Vitamin D: Its Deficiency and Effect of Supplementation on Maternal Outcome

Ashima Taneja1, Shweta Gupta2*, Gurleen Kaur3, Narender Pal Jain4, Jaspreet Kaur5, Satinder Kaur6

Abstract
Objectives: Vitamin D deficiency is on a rise globally and so are the maternal complications related to it. This deficiency can be easily detected and corrected by simple oral supplementation for a better health outcome in pregnancy.

Methods: Antenatal women with no history of Vitamin D intake and first antenatal visit at our hospital between 26 to 28 weeks of gestation or after 34 weeks were tested for levels of Vitamin 25(OH)D. Deficient women (< 30 ng/ml) between 26 to 28 weeks were supplemented and tested again before delivery (Group A). Deficient women after 34 weeks who did not receive supplementation before delivery constituted Group B. Maternal outcome was noted and compared in both the groups.

Results: Out of the 189 Vitamin D deficient women included in the study; 105 (55.5%) were enrolled in Group A and 84 (44.4%) in Group B. 24 (12.7%) women were severely deficient (<4 ng/ml), 134 (70.9%) were deficient (<20 ng/ml) and 28 (14.8%) were vitamin D insufficient (20-30 ng/ml). A statistically significant reduction (p<0.001) was observed in vitamin D deficient women after supplementation in group A. 5.7% women developed preeclampsia in group A as compared to 28.5% in group B (p<0.0001). Higher (13%) incidence of gestational diabetes mellitus was observed in group B as compared to group A (6.6%) though the difference was not significant. A significantly higher incidence of preterm labor was observed in group B (p=0.007).

Conclusion: Vitamin D deficiency is correlated with a higher incidence of preeclampsia, gestational diabetes mellitus and preterm birth. Maternal screening in targeted population and its supplementation is recommended to improve maternal outcome.

Introduction
India is a tropical country where sunshine is found in abundance. Yet people face the deficiency of Vitamin D. Dark pigmented skin, less cutaneous exposure, clothing and use of sunscreens are the common reasons for this deficiency. This deficiency is not satisfactorily diagnosed and adequately treated especially in pregnancy. Vitamin D supplementation during pregnancy improves maternal vitamin D status and may reduce the risk of pre-eclampsia, low birthweight and preterm birth. However, the evidence currently available to directly assess the benefits and harms of the use of vitamin D supplementation alone in pregnancy for improving maternal and infant health outcomes is limited.1 Our study aimed at diagnosing and supplementing vitamin D in pregnancy and finding its effects on maternal outcome.

Material and Methods
This study was done in the department of Obstetrics and Gynaecology from January 1 to December 31, 2015. Antenatal women with no history of Vitamin D intake and first antenatal visit at our hospital between 26 to 28 weeks of gestation or after 34 weeks were tested for levels of Vitamin D after obtaining informed consent. Spot antecubital venous samples were processed on COBAS 6000 (ROCHE) machine by chemiluminescence method and measurement of serum 25-hydroxy vitamin D were taken. Reference range in our lab was: <4 ng/ml (Severe deficiency); <20 ng/ml (Deficiency); 20-30 ng/ml (Insufficiency) and 31-70 ng/ml (Sufficient levels).

Women with chronic hypertension, pregestational diabetes mellitus, renal disease, prior caesarean delivery, any musculoskeletal disorder were excluded from the study. Ethical clearance was obtained from the institutional ethical committee. The data was statistically analyzed using chi square and student’s t test and the results compared.

Results
189 Vitamin D deficient women were included in the study. Of these 105 (55.5%) were in the gestation of 26 to 28 weeks and supplemented with Vitamin D (Group A). 84 (44.4%) women were enrolled after 34 weeks of gestation and could not be supplemented before delivery (Group B).

The severity of vitamin D deficiency was studied in both the groups (Table 1). Out of 189 Vitamin D deficient women 24 (12.7%) had levels less than 4 ng/ml (severely deficient) and 134 (70.9%) women had levels less than 20 ng/ml (deficient). No statistically significant difference was observed in...
deficient women (<20 ng/ml) after supplementation though the p-value was reduced from 9.5% to 1.0% after supplementation (Table 5). Severe vitamin D deficiency between 26-28 weeks were supplemented with vitamin D and its effect was observed (Table 5). Severe vitamin D deficiency was reduced from 9.5% to 1.0% after supplementation though the p-value (0.905) was not statistically significant. A statistically significant reduction (<0.001) was observed in vitamin D deficient women (<20 ng/ml) after supplementation.

Table 1: Severity of vitamin D deficiency in both the groups

<table>
<thead>
<tr>
<th>Vit. D levels (ng/ml)</th>
<th>Description</th>
<th>A (Sample 1 before supplementation between 26-28 weeks) (n=105)</th>
<th>B (Non Supplemented at ≥34 weeks) (n=84)</th>
<th>Total (n=189)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 4</td>
<td>Severely deficient</td>
<td>10 (41.7%)</td>
<td>14 (58.3%)</td>
<td>24 (12.7%)</td>
<td></td>
</tr>
<tr>
<td>Less than 20</td>
<td>Deficient</td>
<td>78 (58.2%)</td>
<td>59 (44.0%)</td>
<td>134 (70.9%)</td>
<td></td>
</tr>
<tr>
<td>20-30</td>
<td>Insufficient</td>
<td>17 (60.7%)</td>
<td>11 (39.3%)</td>
<td>28 (14.8%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Comparison of the vitamin D deficiency according to gravidity in both the groups

<table>
<thead>
<tr>
<th>Vit. D levels (ng/ml)</th>
<th>Description</th>
<th>Groups</th>
<th>Total (n=189)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 4</td>
<td>Severely deficient</td>
<td>Multigravida (n=57)</td>
<td>Primigravida (n=132)</td>
<td>4 (20.8%)</td>
</tr>
<tr>
<td>Less than 4</td>
<td>Deficient</td>
<td>Rural (n=35)</td>
<td>Urban (n=154)</td>
<td>43 (31.4%)</td>
</tr>
<tr>
<td>20-30</td>
<td>Insufficient</td>
<td>Rural (n=35)</td>
<td>Urban (n=154)</td>
<td>9 (32.1%)</td>
</tr>
</tbody>
</table>

Table 6: Maternal outcome in women in both the groups

<table>
<thead>
<tr>
<th>Complication</th>
<th>Group A (Supplemented before delivery) (n=105) (%</th>
<th>Group B (Non Supplemented at ≥34 weeks) (n=84)</th>
<th>Total (n=189)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre eclampsia</td>
<td>6 (5.7)</td>
<td>24 (28.5)</td>
<td>0.00001</td>
<td></td>
</tr>
<tr>
<td>GDM</td>
<td>7 (6.6)</td>
<td>11 (13.0)</td>
<td>0.135</td>
<td></td>
</tr>
<tr>
<td>Preterm labor</td>
<td>9 (8.5)</td>
<td>19 (22.6)</td>
<td>0.007</td>
<td></td>
</tr>
</tbody>
</table>

Discussion

Vitamin D is known to play an important role in bone metabolism through regulation of calcium and phosphate equilibrium. Vitamin D is produced by the body during exposure to sunlight, but is also found in oily fish, eggs and fortified food products. Vitamin D levels can be measured irrespective of fasting and non-fasting state. As vitamin D supplementation sets to be a routine in pregnant women and lactating mothers, there is a need to define the optimum level of vitamin D in this population. Certain institutes recommend a normal level of 20 ng/mL as adequate for pregnant women; however, there is a growing consensus that serum vitamin D levels below 30 ng/ml represents deficiency. The Endocrine Society recommends a higher target of >30 ng/ml in order to achieve optimal skeletal as well as extra-skeletal benefits. These levels can also be applied in pregnancy and during lactation as it correlates with maternal and fetal outcomes. In our study, we observed a higher target of >30 ng/ml in order to achieve optimal skeletal as well as extra-skeletal benefits.
A reduction in the Vitamin D deficiency was observed in pregnant women after supplementation which was statistically significant in severely deficient women. Roth et al also reported a raised mean maternal 25(OH)D concentration at or near delivery as a widespread obstetric outcome after supplementation. Overall, intervention groups attained significantly higher maternal and cord 25(OH)D concentrations than the control groups in their study. They also concluded that a higher regular dose regimens (≥2000 IU/day) led to a greater average increment in maternal delivery.

We observed a significantly higher incidence (28.5%) of preeclampsia in women with vitamin D deficiency who did not receive supplementation before delivery as compared to 5.7% in supplemented group. The etiology of pre-eclampsia is questionable. Literature supports increase in the inflammatory mediators produced by the placenta as a reason of the pathology. Vitamin D is known to have anti-inflammatory properties and there is evidence of an inverse relationship between dietary calcium intake and the incidence of pre-eclampsia. Studies have shown that women who developed pre-eclampsia were found to have lower levels of vitamin D than women who did not with a five-fold increased risk of severe pre-eclampsia. The role of vitamin D deficiency and supplementation in the etiology and prevention of preeclampsia was reviewed in the article by Purswani et al. Their study did not show an independent effect of vitamin D supplementation in preventing preeclampsia.

We observed a higher incidence of gestational diabetes mellitus in vitamin D deficient non supplemented women though it was not statistically significant. Hypovitaminosis D is linked with impaired glucose tolerance and diabetes in the general population. However, the evidence for an association between hypovitaminosis D and gestational diabetes mellitus is debatable. GDM has a similar pathogenesis as T2DM and hence, low levels of maternal 25(OH)D concentrations and development of GDM has been correlated in various studies.

A significantly higher incidence of preterm labor was observed in our study in the non supplemented pregnant women (36.9%) as compared to 13.3% in supplemented women. Vitamin D deficiency has been shown to regulate body inflammatory factor levels that stimulate elevation of uterine contraction hormones, such as prostaglandin, thus causing preterm birth. Zhou et al concluded that maternal circulating 25-OHD deficiency could increase preterm birth risk and so vitamin D supplementation alone during pregnancy could reduce this risk. Whereas Yang et al did not find evidence of an increase in preterm birth risk related to vitamin D level during pregnancy.

We observed a significantly higher incidence of caesarean section rate in the non supplemented group. High prevalence of Vitamin D deficiency in pregnant women and complication of pregnancy like PROM, preterm labor and rate of Caesarean section, gestational hypertension, preeclampsia and diabetes was observed by many authors. Whereas Faustino et al observed that Vitamin D supplementation during pregnancy was associated with increased circulating 25(OH)D levels, birth weight, and birth length, but was not associated with other maternal and neonatal outcomes. Global data have consistently reported associations between maternal Vitamin D deficiency with serious pregnancy complications including pre-eclampsia, gestational diabetes mellitus, infection and cesarean section delivery. Vitamin D supplements during pregnancy improves the women’s vitamin D levels, as measured by 25-hydroxyvitamin D concentrations at term and may reduce the risk of delivering a baby prematurely (less than 37 weeks of gestation), result in a lower risk of high blood pressure and reduce the risk of a low birthweight baby (less than 2500 g).

**Conclusion**

There is a widespread deficiency of vitamin D in the general population and the incidence increases during pregnancy and lactation. Screening of
maternal serum 25-hydroxyvitamin D levels may not be executed due to the cost factor but can be estimated according to the individual clinical circumstances (dark pigmented skin, obesity, less exposure to sunlight, lack of exercise). When vitamin D deficiency is identified during pregnancy, most experts agree that 1,000–2,000 international units per day of vitamin D is safe. We recommend supplementation of vitamin D orally (daily or intermittently) during pregnancy in deficient women to decrease the maternal complications like preeclampsia, gestational diabetes mellitus and preterm birth. Pregnant women should be encouraged to eat a balanced diet, take prenatal supplements regularly and resort to healthy lifestyle measures.

References
