

## Occurrence of Vitamin D deficiency in pregnant women in South India – A preliminary study

Sheela Ravinder S<sup>1\*</sup>, Deepika C<sup>1</sup>, Padmavathi R<sup>1</sup>, KalpanaBalakrishnan<sup>2</sup> and Jaya Vijayaraghavan<sup>3</sup>

<sup>1</sup>Dept. of Physiology, <sup>2</sup>Dept. of EHE, <sup>3</sup>Dept. of Obstetrics & Gynecology, SRMC & RI

Sri Ramachandra University, Porur, Chennai-116, Tamil Nadu, India

\*Corresponding Author E-mail: drsheelaravinder@yahoo.com

### ABSTRACT

#### **Introduction**

Vitamin D deficiency is suspected to be a public health problem in many parts of the world. In addition, vitamin D deficiency is thought to be common among pregnant women and is associated with an increased risk of pre-eclampsia, gestational diabetes and preterm births.

**Objective** - To determine the vitamin D status of antenatal women in the last trimester of pregnancy.

#### **Methods**

**Design** - Cross sectional study.

Biochemical screening of vitamin D status was carried out for one hundred pregnant women in their last trimester. Necessary permission was obtained from the Obstetric department of Sri Ramachandra University. Informed consent was obtained from the subjects. Blood samples from subjects were tested for 25-hydroxyvitamin D (25(OH) D) by chemiluminescence immunoassay at SRMC Biochemical laboratory.

- Vitamin D deficiency - [25(OH)D] < 20 ng/mL or < 50 nmol/L
- Insufficiency - 25(OH)D between 20-30 ng/mL or 50-75 nmol/L
- Sufficiency - 25(OH)D > 30 ng/mL or > 75 nmol/L

#### **Results**

Vitamin D levels have been analyzed for 100 subjects of which 67 were found to be Vitamin D deficient (< 20 ng/ml) 30 were insufficient (between 20-30 ng/ml) and 3 had normal levels of Vitamin D (> 30 ng/ml).

#### **Conclusion**

In view of the high incidence of subnormal vitamin D levels in antenatal women, we recommend biochemical screening in early pregnancy, with subsequent supplementation where indicated. This study may throw light on the need of vitamin D supplementation during pregnancy as a public health intervention for the purpose of improving maternal and infant health outcomes.

**Keywords:** Vitamin D, Deficiency, Pregnancy.

### INTRODUCTION

Vitamin D is essential for absorption of calcium from the intestine and to maintain a healthy mineralised skeleton. Vitamin D has numerous effects on human health and plays a much varied role in health and disease prevention. It affects calcium metabolism, modulates the immune system, cell proliferation and differentiation<sup>1</sup>. Adverse consequences in the mother include increased risk of preeclampsia, gestational diabetes and increased rate of caesarean section. Vitamin D deficiency is becoming highly prevalent in India in spite of being a tropical country with ample sunshine.

A study on 207 mothers from rural and urban North India showed a prevalence of 83.6% and 84.3% of vitamin D deficiency (vitamin D deficiency defined in that study as  $<22.5$  ng/ml), respectively<sup>2</sup>. The incidence of vitamin D deficiency is on the rise and elucidating the importance of this hormone in health and prevention are at the forefront of research.

Vitamin D deficiency is an unrecognized and one of the most common health problems associated with adverse effects on bone mineral homeostasis. Many studies worldwide have reported poor vitamin D status in all age groups, including those in the tropical countries. Children, adults and pregnant women throughout the world, across ethnicity and season are at risk for vitamin D deficiency<sup>3</sup>. There is scarce data about the prevalence of hypovitaminosis D in pregnancy and in the newborn in India<sup>4</sup>.

Vitamin D deficiency and low calcium intake are important risk factors for osteopenia and osteoporosis. Presently, we need to emphasise on adequate vitamin D and calcium intake, to prevent future bone health related conditions like osteoporosis. Foetal calcium is derived from the mother through the placenta. Around 25-30 g of calcium is transported to the foetal skeleton by the last trimester of pregnancy. This study was undertaken to generate serum Vitamin D levels in pregnant women in their last trimester and highlight the important modifiable risk factors like inadequate exposure to sunlight, dietary sources and supplementation.

Based on the study data, preventive measures can be implemented to decrease the deficiency status and thereby the morbidity associated with vitamin D deficiency in the mother & foetus. Health education while conducting the study would be a co-benefit of the study.

#### **Aim:**

To determine the vitamin D status of antenatal women in the last trimester of pregnancy.

### **MATERIAL AND METHODS**

#### **Study Design** - Cross Sectional study

One hundred pregnant women from the Obstetrics department of SRMC were screened for vitamin D status at their antenatal visit. Institutional ethical committee clearance was obtained. Necessary permission for data collection was obtained from the Obstetrics department of Sri Ramachandra University. Written informed consent was obtained from the subjects. Confidentiality regarding data will be maintained. Data collection comprised of standardized questionnaires, anthropometry & detailed information on medical history and medication use. Blood samples from subjects were obtained and tested for 25-hydroxyvitamin D (25(OH)D) by chemiluminescence immunoassay at SRMC Biochemical laboratory.

#### **Statistical analysis**

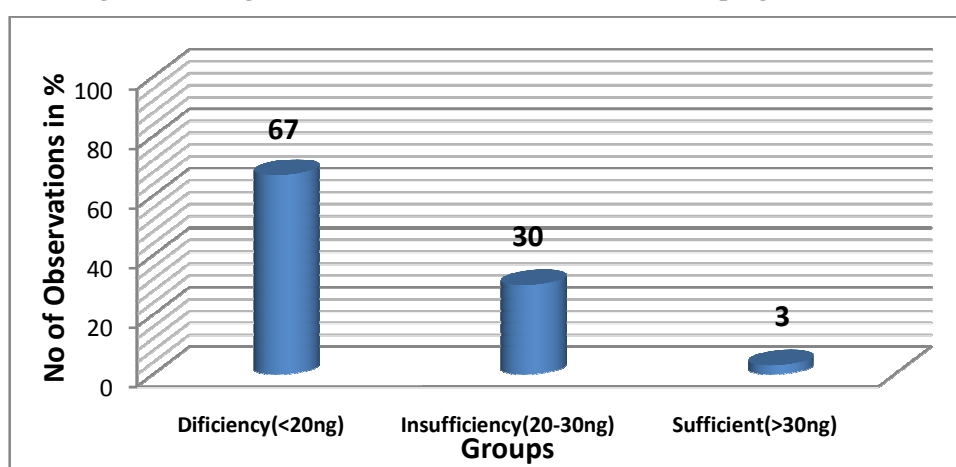
Data analysis was conducted by using SPSS version 11. Data are presented as percentage of different grades of vitamin D levels. The values are expressed as mean $\pm$ SD. Means and standard deviations were used to describe the vitamin D status. Statistical analysis was performed by one sample t test and p value less than 0.05 was considered to be statistically significant.

### **RESULTS**

The most important finding in our study is the unpredictably high occurrence of hypovitaminosis D among pregnant women. Vitamin D levels have been analyzed for 100 subjects of which 67 are found to be vitamin D deficient ( $< 20$  ng/ml) with a mean of  $15.18\pm 3.2$ . Insufficient levels (between 20-30 ng/ml) were observed in 30 subjects with a mean of  $23.06\pm 4.3$  and only 3 had normal levels of vitamin D ( $>30$  ng/ml) with a mean of  $31.6$  ng/ml. (Table-1). The statistical analysis of the distribution of vitamin D levels in the study group was highly significant ( $p = 0.00004$ ).

**Table -1: Distribution of Serum 25 (OH)D levels in pregnant women**

Vitamin D levels	n=100	Mean $\pm$ SD (ng/ml)	p value
Deficient (< 20 ng/ml)	67	15.18 $\pm$ 3.2	0.00004
Insufficient (20-30 ng/ml)	30	23.06 $\pm$ 4.3	
Normal (>30 ng/ml)	3	31.6	

**Fig.1: Percentage distribution of serum 25 (OH)D levels in pregnant women**

## DISCUSSION

During pregnancy the requirement of vitamin D is increased and the synthesis, metabolism and functions of vitamin D compounds throughout gestation are different. It has been proposed that 1,25(OH)<sub>2</sub>D supports implantation, normal pregnancy & fetal growth through release of calcium, and also controls secretion of placental hormones. 24,25(OH)<sub>2</sub>D is synthesized by the placenta which builds up in the bone and may be concerned with the calcification of fetal skeleton<sup>5</sup>. Deficiency of vitamin D alters mineral metabolism in the body and can lead to a decrease in bone mineral density and an increased risk of bone loss (osteoporosis).

In our study we found that two thirds of the participants (67%) had vitamin D deficiency with levels lower than 20ng/ml and a mean of 15.18 $\pm$ 3.2. Around one third of the study group (30%) were insufficient with levels between 20 to 30 ng/ml and a mean of 23.06 $\pm$ 4.3. Only 3 had normal levels of vitamin D (>30 ng/ml) with a mean of 31.6ng/ml. This is in concordance with a study on maternal vitamin D status in pregnant women in South India which revealed that more than 60% of the women had low 25(OH) D concentration (<50 nmol/L or < 20 ng/mL) at 30-week gestation, though there was no association between maternal vitamin D status and birth weight<sup>11</sup>.

Adequate vitamin D intake is crucial to meet the increased requirement in pregnancy, to maintain maternal health, and for prevention of adverse outcomes in the fetus. Vitamin D deficiency during pregnancy is being linked with preeclampsia, gestational diabetes mellitus<sup>6</sup>, and an increased risk for caesarean section delivery. Women with vitamin D deficiency may also have weakness of muscle and bones. A new study has observed that women who develop severe preeclampsia tend to have lower blood levels of vitamin D than healthy pregnant women which entails the possibility that the vitamin plays a role in the complication<sup>7</sup>.

Supplementation with vitamin D reduces the risk of preeclampsia, compared to unsupplemented controls<sup>8</sup>. An uncontrolled trial, supplemented with a multivitamin/mineral supplement and liver oil (containing 900 IU/d vitamin D) at 20 weeks gestation reduced the odds of preeclampsia by 32% with a 95% Confidence Interval of 11-47%<sup>9</sup>. Vitamin D supplementation in early pregnancy needs to be explored for preventing preeclampsia and promoting well-being of the fetus and neonate.

It has been recommended by the Endocrine Society Practice Guidelines that people at risk, including pregnant and lactating women should be screened for vitamin D deficiency<sup>12</sup>. The National Osteoporosis Foundation recommends 400-800IU vitamin D for pregnant women. Vitamin D supplementation is not a part of antenatal care programs in India at present.

A study on rodents concluded that vitamin D is vital for normal bone mineralization during the reproductive period in rats<sup>10</sup>. Vitamin D deficiency is found to be highly prevalent in Indian women, especially pregnant women. Due to the frequent pregnancies coupled with calcium deficiency due to prolonged lactation and decreased intake of calcium in the diet, the calcium demands are high in Indian women.

A recent systematic review established that antenatal vitamin D supplementation improves the vitamin D status of Asian women, improves growth in the infant, thereby decreasing the incidence of rickets in South Asian babies<sup>13</sup>. Current NICE (National Institute for health and Care Excellence) guidance for antenatal care affirms that pregnant women are informed of the importance of adequate vitamin D during pregnancy and later, to maintain good health.

It has been shown in several longitudinal<sup>14-17</sup> and cross-sectional<sup>18-20</sup> studies that, pregnant women have high serum 1, 25(OH)<sub>2</sub>D concentration as compared to non-pregnant young women; Serum 1,25(OH)<sub>2</sub>D rises steadily throughout pregnancy and reaches levels double those of non-pregnant women at term. Vitamin D deficiency in the mother is linked with harmful effects in the foetus/infant & complications for the mother during pregnancy<sup>21</sup>. Foetal and neonatal risks include growth retardation of the foetus, neonatal seizures due to hypocalcemia, and impaired growth and rickets in infancy<sup>22</sup>. Maternal malnutrition and vitamin D deficiency, as seen in Indian women, may lead to severe skeletal weakening during their reproductive period and may have lasting effects on bone health. Hypovitaminosis D and softening of the bones (osteomalacia) have been widely reported among pregnant South Asian women<sup>23,24</sup>. The low exposure to sunlight is compounded for Asian women by decreased outdoor activity, dark colour skin, and excessive clothing that limit sunlight exposure.

After widespread review of literature, the Endo Society guidelines remarks that the previous daily allowance recommended for a pregnant mother is not sufficient. An additional dose of vitamin D may be supplemented to maintain the vitamin D level above the currently accepted optimum of >30 ng/ml and to meet the increasing demands of pregnancy and lactation. The adaptations in the mother vary between gestation and lactation to maintain adequate levels in the growing foetus. The chief adaptive mechanisms to combat the increased demand in the mother are by increased absorption of calcium in the intestine during pregnancy and increased skeletal resorption of calcium during lactation.

Studies from the developed countries show that the impact of the increased calcium demand in the mother during pregnancy and lactation is reversible and does not considerably affect the maternal skeleton. Nevertheless, in our Indian scenario of poor maternal nutrition and early pregnancy before peak bone mass is achieved along with severe vitamin D deficiency, the situation may be different and probably have effects on bone health later in life. Thus, there is a need to increase the intake of vitamin D from foods fortified with vitamin D, and supplements, along with adequate exposure to sunlight to promote good health. Further studies are required to clarify the long-term impact on osteoporosis and elucidate the mechanisms of bone loss and restoration during pregnancy and lactation<sup>25</sup>.

## CONCLUSION

In view of the high incidence of subnormal vitamin D levels in antenatal women, we recommend biochemical screening in early gestation, with subsequent supplementation where indicated.

This study may throw light on the need of vitamin D supplementation during pregnancy as a public health intervention for the purpose of improving maternal and infant health outcomes. It is imperative to highlight the need for improving maternal nutrition, with focus on adequate vitamin D and calcium intake for prevention of bone health related disorders in future. Because of the benefits to mothers and infants and the absence of side effects, vitamin D supplements should be given to all pregnant women during their antenatal visits. Recommendations should be made on informing women of the importance of maintaining adequate vitamin D stores in pregnancy, particularly for those who are at risk for vitamin D deficiency. Education of the public about the beneficial effects of adequate sun exposure to satisfy their body's vitamin D requirements should be implemented. Future studies are essential to determine the true vitamin D requirement during pregnancy not only for maternal skeletal conservation and fetal skeletal development, but also for neural development, immune function and other beneficial effects in the infant as well as in later life.

### REFERENCES

1. Garland CF, Garland FC, Gorham ED, Lipkin M, Newmark H, Mohr SB, et al. The role of vitamin D in cancer prevention. *Am J Public Health*, **96**: 252–61 (2006)
2. Gannagé-Yared MH, Chemali R, Yaacoub N, Halaby G. Hypovitaminosis D in a sunny country: Relation to lifestyle and bone markers. *J Bone Miner Res*. **15**:1856–62 (2000)
3. Holick MF, Chen TC. Vitamin D deficiency: A worldwide problem with health consequences. *Am J Clin Nutr*. **87**: S1080–6(2008)
4. Sachan A, Gupta R, Das V, Agarwal A, Awasthi PK, Bhatia V. High prevalence of vitamin D deficiency among pregnant women and their newborns in northern India. *Am J Clin Nutr*. **81**: 1060–4 (2005)
5. Shin JS, Choi MY, Longtine MS, Nelson DM. Vitamin D effects on pregnancy and the placenta. *Placenta*; **31**: 1027–34 (2010)
6. MacKay AP, Berg CJ, Atrash HK. Pregnancy-related mortality from preeclampsia and eclampsia. *Obstet Gynecol*. **97**: 533–8 (2001)
7. Merewood A et al, Association between Vitamin D deficiency and primary caesarean section; *J Clin Endocrinol Metab*. **94**: 940 (2009)
8. Marya RK, Rathee S, Manrow M. Effect of calcium and vitamin D supplementation on toxemia of pregnancy. *Gynecol Obstet Invest*. **24**: 38–42 (1987)
9. Olsen SF, Secher NJ. A possible preventive effect of low-dose fish oil on early delivery and preeclampsia: Indications from a 50-year-old controlled trial. *Br J Nutr*. **64**: 599–609 (1990)
10. Marie PJ, Cancela L, Le Boulch N, Miravet L. Bone changes due to pregnancy and lactation: Influence of vitamin D status. *Am J Physiol*. **251**: E400–6 (1986)
11. Harinarayan CV, Ramalakshmi T, Prasad UV, Sudhakar D, Srinivasarao PV, Sarma KV, et al. High prevalence of low dietary calcium, high phytate consumption, and vitamin D deficiency in healthy south Indians. *Am J Clin Nutr*. **85**: 1062–7 (2007)
12. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: An Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. **96**: 1911–30 (2011)
13. Brooke OG, Brown IR, Cleeve HJ, Sood A. Observations on the vitamin D state of pregnant Asian women in London. *Br J Obstet Gynaecol*. **88**: 18–26 (1981)
14. Seki K, Makimura N, Mitsui C, Jirata J, Nagata I, Calcium-regulating hormones and osteocalcin levels during pregnancy: a longitudinal study. *Am J Obstet Gynecol*, **164**: 1248-1252 (1991)
15. Ardawi MSM, Nasrat HAN, BA'Aqueel HS, Calcium-regulating hormones and parathyroid hormone-related peptide in normal human pregnancy and postpartum: a longitudinal study. *Eur J Endocrinol*, **137**: 402-409 (1997)

16. Ritchie LD, Fung EB, Halloran BP, et al, A longitudinal study of calcium homeostasis during human pregnancy and lactation and after resumption of menses. *Am J Clin Nutr*, **67**: 693-701 (1998)
17. Uemura H, Yasui T, Kiyokawa M, et al, Serum osteoprotegerin/osteogenesis-inhibitory factor during pregnancy and lactation and the relationship with calcium-regulating hormones and bone turnover markers. *J Endocrinol*, **174**: 353-359 (2002)
18. Whitehead M, Lane G, Young O, et al, Interrelations of calcium-regulating hormones during normal pregnancy. *Br Med J (Clin Res Ed)* **283**: 10-12 (1981)
19. Bouillon R, Van Assche FA, Van Baelen H, Heyns W, De Moor P, Influence of the vitamin D-binding protein on the serum concentration of 1,25-dihydroxyvitamin D<sub>3</sub>. Significance of the free 1,25-dihydroxyvitamin D<sub>3</sub> concentration. *J Clin Invest*, **67**: 589-596 (1981)
20. Kuoppala T, Tuimala R, Parviainen M, Koskinen T, Ala-Houhala M, Serum levels of vitamin D metabolites, calcium, phosphorus, magnesium and alkaline phosphatase in Finnish women throughout pregnancy and in cord serum at delivery. *Hum Nutr Clin Nutr*, **40**: 287-293 (1986)
21. Barrett H, McElduff A. Vitamin D and pregnancy: An old problem revisited. *Best Pract Res Clin Endocrinol Metab*. **24**: 527–39 (2010)
22. Marya RK, Rathore S, Dua V, Sangwan K. Effect of vitamin D supplementation during pregnancy on foetal growth. *Indian J Med Res*. **88**: 488–92 (1988)
23. Dunne F, Walters B, Marshall T, Heath DA. Pregnancy associated osteoporosis. *Clin Endocrinol (Oxf)* **39**: 487–90 (1993)
24. NKritz-Silverstein D, Barrett-Connor E, Hollenbach KA. Pregnancy and lactation as determinants of bone mineral density in postmenopausal women. *Am J Epidemiol*. **136**: 1052–9 (1992)
25. Sachan A, Gupta R, Das V, Agarwal A, Awasthi PK, Bhatia V. High prevalence of vitamin D deficiency among pregnant women and their newborns in northern India. *Am J Clin Nutr*. **81**: 1060–4 (2005)
26. Goswami R, Gupta N, Goswami D, Marwaha RK, Tandon N, Kochupillai N. Prevalence and significance of low 25-hydroxyvitamin D concentrations in healthy subjects in Delhi. *Am J Clin Nutr*. **72**: 472–5 (2000)
27. Goswami R, Mishra SK, Kochupillai N. Prevalence and potential significance of vitamin D deficiency in Asian Indians. *Indian J Med Res*. **127**: 229–38 (2008)