Section: Obstetrics and Gynaecology

Original Research Article

MATERNAL SERUM VITAMIN D3 LEVELS IN PRETERM AND TERM DELIVERIES IN LOW RISK PARTURIENTS

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Corresponding Author:
Dr. Syeda Maisarah Imam,
Email: maisarahimam.mi@gmail.com

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Bhanumathi Vasudeva[1], Sharadha Govindaraju[1], Annu Murali M[2], Syeda Maisarah Imam[1], Ashok Kumar Devoor[2]

[1]Junior Resident, Department of Obstetrics and Gynaecology, Vani Vilas, BMCRI,Bangalore, India
[2]Associate Professor, Department of obstetrics and Gynaecology, Vani Vilas Hospital, BMCRI, Bangalore. India

Abstract

Background: Preterm labour is defined as one where the labour starts before 37th completed weeks (259days), counting from the first day of last menstrual period. Prematurity, resulting from preterm birth, is the leading cause of perinatal morbidity and mortality, with attendant effects on maternal health and also on the emotional and socioeconomic wellbeing of the family. The objective is to determine the level of serum vitamin D in a matched population of women with preterm and term deliveries. **Materials and Methods:** In the current study, women who gave birth prematurely (defined as before 37 weeks) and term (defined as after 37 weeks) at the labour unit of hospitals affiliated with BMCRI were compared. After birth, samples of the mother's venous blood were taken, and pertinent information was gathered using a proforma. A vitamin D enzyme-linked immunoassay kit was used to measure the serum's 25-hydroxy vitamin D levels. **Result:** There was no significant difference in parity (P=0.841), BMI (P=0.104), religion (P=0.86), booking status (P=1), skin color (P=0.361) or dressing style (P=0.841) between the preterm and term groups. There were, however, significant differences in vitamin D levels (P<0.001), between the two groups of parturients. Overall, 85 (85%) of the 100 study women had vitamin D deficiency. 49 (49%) women with preterm delivery had low serum vitamin D level as compared with 36 (36%) women with term delivery (P<0.001). **Conclusion:** Serum 25-hydroxy vitamin D deficiency was more prevalent among women with preterm delivery than among those with term delivery. And Preterm delivery has high morbidity and mortality. It is therefore important for women to have optimized serum vitamin D levels in pregnancy to reduce this adverse pregnancy outcome.

INTRODUCTION

In the field of medicine, awareness of the numerous roles that vitamin D plays in the body is still growing. A fat-soluble vitamin called vitamin D has both classical and non-classical actions. In addition to its non-classical effects, which include its antibacterial influence via complex interactions between vitamin D and the immune system, its classical benefits include preserving the skeleton by regulating calcium and phosphate homeostasis. After monocyte activation, vitamin D supplementation increases the synthesis of the antibacterial protein cathelicidin,[1] According to the maternal vitamin D status, the placenta converts vitamin D from its most readily available form, 25-hydroxy vitamin D, to its metabolically active form, 1,25-dihydroxyvitamin D, which has immunomodulatory effects.[2,3]

Preterm birth is the main cause of perinatal morbidity and mortality. As a result, mother health as well as the psychological and financial well-being of the family are significantly impacted. Preterm births of newborns are anticipated to occur in 15 million cases annually, and this figure is expected to rise.[4]reterm birth rates, according to estimates from 184 nations, range from 5% to 18%, and more than 60% of preterm newborns are born in Africa and south Asia.[4] Preterm birth complications are the main cause of death in children under the age of five.

Placental infection and inflammation are more common in preterm deliveries brought on by premature rupture of the membranes or spontaneous preterm labour. Such placental infections and inflammation are suppressed in part by vitamin D. When compared to women with normal vitamin D levels, studies have shown an increased prevalence of premature delivery in women with vitamin D insufficiency.[5,6]

Humans' vitamin D levels are affected by a number of variables, including the length of time that crucial skin areas are exposed to sunshine, skin type, clothing type, access to a diet high in vitamin D, body mass index, and the presence of chronic diseases, among others. In order to ascertain whether there is a correlation between low blood vitamin D levels and preterm delivery among pregnant women, the current study set out to measure the levels of serum vitamin D in a matched group of women who had preterm and term deliveries.

MATERIALS AND METHODS

This case control study was done among patients admitted in hospitals attached to Bangalore Medical College and Research Institute with the approval from the institutional ethical committee. Duration of study was February 2021 to August 2022.

Inclusion Criteria

- Patients willing to give informed written consent. (Annexure 1)
- Case-preterm delivery control-term delivery
- Women with singleton gestation
- Women with >28weeks of gestation
- No known comorbidities
- No habits of smoking / alcohol

Exclusion Criteria

- Patients not willing to give informed consent.
- Women with less than 28 week of gestation
- Women with previous preterm delivery
- Women with multifetal gestation
- Known medical condition before or during pregnancy
- Women with uterine anomalies
- Women with smoking/ alcohol habits/ drug abuse

Sample Size

The sample size was estimated on the basis of previous studies [7,8] conducted by Oluwole et al

$N = \frac{(Z\alpha - Z1-\beta)^2 [P_1(100-P_1) + P_2(100-P_2)]}{d2}$

$= \frac{(1.96+0.84)^2 (1787.11+465.99)}{(13)^2}$

= 51.19

Therefore the sample size is calculated to be 50 in each group would be required to ensure at least 80% power to detect the anticipated between-group differences, allowing for an attrition or non-response rate of 10%.

Methodology

the patients fulfilling the inclusion criteria will be enrolled for the study after obtaining informed consent. Case record form with follow up chart will be filled for each.

Procedure of Study

- A structured interviewer-administered questionnaire will be used for data collection.
- Gestational age will be based on the participants' last normal menstrual period, and confirmed or modified by a first- or early second-trimester ultrasound.
- Maternal socio demographic data and characteristics such as skin color and clothing type among others will be obtained at presentation and from medical records
- Thorough clinical examination including General Physical Examination, vitals, systemic examination will be done
- Patients routine investigations such as CBC, RBS, USG etc will be collected
- A venous blood sample will be collected immediately after delivery and sent to the laboratory
- The samples will then be centrifuged, and the serum will stored at −20oC until analysis. The level of total 25-hydroxyvitamin D in each serum sample was measured by using a CLIA (Chemiluminiscent immunoassay).
- Vitamin D levels obtained. Low serum vitamin D will be defined as a level below 30 ng/mL.

Since the sample size was 100, normality was checked using Kolmogorov-Smirnov test. Kolmogorov-Smirnov test showed $p < 0.05$ and > 0.05 for some variables. Hence both parametric tests and non-parametric tests were used in the study.

RESULTS

The mean age of women was 24.32 ± 3.88 years for those with preterm delivery 24.30 ± 3.9 years for those with term delivery (P=0.980). There was no significant difference in parity (P=0.841), BMI (P=0.104), religion (P=0.86), booking status (P=1), skin color (P=0.361) or dressing style (P=0.841) between the preterm and term groups.

Table 1: Distribution according to other characteristics

Mann Whitney U test statistics					
Variables		**Median**	**IQR**	**Z score**	**P-value**
Gestational age	Case	35	34 – 36	-8.249	< 0.0001*
	Control	39	38 – 40		
Vitamin D levels	Case	25	19.75 – 27	-5.272	< 0.0001*
	Control	28	26 – 31		
BMI	Case	26	22 – 28	-1.625	0.104
	Control	27	23.5 – 29		

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Birthweight	Case	3	2 – 3	-1.417	0.157
	Control	3	2 - 3		

Table 2: Distribution according to parity

Group		PARITY		Total	P-value
		PRIMI	MULTI		
Control	Count	28	22	50	0.841
	%	56.0%	44.0%	50.0%	
Case	Count	27	23	50	
	%	54.0%	46.0%	50.0%	
Total	Count	55	45	100	
	%	100.0%	100.0%	100.0%	

Table 3: Distribution according to religion

Group		Religion			Total	P-value
		Hindu	Muslim	Christian		
Case	Count	21	27	2	50	1
	%	42.0%	54.0%	4.0%	50.0%	
Control	Count	21	27	2	50	
	%	42.0%	54.0%	4.0%	50.0%	
Total	Count	42	54	4	100	
	%	100.0%	100.0%	100.0%	100.0%	

Table 4: Distribution according of still birth

Group		Still birth		Total	P-value
		NO	YES		
Case	Count	48	2	50	<0.0001
	%	96.0%	4.0%	50.0%	
Control	Count	50	0	50	
	%	100.0%	0%	50.0%	
Total	Count	98	2	100	
	%	100.0%	100.0%	100.0%	

Table 5: Distribution according of NICU admission

Group		NICU		Total	P-value
		NO	YES		
Case	Count	38	12	50	<0.001
	%	76.0%	24.0%	50.0%	
Control	Count	49	1	50	
	%	98.0%	2.0%	50.0%	
Total	Count	87	13	100	
	%	100.0%	100.0%	100.0%	

There were, however, significant differences in vitamin D levels (P<0.001), NICU admission and stillbirth between the two groups of parturients.

Table 6: Distribution according to skin colour

Group		Skin colour		Total	P-value
		LIGHT	DARK		
Case	Count	26	24	50	0.766
	%	52.0%	48.0%	50.0%	
Control	Count	23	27	50	
	%	46.0%	54.0%	50.0%	
Total	Count	49	51	100	
	%	100.0%	100.0%	100.0%	

Overall, 85 (85%) of the 100 study women had vitamin D deficiency. 49 (49%) women with preterm delivery had low serum vitamin D level as compared with 36 (36%) women with term delivery (P<0.001).

Table7: Distribution according of vitamin D levels

Group		Vitamin D		Total	P-value
		< 30 ng/ml	> 30 ng/ml		
Case	Count	49	1	50	< 0.0001*
	%	98.0%	2.0%	50.0%	
Control	Count	36	14	50	
	%	72.0%	28.0%	50.0%	
Total	Count	85	15	100	
	%	100.0%	100.0%	100.0%	

Table 8: Distribution according to dressing

Group		Age category		Total	P-value
		Uncovered	Covered		
Case	Count	22	28	50	0.841
	%	44.0%	56.0%	50.0%	
Control	Count	23	27	50	
	%	46.0%	54.0%	50.0%	
Total	Count	98	2	100	
	%	100.0%	100.0%	100.0%	

DISCUSSION

Vitamin D deficiency is widely prevalent all across the globe. The discovery of non classic functions of vitamin had lead the researchers to unveil the association between vitamin D deficiency and various disease processes. This resulted in the emergence of the concept that maintenance of optimum 25(OH)D levels in the blood is required for Vitamin D regulation of a large number of physiologic functions beyond that of the classic actions involved with bone mineral metabolism. Therefore vitamin D deficiency during pregnancy may not only impair maternal skeletal preservation and fetal skeletal formation but also be vital to the fetal "imprinting" that may affect chronic disease susceptibility soon after birth as well as later in life. This prospective observational study was undertaken to establish the association between maternal hypovitaminosis D and preterm delivery.

Our study demonstrated a very high prevalence of vitamin D deficiency among pregnant women which is astonishing as India being a tropical country with abundance of sunshine throughout the year. Various studies conducted in India and other countries across the world have also revealed high prevalence of vitaminD deficiency.

The current study discovered that maternal hypovitaminosis D was substantially related with preterm birth and that vitamin D deficiency was rather prevalent among parturients. These results might have long-term repercussions for women's preterm delivery prevention.

The overall prevalence of vitamin D deficiency recorded in the present study was 85%, which is approximately three times of the prevalence of 29% reported in a prospective study conducted in similar settings in Lagos.[9]The population of participants recruited in these two studies were mostly not well educated and likely to consume diets that are deficient in vitamin D and other nutrients as compared with women who delivered outside the health facilities. In studies in the United States and China the reported prevalence of vitamin D deficiency was 70% and 50%, respectively.[10,11] Several studies have shown that serum 25-hydroxy vitamin D deficiency is higher among dark-skinned women than among lighter skin women,[12-14] because dark-complexioned women possess more melanin, which protects their skin against damage from ultraviolet B exposure as compared with fair-skinned and white women. The present study might differ from these other studies because it was conducted in India where a considerable proportion of women wear full-coverage clothing, as reflected in the present findings. The women are therefore exposed to less sunlight, which is the major source of naturally occurring vitamin D.[15,16]

The present study showed that the prevalence of vitamin D deficiency was higher among women with preterm delivery than among those with term delivery. This finding is supported by a previous meta-analysis that found that vitamin D deficiency was a significant risk factor for preterm birth., 5 Several other studies comparing preterm and term delivery also found a higher prevalence of vitamin D deficiency among women with preterm than among those with term delivery. However, other studies by Gbadegesin et al,[9] in Lagos, Nigeria, and Yang et al,[17] in Guangdong, China, found no association between vitamin D deficiency and pregnancy complications including preterm delivery.

The study has some limitations. Although, similar to previous studies, the study found that vitamin D deficiency is more prevalent among preterm deliveries as compared with term deliveries, a cause and effect relationship cannot be established because of the study design employed. Another limitation was the difficulty in extracting reliable information on the intake of vitamin D-rich diets from the study women, and this factor might have had a direct or indirect influence on the observed association noted in the study. Sample size being small reduces the power of study.

CONCLUSION

In conclusion, the present study showed that serum 25-hydroxy vitamin D deficiency was more prevalent among women with preterm delivery than among those with term delivery. It is therefore important for women to have optimized serum vitamin D levels in pregnancy to reduce this adverse pregnancy outcome. However, a large, well-designed, multicenter, randomized control trial is recommended to further validate the role of routine prenatal vitamin D supplementation in improving maternal and perinatal outcomes including preterm delivery.

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