish and milk, and vitamin D fortified foods.[2,3]

Vitamin D is an essential fat-soluble vitamin that modulates calcium, phosphorous, and bone metabolism.[4,5] However, the broad tissue distribution of its receptors in the human body suggest its role in the normal physiological responses of various body systems.[4,5] VDD, therefore, has broad multi-system health implications. It is associated with skeletal disorders, cardiovascular disease, diabetes, cancer, and infectious and autoimmune diseases.[6-8] Moreover, a multitude of studies that link VDD to adverse maternal and perinatal outcomes have been published in recent years[9-13] Some of these outcomes include pre-eclampsia,[14] gestational diabetes as well as congenital rickets in newborn infants.[15]

In 2008, the Endocrine Society published guidelines for the evaluation, treatment, and prevention of vitamin D deficiency.[16] To combat the high prevalence of VDD in India, The Endocrine Society of India released guidelines in 2015 that recommend 1000 IU for pregnant women after 12 weeks' gestation, and 1000–2000 IU for adults.[17] Studies have shown that vitamin D supplementation of up to 4000 IU/day during pregnancy is safe and effective in addressing VDD.[18]

We previously reported VDD prevalence of 81% and 64% in pregnant and non-pregnant women, respectively, attending a private hospital in Bengaluru, India, underscoring the need for state-wide vitamin D supplementation programs. In this follow-up study, we report on the impact of vitamin D supplementation during pregnancy. Our findings corroborate other studies that have reported high VDD prevalence in pregnant women in India and the potential of interventional oral vitamin D supplementation.

Objectives of the Study

The objectives of this study were

1. to explore the prevalence of VDD among pregnant women at a multi-specialty hospital in Bengaluru, India and
2. to study the impact of daily oral vitamin D supplementation in pregnancy and
3. to explore population-based remedies.

MATERIALS AND METHODS

This was a single center, open label clinical study carried out with Institutional Review Board approval at Divakars Specialty Hospital in Bengaluru, India, from June 2017 to January 2018. All women attending the hospital for prenatal care were considered for the study. The inclusion criteria were: a) confirmed pregnancy of 14 weeks of gestation at the time of consent and b) ability to give consent and comply with the study's oral vitamin D supplementation regimen. Women with pregnancies greater than 14 weeks of gestation as calculated by last menstrual period were not eligible to participate. In addition, pregnant women with pre-existing calcium or parathyroid conditions, chronic hypertension and active thyroid disease were also excluded.

Following enrollment into the study, baseline serum vitamin D levels were measured along with blood tests carried out as part of routine maternity care. The participants were then given oral vitamin D supplementation at 1000 IU per day to be taken throughout the rest of the pregnancy. The participants were encouraged to keep a daily diary in which they would record any adverse effects. Serum vitamin D levels were measured again on Day 3 postpartum.

All blood samples were processed at the Divakars Specialty Hospital. Serum 25(OH)D was measured by chemiluminescent immunoassay. The vitamin D status of the women was classified as follows: serum 25(OH)D levels <20 ng/ml = vitamin D deficiency (VDD); levels >20 - <30 ng/ml = vitamin D insufficiency (VDI) and levels >30 ng/ml = vitamin D sufficient (VDS). Data on the serum vitamin D levels for each patient were entered into a Microsoft® Excel spreadsheet for analysis along with the patient's demographic data. The statistical analysis was carried out using Microsoft® Excel 2010. Data were compiled as percentages and means and standard deviations. A paired t-test was conducted to determine significance of the difference between means.

RESULTS

Two hundred pregnant women were enrolled into the study. The mean age of the participants was 29±4 years. The mean serum vitamin D level at baseline was 11±93 ng/mL and on Day 3 postpartum it was 24.42±10.93 ng/mL, a statistically significant change ($p < 0.001$) (Table 1).

At baseline 86.5% (n =173) women were vitamin D deficient, 12.5% (n = 25) were vitamin D insufficient and 1% (n = 2) were vitamin D sufficient.

The corresponding figures at the end of the study were 37% (n =74) VDD, 32.5% (n = 65) VDI and 30.5% (n = 61) VDS. (Table 1). A total of 60 (30.3%) participants who at the beginning of the study were vitamin D deficient and insufficient achieved vitamin D sufficiency at the end of the study period (Table 2). There were no adverse effects reported as a result of taking the vitamin D supplements.

Variable	Baseline (n = 200)	Three Days Postpartum (n = 200)
Serum 25(OH)D (ng/mL)		
Average	11.93±7.26	24.42±10.93[#]
< 20 (deficient)	173(86.5%)	74(37)
20–30 (insufficient)	25(12.5%)	65(32.5)
> 30 (sufficient)	2(1%)	61(30.5)
Total	200 (100)	

Table 1. Serum 25(OH)D Values at Baseline and Three Days Postpartum

[#]P <0.001 indicating mean change in serum 25(OH)D is significant.

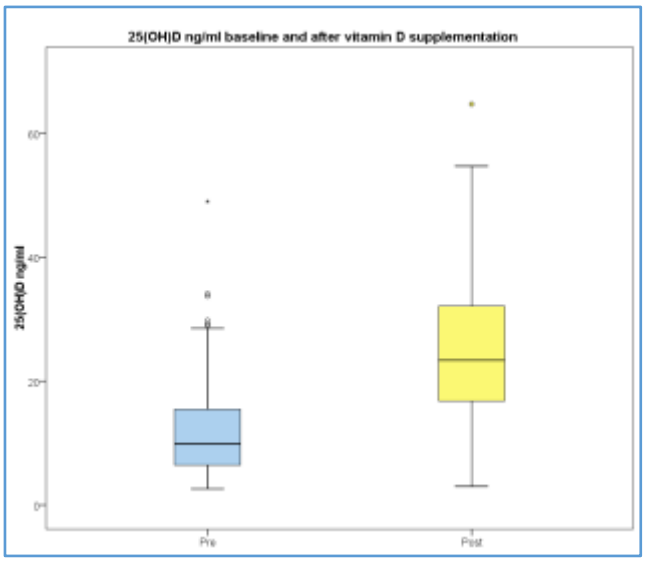

Figure 1

Variable	Final Vitamin D Status of Women who were Deficient at Baseline (n = 173)	Final Vitamin D Status of Women who were Insufficient at Baseline (n = 25)
Serum 25(OH)D (ng/mL)		
<20 (deficient or insufficient)	129(74.6)	9(36)
>30 (sufficient)	44 (25.4)	16(64)

Table 2. Number of Pregnant Women who Achieved Vitamin D Sufficiency at the End of the Study

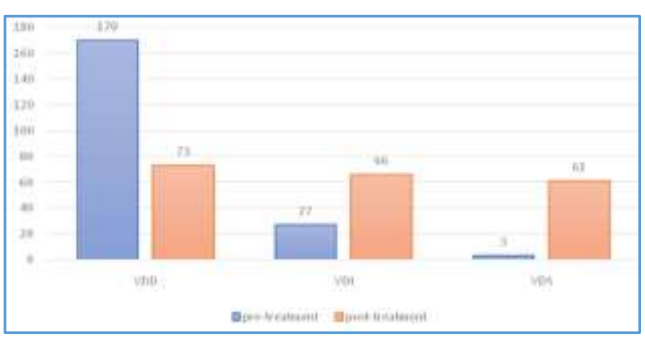

Figure 2

DISCUSSION

We found high VDD levels among otherwise healthy pregnant women attending a private hospital in Bengaluru, India, with the mean serum 25(OH)D values consistent with the 9.28–23.4 ng/mL range reported in previous studies in India.[19–21] Furthermore, the VDD prevalence of 86.3% found in this study, although higher than those reported in the literature for pregnant women, which are as high as 84%,[21] falls within the range for VDD prevalence reported in India.

In a seminal six-year randomized clinical trial assessing the safety and efficacy of vitamin D supplementation in pregnant women in the United States, Hollis et al.[18] found that 4000 IU/day was safe and effective for achieving vitamin D sufficiency in pregnant women and their neonates. An open-label randomized clinical trial in the states of Jammu and Kashmir, India, studying the efficacy and safety of vitamin D supplementation in pregnant women found that 2000 IU/day (n = 18) or 60, 000 IU/ month (n = 23) was effective in restoring vitamin D sufficiency.[22] Other studies in India conducted with both monthly bolus concentrations of up to 120,000 IU/month[23] and daily vitamin D supplementation of up to 4000 IU/day[24] have reported improved vitamin D sufficiency in pregnant women as well. We found that 1000 IU/day, a dose based on the current guidelines by the Endocrine Society of India, starting during the 14th week of gestation increased the mean serum 25(OH)D levels of the study cohort and restored the vitamin D sufficiency of 30% of women who were previously vitamin D insufficient or deficient. It is plausible that higher doses would have resulted in a greater percentage of women with vitamin D sufficiency, as Mir et al.[22] reported that 2000 IU/day restored the vitamin sufficiency of 80.5% of study participants. Future studies on the optimal vitamin D supplementation dose for pregnant women are, therefore, still needed.

Vitamin D plays a role in ensuring good maternal and neonatal health outcomes. Pre-eclampsia, one of the leading causes of maternal mortality and morbidity worldwide, is associated with VDD.[25] Gestational diabetes mellitus (GDM), which results in poor maternal and neonatal outcomes, in addition to increasing the risk of cardiovascular disease, type 2 diabetes, and obesity, has also been found to have a higher prevalence in women with VDD.[26] Vitamin D metabolism is greatly altered during pregnancy, especially as demands for nutrients such as calcium, whose metabolism vitamin D modulates, by the developing foetus increase - during the last trimester, the skeleton of the foetus begins to calcify, thereby increasing maternal demand for calcium;[27] moreover, levels of 1, 25(OH)2 D, which are responsible for enhancing intestinal calcium absorption, have been shown to increase. Thus, ensuring vitamin D sufficiency through vitamin D supplementation during pregnancy, which is an easy, affordable, and accessible approach, can help ensure normal foetal development, in addition to safeguarding maternal health, especially in a population that is already high risk for VDD.

We acknowledge a number of limitations in his study. Parathyroid hormone (PTH) levels have been used to determine the appropriate cut off level of serum 25(OH)D to define VDD in a particular population;[28,29] however, in this study, the PTH levels of the study participants were not measured. In addition, as participants were asked to self-report their adherence to the oral vitamin D regimen, we have no way of knowing with certainty whether the participants strictly adhered to the regimen.

CONCLUSION

The Indian population has a high prevalence of VDD. Oral vitamin D supplementation of as little as 1000 IU/day significantly reduces the incidence of VDD; but our study suggests that this is not the optimal dose as the ideal would be to give a dose that eradicates VDD completely in pregnancy. The advice from the Indian Endocrine Society

therefore needs to be revised, and additional research is required to establish the optimal dose that is both safe and effective in the total eradication of VDD.

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