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Study of prevalence of pre-eclampsia in Vitamin D supplemented vs none supplemented primigravida mothers

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Abstract
Background: Pre-eclampsia is a significant co-morbidity which can have adverse effect on maternal and neonatal outcomes. Recent evidence have suggested that there is a causal association between low levels of vitamin D and development of pre-eclampsia in nulliparous women.
Aims and Objectives: To evaluate prevalence of pre-eclampsia in Vitamin D supplemented and non supplemented primigravida mothers.
Materials and Methods: A total of 100 primigravida mothers were recruited in the study and divided in to two groups of 50 subjects each. The recruitment was done prior to 20 weeks of gestation wherein 50 patients of interventional group received Vitamin D supplements along with regular antenatal care. Rest 50 patients received only the regular antenatal care.
Results: At baseline, hypovitaminosis D in interventional group was noted to be 40% (n=20). A total of 2 patients developed pre-eclampsia in interventional group whereas 9 patients developed pre-eclampsia in control group. The difference was significant with a higher prevalence of pre-eclampsia in control group that did not receive vitamin D supplementation.
Conclusion: Vitamin D supplementation should be considered as an essential component in antenatal care which can be associated with lowering the incidence of pre-eclampsia.

Keywords: pre-eclampsia, vitamin D, hypovitaminosis D

Introduction
Calcium and bone metabolism in adults depend heavily on concentrations of vitamin D and its active metabolite 1,25-dihydroxyvitamin D [1,25$(OH)_2$D]. Without 1,25$(OH)_2$D, the body cannot absorb calcium and phosphorus adequately, secondary hyperparathyroidism supervenes, the skeleton loses mineral content (secondary osteoporosis), and new bone is not adequately mineralized (rickets or osteomalacia) [1]. During pregnancy and lactation, mothers provide large amounts of calcium to the developing fetus and suckling neonate, respectively [2, 3]. Of late research have noted association of adverse maternal and neonatal health indices including preeclampsia with deficiency of vitamin D [4].
In this interventional comparative study we evaluated role of vitamin D supplementation on development of pre-eclampsia in primigravida mothers.

Materials and methods
A total of 100 patients were recruited in the study after obtaining due informed consent. The study details and procedures were explained to subjects in their native language. Patients unwilling to give an informed consent were excluded from the study.

Inclusion criteria
- Primigravida
- Age above 18 years
- Willing to give informed consent

Exclusion criteria
- Age below 18 years
- Patients with significant co-morbidities such as pre-existing hypertension, diabetes mellitus, malignancies, etc.
- Patients with any disorders affecting levels of vitamin-D

Patients satisfying the inclusion criteria were included and divided in to 2 groups of 50 subjects each. Interventional group underwent baseline vitamin D estimation and were given weekly oral supplements of Vitamin D (60,000 IU) until delivery. Both the groups received regular antenatal care. Incidence of pre-eclampsia was noted at any point of time subsequent to recruitment into the study.

Results

Table 1: Mean levels of Vitamin D at baseline

Vit D (ng/ml)	Study group
Mean	21.4
SD	7.6

Table 2: Baseline Vitamin D status

Status of Vitamin D level	Study group
Adequate (>/= 30ng/ml)	5
Insufficiency (20-29 ng/ml)	24
Deficiency (7 to <20 ng/ml)	19
Severe deficiency(<7ng/ml)	2
Total with less than normal	45

Table 3: Incidence of pre-eclampsia

Pre-eclampsia	Study group	Control group
Yes	2	10
No	48	40
P value	0.0277	
Inference	Significantly higher incidence of pre-eclampsia in control group	

Discussion

As observed from our study the baseline data suggests less than normal Vitamin D levels in 45 (90%) of the patients in study group. The mean Vitamin D levels at baseline were 21.4ng/ml (SD:7.6). Adequate levels of vitamin D are considered when the levels are above 30ng/ml. The study group was subsequently given vitamin D supplements and over the course of pregnancy it was noted that 2 patients in study group developed pre-eclampsia compared to 9 in the control group. The difference was significant (P=0.0277; Fischer's exact test).

Various studies have tried to correlate vitamin D deficiency with adverse maternal health outcomes as below:

Haugen M *et al.* [5] considering only the intake of vitamin D from supplements, authors found a 27% reduction in risk of preeclampsia (OR = 0.73 [0.58–0.92]) for women taking 10–15 μg/d as compared with no supplements. Bodnar LM *et al.* [6] noted monotonic dose-response relation between serum 25(OH)D concentrations at less than 22 wk and risk of preeclampsia. They observed that Maternal vitamin D deficiency may be an independent risk factor for preeclampsia. Baker AM *et al.* [7] in a nested case control study noted that Midgestation maternal 25(OH)D concentration was lower in women who subsequently developed severe preeclampsia compared with controls. Achkar M *et al.* [8] noted that Maternal vitamin D deficiency early in pregnancy defined as 25(OH)D <30 nmol/L may be an independent risk factor for PE. The relevance of vitamin D supplementation for women of childbearing age should be explored as a strategy for reducing PE and for promoting a healthier pregnancy. Wetta LA *et al.* [9] on contrary noted that Midtrimester maternal vitamin D was not significantly associated with preeclampsia <37 weeks or spontaneous preterm birth <35 weeks. Behjat Sasan S *et al.* [10] noted Vitamin D supplementation therapy in pregnancy could help in reducing the incidence of gestational hypertension/preeclampsia. Our study is similar to research by other workers showing association between vitamin D levels and development of pre-eclampsia.

Limitations

1. A smaller sample size that cannot be extrapolated to regional and national trends.
2. Effect of vitamin D supplementation on other indicators of maternal health was not evaluated.
3. Foetal wellbeing and neonatal outcomes were not compared between the groups.
4. The study was not blinded which may lead to inherent bias.

Conclusion

As observed from our study a high number of primigravida mothers tend to have hypovitaminosis D when evaluated before 20 weeks of gestational age. Supplementation of Vitamin D in form of oral tablets at dose of 60,000 IU/week was associated with lower incidence of pre-eclampsia in primigravida mothers. In a country like ours with less than satisfactory mother and child health parameters Vitamin D supplementation will serve as an useful adjunct in preventing development of pre-eclampsia, thereby leading to better maternal and neonatal outcomes.

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