



CALCIUM AND HYPOVITAMINOSIS D AMONG PREGNANT WOMEN AND THEIR NEWBORNS IN SOUTH INDIAN POPULATION

Gynecology

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ABSTRACT

Pregnancy is characterised by physiological changes in mineral metabolism, to allow calcium accretion in the fetal skeleton. Vitamin D insufficiency to pregnant women has been associated with a number of adverse consequences, and has been recognized as a public health concern in pregnant women and their infants. 382 pregnant women attending the antenatal clinic with 26-28 weeks gestation with single viable pregnancy were selected into the study group. 214 women who are admitted to the labour ward directly were treated as the control group. *The present study evaluated serum 25-hydroxyvitamin D3 [25(OH)D3], Calcium, concentrations in healthy term newborns and their mothers* and Anthropometric measurements of the newborn was taken within 6 hrs after delivery. The maternal hypovitaminosis D is real public health problem. The prevention is necessary, by the systematic vitamin D supplementation for pregnant women. *Vitamin D supplementation campaigns which should cover pregnant women and the newborn to prevent maternal and perinatal vitamin D deficiency should be implemented especially in risk areas.* More investigation is needed to find the exact cause of and factors that contribute to hypovitaminosis D in women in our country.

KEYWORDS

cord blood, hypovitaminosis D, Parathyroid hormone, sunlight, dietary calcium.

Introduction:

Vitamin D deficiency has been demonstrated to be prevalent in India (1) and particularly in rural Andhra Pradesh and despite of good sunshine exposure (2) but still vitamin D deficiency be seen south part of India which is closer to tropics is not clear. Vitamin D deficiency leads to many disorders including osteomalacia and rickets (3). Circulating maternal Vitamin D is the sole source for the foetal Vitamin D and the neonatal Vitamin D levels are highly correlated with maternal levels (4- 7). Due to deficient stores in the fetus, the newborns may suffer from neonatal rickets and hypocalcaemia (8-9).

Vitamin D binding proteins also increase during pregnancy secondary to high oestrogen levels, but the 25-hydroxyvitamin D (25(OH)D) level, the single best nutritional indicator of vitamin D status. Low maternal vitamin D levels during pregnancy have been associated with a plethora of adverse neonatal outcomes, including small for gestational age and preterm births, detrimental effect on offspring bone and teeth development, and risk of infectious diseases. However, maternal 25(OH)D level remains an important parameter that should be assessed during pregnancy because the fetus is totally dependent on the mother for 25(OH) (10). An observational study reveals that neonatal vitamin D is primarily determined by maternal contributions: implications of a new assay on the roles of vitamin D forms (11).

Previous Indian studies (1-2, 6) on vitamin D status in pregnant were conducted in North India and so far no data is available from south India, an area with different food habits and cultural practices. Based on these back ground present study was carried in south Indian population. In view of reasons stated above the study was undertaken in pregnant women and their newborn children.

Our aim is to determine the prevalence of hypovitaminosis D and the effect of Vitamin D supplementation during third trimester of pregnancy. By estimating serum bone mineral markers of Vitamin D and calcium metabolism in pregnant women and in the cord blood. To explore the effect of vitamin D supplementation on anthropometric measurements of newborns of the subjects.

Material and Methods|:

The study was conducted in P.K. Das Institute of Medical sciences. Healthy pregnant women at 24 – 28 weeks gestation with single viable pregnancy and the women attending the antenatal clinic were explained about the presumed beneficial effects of Vitamin D supplementation during pregnancy were recruited in this study.

382 pregnant women attending the antenatal clinic with 26-28 weeks gestation with single viable pregnancy were selected into the study group. 214 women who are admitted to the labour ward directly were treated as the control group. Written and informed consent was obtained from all the studied subjects. All the recruited antenatal women were supplemented with 1000 mg of calcium lactate and advised to take daily till term. Vitamin-D supplementation: The study group women were supplemented with Vitamin D 60,000 IU / Month at monthly intervals during the third trimester.

3 ml of blood samples was collected before delivery after admission into labour ward for vitamin D (25(OH)D), alkaline phosphatase and calcium, collected samples were centrifuged at 2000rpm for 15 minutes for further analysis. At the time of delivery cord blood was collected. 10 ml of cord blood was collected from placental end of the cord while placenta is still insitu. Sera was separated for vitamin D (25(OH)D), alkaline phosphatase and calcium analysis and 3rd day and their neonates 3rd post partum day blood sample was collected for further biochemical analysis. Anthropometric measurements of the newborn was taken within 6 hrs after delivery for birth weight, crown heel length, Head Circumference, mid upper arm circumference and largest diameter of anterior fontanelle.

Statistical Analysis:

The data were presented as mean with SD. Statistical analysis were done by using Microsoft Excel and SPSS for windows version 11.5 (SPSS, Inc., Chicago). A P-value less than 0.05 were considered statistically significant.

Results:

Table.1: Shown Mean SD of Base line characteristics of patients and

controls.

Table.2: Shown Mean SD of vitamin D in serum and cord blood, PTH and calcium levels of patients and controls.

Table.3: Shown Mean SD of Birth weight and circumference of patients and controls.

Total 382 women patients recruited and 107 had completed data and healthy controls were 214 women recruited and 110 had complete data. Significant difference was observed between cases and control in age, duration of sun exposure, supplemental calcium in mg / day and weight at term in kg ($P < 0.005$) and no significant difference was observed height in cm. Serum 25(OH)D level at term in subjects supplemented with vitamin D was higher in supplemented group (19.2729.012 ng/ml) when compared with control group ($P < 0.01$). Serum 25(OH)D level in cases, women who received vitamin D of 60,00 IU each in last trimester was not different from their 25(OH)D at the time of recruitment (p NS) where as PTH was high at the time of recruitment ($P < 0.005$). Neonatal calcium levels among babies with normal 25(OH) D ($> 10\text{ng/ml}$). Prevalence of neonatal hypocalcemia among neonates with normal cord blood 25(OH)D ($> 10\text{mg/ml}$) in the supplemented group was 38.31% and in the unsupplemented group it was 28.82%. Neonatal cord blood 25(OH)D was $> 10\text{mg/dl}$ in 71 babies (67.21%) born to unsupplemented subjects and 39 babies (35.54%) had $< 10\text{ng/dl}$. In the supplemented group 52 babies (48.59%) had 25(OH)D $> 10\text{ng/dl}$ and 58 babies (51.4%) had $< 10\text{ng/dl}$. If the serum 25(OH)D was $< 30\text{ng/ml}$ it is considered as hypovitaminosis D. The serum 25(OH)D level in cases at the time of recruitment was high (19.3812.112) compared to 25(OH)D level at term (19.279.012). Controls despite having high sun exposure had lower S. Vitamin D levels than cases at term. Serum calcium was found to be lower in cases rather than controls. However none of the babies born to either cases or controls had neonatal hypocalcemia. Effects of vitamin D supplementation on the nutrition of the newborn was evident by the fact that cases (recruited subjects supplemented with vitamin D) gave birth to babies with higher birth weight than controls ($P < 0.001$). The head circumference and mid upper arm circumference of the babies born to subjects supplemented with vitamin D was higher compared to unsupplemented subjects ($P < 0.001$).

Discussion:

Current available data indicate that vitamin D supplementation during pregnancy reduces the risk of preterm birth, low birth weight, dental caries of infancy, and neonatal infectious diseases such as respiratory infections and sepsis. Low doses of vitamin D during pregnancy have been reported to be safe, at least in the short term. No results are yet available regarding the potential long-term side effects of vitamin D supplementation on neonatal health, thus further high-quality research is needed in order to follow up the health of offspring of mothers supplemented with vitamin D during pregnancy.

The most important finding in our study is unexpectedly high prevalence of hypovitaminosis D among pregnant women. Hypovitaminosis D and osteomalacia among pregnant South Asian women have been widely reported (6). Previous studies were from temperate regions such as the United Kingdom and Norway (11), where the already low availability of overhead sun is compounded for Asian women by poor outdoor activity, pigmented skin and excessive clothing. We expected to find a higher serum 25(OH)D concentration in vitamin D supplemented women in our study. However the results were contrary to expectation with supplemented and unsupplemented women having equally low mean serum concentrations and equally high prevalence of the vitamin D deficiency. In non-Western countries, more than half of the pregnant women who were beyond their first trimester had 25(OH)D levels below 75 nmol/L ; these include countries such as India, (12). Vitamin D plays an important role during pregnancy and this has been demonstrated by findings on nuclear vitamin D receptors (VDRs) and vitamin-D-activating 1α -hydroxylase in pregnancy-specific tissues, i.e. the decidua and placenta (13)

Other words 60,000 IU of vitamin D monthly in last trimester was not sufficient to elevate vitamin D status of the subjects. However it still had same physiological effect in terms of lowering the serum PTH. In the present study high prevalence of vitamin D deficiency serum in pregnant women is probably due to occupation dress code and duration

of exposure to sunlight of the rural subjects, who are agricultural labourers working for about 8 hrs a day in sunlight. In the region where the study was conducted season has little impact on cutaneous synthesis of vitamin D. The cut off of $10\text{ ng } 25(\text{OH})\text{D/ml}$ is used for defining hypovitaminosis D in newborns. The corresponding 25(OH)D value in mothers was 30 ng/ml . Accordingly 76.63% women in the supplemented group and 87.27% in the unsupplemented group was considered to have hypovitaminosis D. In the neonates 58 babies (54.2%) in the supplemented group and 82 babies (74.54%) in the unsupplemented group were considered to have hypovitaminosis D. Vitamin D supplementation particularly in the form single dose at monthly intervals is well tolerated, starting from the 6th month does not have any action on embryogenesis (14). The administration of 5mg in the 7th or 8th month of the pregnancy results in a significant modification in maternal and cord calcium levels producing levels comparable to those observed with a daily dose of 1200U during the last trimester. Like previous studies the present study found that levels of 25(OH)D appear to be higher in maternal than cord blood. In the cord blood the 25(OH)D level in the supplemented group was higher compared to unsupplemented group. Concerning safety, low doses of vitamin D during pregnancy have been reported to be safe, at least in the short term. No results are yet available regarding the potential long-term side effects of vitamin D supplementation on neonatal health, thus further high-quality research is needed in order to follow up the health of offspring of mothers supplemented with vitamin D during pregnancy.

Maternal vitamin D has been shown to have its main impact on offspring birth weight and bone mass as well as immunity. Current available data indicate that vitamin D supplementation during pregnancy reduces the risk of preterm birth, low birth weight, dental caries of infancy, and neonatal infectious diseases such as respiratory infections and sepsis.

We have shown that low maternal 25 (OH)D in case pregnancy is associated with increased anterior fontanelle diameter decreased mid upper arm circumference. Vitamin D deficiency among pregnant woman is preventable and treatable but it is increasingly reported from around the world, especially among women with dark skin living at higher latitudes and among women who rarely expose their skin to sunlight.

Investigators are mainly for women in the temperate climates especially those with greater skin pigmentation and for women living in tropical regions (15). On the basis of our results we conclude that such recommendations perhaps also warranted for pregnant Indian women so that they remain healthy and provide adequate vitamin D to their fetus.

Evidence-based interventions to improve maternal and fetal nutrition, such as for Vitamin D, are accompanied by a decrease of the impact on the health of their children. Moreover, it is suggested to increase the awareness of people, especially women, about the factors affecting vitamin D status. These factors include consuming rich sources of vitamin D, exposure to sunlight, and also emphasizing the prescription of vitamin D supplements to infants.

Conclusion:

The maternal vitamin D deprivation is a real public health problem. The impact of deficiency is found in both of mother and newborn. The supplementation by vitamin D has become systematic for pregnant women at the third trimester in India. An increase in birth weight, mid upper arm circumference and head circumference of the babies of vitamin D supplemented mothers. Maternal vitamin D has been shown to have its main impact on offspring birth weight, long-term side effects of vitamin D supplementation on neonatal health, thus further high-quality research is needed in order to follow up the health of offspring of mothers supplemented with vitamin D during pregnancy. Large-scale studies in different geographical locations are necessary to identify the true role of Vitamin D on the health of pregnant women. Vitamin D supplementation campaigns which should cover pregnant women and the newborn to prevent maternal and perinatal vitamin D deficiency should be implemented especially in high risk areas. More investigation is needed to find the exact cause of and factors that contribute to hypovitaminosis D in women in our country.

Table.1: Shown Mean $\pm$ SD of Base line charecterstics of patients and controls.

Variables	Cases	Controls	P Value
Age (years)	22.321.82	22.692.54	P<0.001
Duration of sun exposure for 3 months(minutes)	60.4279.01	159.6899.12	P<0.001
Supplemental calcium (mg/day)	1000.00	275.54111.01	P<0.001
Height (cm)	155.724.26	155.103.68	P=NS
Weight at term(kg)	57.166.01	55.342.60	P=NS < 0.005

Table.2: Shown Mean $\pm$ SD of vitamin D in serum and cord blood, PTH and calcium levels of patients and controls.

Parameters	Cases	Controls	P Value
Serum 25(OH)D at term	19.2729.012	16.0497.066	<0.05
Cord blood 25(OH)D	13.1236.615	7.7022.886	<0.001
Maternal plasma PTH at term	19.38312.112	24.93812.508	<0.01
Neonate S. calcium on day3	8.991.69	9.891.8	<0.005
Neonate S. PTH	32.93223.098	43.65234.165	<0.01

Table.3: Shown Mean $\pm$ SD of Birth weight and circumference of patients and controls.

Weight/ circumference	Cases	Controls	P Value
Birth weight of baby (kg)	3.000.28	2.850.21	< 0.001
Crown heel length of baby (cm)	50.061.21	50.411.36	NS
Largest Anterior Fontanelle diameter (cm)	1.1630.08	1.1950.06	<0.05
Head circumference (cm)	32.840.72	32.520.84	<0.05
Mid upper arm circumference (cm)	9.110.16	8.960.15	<0.001

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