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Research Article
Pregnancy

The prevalence of Vitamin D deficiency in pregnancy and neonatal outcomes

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Introduction: Vitamin D is an essential fat-soluble vitamin and has multiple functions. It affects calcium metabolism, modulates the immune system, cell proliferation, and differentiation. **Objective**: To study the prevalence of vitamin D deficiency in pregnant women and neonatal outcome in a tertiary care hospital, to study the association between maternal vitamin D and medical disorders, and to correlate maternal vitamin D deficiency with neonatal vitamin D levels and neonatal outcomes. **Materials and Methods**: This cross-sectional and observational study was conducted over a period of one year on 355 antenatal women admitted for safe confinement. 4 ML of whole blood was collected from median ante-cubital fossa and vitamin D levels were assessed using ELFA [Enzyme Linked Fluorescent Assay] following delivery, and 2ml of cord blood was also collected and sent for Vitamin D levels. **Results:** Out of the total study population, 12.96% (46) had adequate levels of vitamin D, the majority - 74.65% (265) had insufficient vitamin D levels, and 12.39% (44) had severe vitamin D deficiency. The overall deficiency among neonates was 95.22%. No significant association was found between vitamin D deficiency and maternal complications, except for the mode of delivery which was statistically significant with a P-value of 0.04. **Conclusion:** This study reaffirms that vitamin D deficiency is on the increase and therefore needs intervention by biochemical screening and corrective measures during pregnancy.

Keywords: Vitamin D deficiency, Prevalence, Pregnancy, Maternal outcomes, Neonatal outcomes

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Introduction

Vitamin D is an essential fat-soluble vitamin and has multiple functions. It affects calcium metabolism, modulates the immune system, cell proliferation, and differentiation [1]. Vitamin D and its metabolites are hormones and hormone precursors rather than vitamins.

It is unique among vitamins as it is made from skin exposure to sunlight. Other sources are from diet and dietary supplements. Adequate Vitamin D intake is associated with a lower risk of cancer, [2] cardiovascular diseases, [3] autoimmune diseases, neurological disorders, and diabetes.

The prevalence of vitamin D deficiency has increased and continues to be a major public health problem in many countries. Over 2 billion people suffer from vitamin D deficiency. Vitamin D deficiency is becoming highly prevalent in India, in spite of being a tropical country.

It has been reported in all age groups including toddlers, schoolchildren, pregnant women, and their neonates, and adult males and females residing in rural and urban India [4,5]. It is common in dark-skinned persons, veiled populations living at various altitudes. The worldwide prevalence of vitamin D deficiency ranges from 18-84% [6].

Vitamin D deficiency is an unrecognized and one of the most common health problems associated with adverse effects on bone mineral homeostasis.

Vitamin D deficiency during pregnancy is associated with multiple adverse health outcomes in mothers like bacterial vaginosis, [7] preterm labor, gestational diabetes, preeclampsia, and increased cesarean section.

In newborns it is associated with SGA, neonatal hypocalcemia, seizures, infantile heart failure, enamel defects, large fontanels, congenital rickets, and in children, low mineral density, rickets, type 1 diabetes, and eczema are seen.

Pregnant women in India have shown a prevalence of vitamin D deficiency of 84% which correlated significantly with serum 25(OH)D status of their newborns [8].

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 < 22.9 ng/ml) respectively [9].

Materials and Methods

One year cross-sectional and observational study was conducted from 1st June 2018 to 30th May 2019 on 355 pregnant women admitted for delivery. Institutional ethical committee clearance was obtained. The selected patients were briefed about the nature of the study, details of the test, and written consent was obtained. Women with multiple pregnancies, with pre-existing disorders like the history of thyroid, parathyroid, adrenal disease, hepatic or renal failure, gastrointestinal disorders, Type 1 DM were excluded. Women on therapeutic vitamin D supplementation, antiepileptics, and antitubercular drugs were also excluded.

Demographic data like age, obstetric history along with relevant history was recorded in a predesigned proforma. About 4 ml of venous blood was collected from the median antecubital fossa into plain tube following delivery, and 2ml of cord blood was also was collected and sent for serum Vitamin D levels. The sample was centrifuged at 2000 rpm and the serum was processed using Enzyme-Linked Fluorescent Assay (ELFA) with Vidas equipment.

Table-1: Based on serum levels patients were divided into four groups.

Group	Serum 25(OH) D level ng/ml
1. Severe deficiency	≤ 10
2. Insufficiency	11-29
3. Adequacy	30-100
4. Toxicity	>100

Association of vitamin D deficiency with maternal outcomes such as gestational hypertension, pre-eclampsia, gestational diabetes, abruption, oligohydramnios, preterm labor, mode of delivery, and maternal obesity were studied. Association of neonatal outcomes like gestational age at term, 1 minute APGAR, birth weight (AGA/SGA/LGA), fetal growth restriction, IUD/stillbirth, NICU admission, and congenital anomalies were studied.

Statistical Analysis: The data was collected in a pre-designed format. Data analysis was done by Epi Info 7.2.14 version and Microsoft Excel (SPSS 19th version). Results were expressed as Mean and Median for descriptive statistics. Chi-square test (mid exact p-value) was used to see the association between two groups appropriately. The p-value < 0.05 was considered as statistically significant. The correlation was done to test the association between maternal and neonatal vitamin D levels.

Results

The most important finding in the present study is the unpredictably high occurrence of hypovitaminosis among pregnant women. The majority, 74.65% (265) had insufficient vitamin D levels, followed by 12.96% (46) who had adequate levels of vitamin D and 12.39% (44) who had severe deficiency. The overall deficiency among mothers was 87.04%. The mean value of Vitamin D among mothers was 20.5456+/- 7. 542ng/ml.

Table-2: Prevalence of Vitamin D Deficiency in Pregnancy

Vitamin D status	Mean±SD (ng/ml)	Frequency	Percentage (%)
Severe Deficiency	1.3205±3.3635	44	12.39
Insufficiency	18.8686±5.0048	265	74.65
Adequate	33.8978±4.7253	46	12.96
Total	20.5456±7.5427	355	100

In the present study, out of the total study population among neonates, the majority 70.99% (252) had insufficient vitamin D levels with a mean value of 16.9294 ± 4.8933ng/ml, followed by 24.23% (86) who had severe deficiency with a mean value of 2.3942 ±4.1155ng/ml and 4.79 (17) who had adequate levels of vitamin D with a mean value of 31.8353 ± 2.9242ng/ml. The overall deficiency among neonates was 95.22% with a mean value of 17.2278 ± 6.2047ng/ml.

Table-3: Prevalence of Vitamin D Deficiency in Neonates

Vitamin D status	Mean±SD(ng/ml)	Frequency	Percentage (%)
Severe Deficiency	2.3942±4.1155	86	24.23%
Insufficiency	16.9294±4.8933	252	70.99%
Adequate	31.8353±2.9242	17	4.79%
Total	17.2278±6.2047	355	100%

In this study, a positive correlation was observed between maternal and neonatal vitamin D levels with R-value =0.871410044, whose corresponding P-value for 355 pairs is < .00001 which is statistically significant.

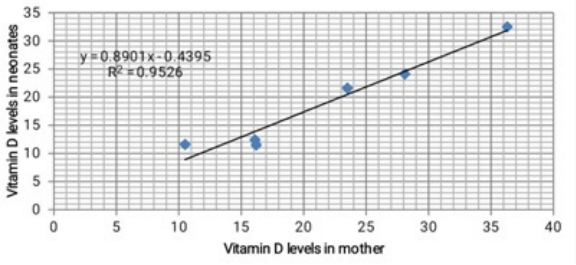

Fig-1: Correlation between Maternal and Neonatal Vitamin D Levels.

Table-4: Vitamin D Deficiency and Mode of Delivery.

Vitamin D status	Normal and Instrumental	LSCS	Total	P-value
Severe Deficiency	30 (8.45%)	14 (3.94%)	44 (12.39%)	0.04 (Significant)
Insufficiency	138 (38.87%)	127 (35.77%)	265 (74.65%)	
Adequate	31 (8.73%)	15 (4.22%)	46 (12.96%)	
Total	199 (56.05%)	156 (43.94%)	355 (100%)	

In the present study, maternal complications like gestational hypertension, preeclampsia, gestational diabetes, abruption, oligohydramnios, preterm labor, and maternal obesity were studied. There was no significant association found between vitamin D deficiency and maternal complications. Operative deliveries were found to be more statistically significant with a P-value of 0.04, especially severely deficient patients.

Parameters like duration of exposure to the sun, use of sunscreen, use of dairy products, dressing style, and use of multivitamin tablets in pregnant women were also studied, none of which showed a significant association. The neonatal parameters and complications like gestational age, 1-minute APGAR, birth weight (AGA/SGA/LGA), fetal growth restriction, IUD/stillbirth, NICU admission, and congenital anomalies were studied. There was no significant association found between vitamin D deficiency status and neonatal complications.

Discussion

1, 25 – dihydroxy vitamin D [1,25 (OH)2 D] is the major steroid hormone involved in mineral ion homeostasis regulation. Vitamin D and its metabolites are hormones and hormone precursors rather than vitamins since in the proper biologic setting, they can be synthesized endogenously. During pregnancy, maternal hemodilution is accompanied by a number of physiological changes into both vitamin D metabolism and maternal body composition; such adaptations lead to differences in the determinants of response to vitamin D supplementation between pregnant and non-pregnant women [10]. Although the food may provide small amounts of both vitamin D3 (cholecalciferol) and vitamin D2 (ergocalciferol), exposure to the sun is by far the major source of

Vitamin D to the body, the vitamin being synthesized from cholesterol derivatives. Vitamin D is carried up to the liver and hydroxylated to 25(OH)D or calcidiol; circulating 25(OH)D concentration is often used as an indicator of vitamin D status, due to its high concentration and larger half-life in comparison to the active form, but this inactive form of vitamin D requires further hydroxylation into the kidneys to 1,25-dihydroxyvitamin D (1,25[(OH]2D) or calcitriol, which is the active form of vitamin D [11].

In the present study out of the total study population, the majority of 265 (74.65%) had insufficient vitamin D levels, followed by 46 (12.96%) who had adequate levels of vitamin D and 12.39% (44) who had severe deficiency. The overall deficiency among mothers was 87.04%. The mean value of vitamin D among mothers was 20.5456 ± 7. 542ng/ml.

In concurrence to the present study, the following studies showed a similar prevalence rate of vitamin D in India and worldwide: A study carried by Sheela Ravinder S et al [12] Chennai (Tamil Nadu) demonstrated the prevalence of Vit D deficiency of 97%; Shweta Gupta et al [13] Ludhiana (Punjab) illustrated the prevalence of Vit D deficiency of 94.5%; Dipali Prasad et al [14] Patna (Bihar) showed the prevalence of Vit D deficiency of 88%; Shailaja Nageshu et al [15] Kuppam (AP) showed the prevalence of Vit D deficiency of 67.6% and study at Femina Women's Hospital [16] Hyderabad (Telangana) showed the prevalence of Vitamin D deficiency of 56%.

In the present study, out of the total study population, the majority 252 (70.99%) had insufficient vitamin D levels with a mean value of 16.9294±4.8933ng/ml, followed by 86 (24.23%) who had severe deficiency with a mean value of 2.3942 ± 4.1155ng/ml and 17(4.79%) who had adequate levels of vitamin D with a mean value of 31.8353±2.9242ng/ml. The overall deficiency among neonates of the mothers was 95.22%. The mean value of vitamin D among mothers was 17.2278±6.2047ng/ml. The result of the present study is comparable with the study done by Yuanliu Wang et al [17] that revealed the overall deficiency was 83.27%, among neonates. The mean value of vitamin D among neonates was 15.23±5.43ng/ml. In the present study, a positive correlation was observed between the maternal and neonatal vitamin D levels with an R-value of R= 0.871410044, whose corresponding P-value for 355 Study pairs is < .00001 which is statistically significant. It means that as the levels of vitamin D in the mother increases, a steady increase in the fetal or neonatal levels can be observed.

The present study correlates with the study done by Yuanliu Wang et al [17] and Sachan et al [8] observed a positive correlation between the vitamin D levels of mother and neonates with an R-value of 0.879 and 0.79 respectively which is statistically significant with a corresponding P-value < 0.001 seen in both the studies.

A study was done by Yuanliu Wang et al, [17] among 1978 mother-neonate pairs from Liuzhou city, China during 2015-2016. The study concluded that the mean concentrations of 25- hydroxyl vitamin D (25(OH)D were 16.17±6.27 and 15.23±5.43ng/ml in the mother and neonate groups, respectively, and the prevalence values of Vitamin deficiency in the two groups were 78.18% and 83.27%, respectively. Vitamin D-calcium co supplementation during pregnancy improved the vitamin D deficiency in both the maternal and neonatal groups (a OR 0.56, 0.66; P<0.001). Maternal Vitamin D deficiency significantly increased the risk of neonatal low birth weight (LBW) (a OR 2.83; P = 0.005) and small-for-gestational-age (SGA) (a OR 1.17; P = 0.015). There was a positive correlation between maternal and neonatal Vitamin D deficiency (r = 0.879, P< 0.001).

In the present study, among 355 women, 199(56.05%) had Vaginal delivery and 156(43.94%) had LSCS. It was observed that 31(8.73%) who had adequate levels of vitamin D had a normal vaginal delivery and instrumental delivery and 15(4.22%) who had adequate levels of vitamin D had LSCS. The association was drawn taking adequate levels as one group and severe deficiency, insufficiency as another group. Association between vitamin D levels and C-section was statistically significant (P=0.04)

A study was done by Nalini Sharma et al, [18] among 177 antenatal women in North-Eastern India, where the study subjects were divided into three groups. Deficient group where 25(OH) levels < 20 ng/ml, insufficiency < 32ng/ml and sufficient group > 32 ng/ml, Vitamin D deficiency was present in 84.18% subjects. Vitamin D insufficiency was present in 12.44% subjects. Lower levels of vitamin D were associated with maternal (preeclampsia, cesarean section) and fetal outcomes (low birth weight babies) with a P-value of < 0.05.

Conclusion

This study confirms that vitamin D deficiency is on the increase in pregnant women. Based on the findings of the present study it may be concluded that the prevalence of vitamin D deficiency was as high as 87.04% in spite of the study being done in India, a country with ample sunshine. Vitamin D supplementation during pregnancy can improve vitamin D levels in both mothers and neonates.

What does the study add to the existing knowledge

Universal screening of pregnant women for vitamin D deficiency could be taken up if the cost of screening is achievable at more economical rates. Vitamin D supplementation during pregnancy may help in reducing operative deliveries. It was found that there was no significant association between vitamin D deficiency and between maternal and fetal outcomes. To establish a strong association between vitamin D deficiency and various antenatal and neonatal complications further studies with large subject groups could be of help in asserting the association.

Author's contribution

Dr. Susheela Gayam: Concept, manuscript preparation

Dr. Summaya Fatima: Study design

Dr. Neelima C: Data analysis

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