

Maternal Vitamin D Status and Preterm Birth: A Cross-Sectional Comparative Study in Northwestern Nigeria

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ABSTRACT: Introduction: One of the most common causes of neonatal morbidity and mortality, particularly in sub-Saharan Africa, is pre-term delivery. Maternal vitamin D deficiency has been linked to various adverse pregnancy outcomes, such as preterm delivery, yet findings remain inconsistent and limited, especially in low and middle-income countries like Nigeria. Therefore, this study aimed to assess maternal vitamin D levels and their association with preterm delivery at Usmanu Danfodiyo University Teaching Hospital (UDUTH), Sokoto.

Methods: A cross-sectional comparative study was conducted over five months among parturients at Usmanu Danfodiyo University Teaching Hospital (UDUTH), Sokoto. A total of 120 participants (60 per group) were recruited through systematic sampling and randomly allocated to two groups: those with preterm delivery (28 to <37 weeks) and those with term labour (≥ 37 weeks). Maternal serum vitamin D levels were measured using a solid-phase ELISA (Monobind Inc., USA). Data analysis was performed using SPSS. Chi-square tests were used to detect associations and identify predictors, respectively, at a 0.05 level of significance.

Results: The mean serum vitamin D level in the preterm group was 26.67 ± 14.97 , whereas in the term group, it was 49.55 ± 18.10 . The prevalence of low serum vitamin D levels among parturients with preterm delivery was 76.7%, compared to 15% in those with term delivery. There was a statistically significant association between serum vitamin D levels and gestational age: parturients with preterm delivery had lower vitamin D levels than those with term delivery. ($\chi^2 (1) = 43.502$, $p < 0.05$).

Conclusion: The present study demonstrated that serum vitamin D deficiency was more common among women with preterm delivery than those with term delivery. Therefore, measuring serum vitamin D during pregnancy may prove to be a useful tool in predicting the onset of preterm labour.

Keywords: *Preterm, Vitamin D, 25-Hydroxyvitamin D*

Introduction

The prevalence of prematurity has risen recently, with the number of preterm births increasing by approximately 30% since 1981. (1) Preterm delivery is defined as birth occurring after reaching the age of viability. It significantly contributes to neonatal morbidity and mortality, with around 1.1 million newborn deaths each year. (2) It is also a leading cause of death among children under five worldwide and remains a primary factor in causing disabilities and long-term health issues later in life. (2) Nearly one million preterm newborns die from complications related to prematurity, either directly or indirectly. Alarmingly, more than 60% of these 15 million preterm babies worldwide are born in sub-Saharan Africa and South Asia. (3) In the United States, preterm births complicate about 12% of all pregnancies and account for 75%

of neonatal deaths not due to congenital abnormalities. In the United Kingdom, 7.4% of live births were preterm. (3,4) In Nigeria, preterm births range between 773,597 and 871,000 annually, representing a prevalence rate of 12.2%, with direct preterm complications causing 98,300 deaths among children under five. (3)

Vitamin D is essential for healthy human growth and development and functions as a fat-soluble metabolite crucial for the proper regulation of various bodily functions. (5) Maternal vitamin D deficiency or insufficiency has been linked to numerous adverse maternal and fetal outcomes. These include conditions such as gestational diabetes mellitus (GDM), preeclampsia, and small for gestational age (SGA) births, as well as other tissue-specific disorders. This deficiency is widely recognised as a prevalent and significant public health concern globally, particularly regarding its impact on pregnant women. (5) Several studies have indicated a higher occurrence of preterm delivery among women with vitamin D deficiency compared to those with adequate vitamin D levels. (5–8) Wagner et al. found that pregnant women with serum vitamin D concentrations below 20 ng/mL were 3.81 times more likely to experience preterm birth than those with levels exceeding 40 ng/mL.(9) Similarly, Bodnar et al. reported that the risk of preterm birth decreased significantly as serum concentrations of 25-hydroxyvitamin D increased, reaching a notable reduction around 36 ng/mL before stabilising or plateauing. (10) Shibata et al. also found that lower vitamin D levels among pregnant women in Japan were associated with an increased risk of preterm birth. (11) Conversely, Zhou et al. reported that vitamin D insufficiency was linked to a reduced risk of preterm birth. (12) They observed that in Southern China, preterm births occurred more frequently among women with high maternal 25(OH)D levels of 30 ng/mL compared to those with lower (20 ng/mL) and medium (20–30 ng/mL) levels. (12) On the other hand, some studies have not found any correlation between vitamin D levels and the occurrence of preterm births. (13) According to research by Flood-Nichols et al. and Rodriguez et al., there is no association between vitamin D insufficiency during pregnancy and preterm birth. (13,14)

Considering the potential health risks, the high prevalence of preterm birth, the importance of these nutrients during pregnancy, the possibility for interventions, and

the wider public health and economic consequences of preterm birth, research on serum vitamin D levels in pregnant women and their connection to preterm delivery is justified. Such studies can improve clinical practice and public health strategies, and offer insights into maternal and neonatal health. Additionally, there is a lack of local studies on this effect in my environment. The aim of this study is to determine serum vitamin D levels among pregnant women at Usmanu Danfodiyo University Teaching Hospital, Sokoto, and to evaluate their association with preterm delivery.

Methodology

It was a cross-sectional comparative study conducted over five months among parturients at Usmanu Danfodiyo University Teaching Hospital (UDUTH) in Sokoto. A total of 120 participants (60 per group) were recruited through systematic sampling and randomly assigned to two groups: those with preterm delivery (28 to <37 weeks) and those with term labour (≥ 37 weeks). Participants mainly ranged in age from 16 to 45 years, with singleton pregnancies, and were excluded if they had a history of preterm birth, severe systemic illness, HIV infection, multiple gestations, substance use, polyhydramnios, or significant intercurrent illness. Maternal serum Vitamin D levels were measured using a solid-phase ELISA (Monobind Inc., USA). A 5 mL sample of venous blood was collected aseptically, centrifuged, and then analysed. The absorbance was read at 450 nm. Data analysis was performed using SPSS, with Chi-square tests employed to identify associations at a 0.05 level of significance.

Results.

MEAN SERUM VITAMIN D LEVEL AMONG THE STUDY PARTICIPANTS

Table 1 illustrates the serum vitamin D levels of the study participants. In Group 1 (preterm), approximately 76.7% had low serum vitamin D levels, while 23.3% had normal levels. Conversely, in Group 2 (term), about 85% of participants had normal vitamin D levels, with 15% having low levels. The mean serum vitamin D level in the preterm group was 26.67 ± 14.97 , compared to 49.55 ± 18.10 in the term group.

TABLE 1. MEAN SERUM VITAMIN D LEVEL AMONG THE STUDY PARTICIPANTS

| Serum Vitamin D | Group 1 (Preterm) N (%) | Group 2 (Term) N (%) | Total = 120 |
|---------------------------------|------------------------------------|---------------------------------|--------------------|
| Low (<30ng/ml) | 46.0(76.7) | 9.00(15) | 55.0(45.8) |
| Normal (\geq 30ng/ml) | 14.0(23.3) | 51.0(85) | 65.0(54.2) |
| Total | 60.0(100) | 60.0(100) | 120(100) |
| Mean \pm SD | 26.67 \pm 14.97 | 49.55 \pm 18.10 | 38.12 \pm 20.14 |
| Range (min – max) | 6.67 – 63.05 | 13.45 – 92 | 6.67 – 92.00 |

ASSOCIATION BETWEEN SERUM LEVELS OF VITAMIN D WITH PRETERM DELIVERY

There was a significant link between serum vitamin D levels and preterm delivery: participants with preterm delivery had lower vitamin D levels than those with full-term delivery (χ^2 (1) = 43.502, $p < 0.05$). The value of $CC = 0.526$ indicates a moderate association between vitamin D serum levels and preterm delivery. The $RR = 5.111$, with a confidence interval (LCI, UCI) = (2.754, 9.485), signifies an increased risk of preterm delivery at low vitamin D levels.

TABLE 2. ASSOCIATION BETWEEN SERUM LEVELS OF VITAMIN D WITH PRETERM DELIVERY

| Gestational Age Level | Vitamin D Level | | Total | Chi-square (χ^2) | df | P-value |
|------------------------------|------------------------|---------------|--------------|---|-----------|----------------|
| | Low | Normal | | | | |
| Preterm | 46 | 14 | 60 | 43.502 | 1 | <0.001 |
| Term | 9 | 51 | 60 | | | |
| Total | 55 | 65 | 120 | | | |
| CC | 0.526 | | | | | |
| RR (LCI, UCI) | 5.111 (2.754, 9.485) | | | | | |
| OR (LCI, UCI) | 18.619 (7.365, 47.067) | | | | | |

CC=Contingency Coefficient, RR=Relative Risk, OR=Odds Ratio, LCI=Lower Confidence Interval, UCI= Upper Confidence Interval

RECEIVER-OPERATOR CHARACTERISTIC (ROC) CURVE OF SERUM VITAMIN D LEVEL FOR PREDICTION OF PRETERM LABOUR

The Receiver Operating Characteristics (ROC) curve for serum Vitamin D is illustrated in Figure 1 below. The area under the curve (AUC) was 0.833 (95% confidence interval 0.759-0.906, $p=0.000$) as shown in Table 3. Sensitivity and specificity for various serum Vitamin D cut-off values are listed in Table 3. The cut-off value offering the highest sensitivity and specificity was 28.3, with 87% sensitivity and 72% specificity. At this threshold, the positive predictive value was 75% and the negative predictive value was 80%.

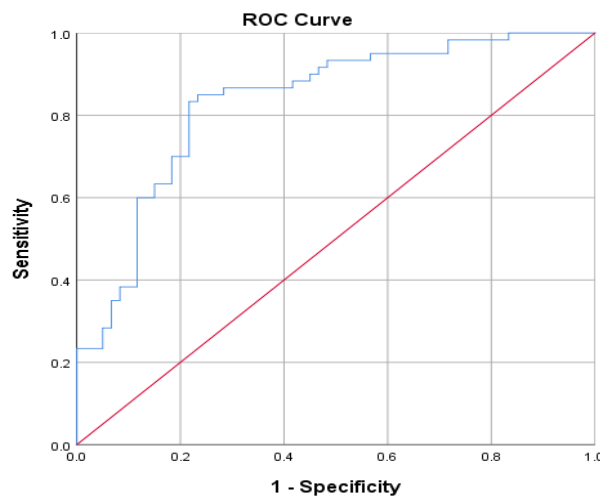


Figure 1: Receiver-operator characteristic curves of serum vitamin D level

Area Under the Curve

| | Cut of value | Sensitivity | Specificity | Std. Error ^a | Asymptotic Sig. ^b | AUC | 95% Confidence interval (CI) | |
|-------------------------|--------------|-------------|-------------|-------------------------|------------------------------|-------|------------------------------|-------|
| | | | | | | | Lower bound | S |
| Serum Vitamin D (ng/ml) | <28.3 | 87.0 | 72.0 | 0.037 | 0.000 | 0.833 | 0.759 | 0.906 |

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Co-ordinates of the curve

| Cut-off values | Sensitivity | 1-Specificity |
|----------------|-------------|---------------|
| 27.8850 | 0.867 | 0.333 |
| 28.0150 | 0.867 | 0.317 |
| 28.0650 | 0.867 | 0.300 |
| 28.3650 | 0.867 | 0.283 |
| 28.8300 | 0.850 | 0.283 |
| 29.0450 | 0.850 | 0.250 |
| 30.5250 | 0.850 | 0.233 |
| 32.3850 | 0.833 | 0.233 |

Discussion

This study observed that most patients (40.00%) in group I and (51.70%) in group II came from lower-class families. Socioeconomic status was not statistically significant ($p < 0.162$) between the two groups. This aligns with a study by Bhat et al. (15), which found that the majority of patients in both preterm and term groups belonged to low socio-economic classes. This contrasts with a study by Siddika et al. (16), which found that most of their subjects, both preterm and term, belonged to the middle socio-economic status (66.7% and 86.7%, respectively).

In this study, 51.70% of women in the term comparator group were primiparous, while 48.30% were multiparous; in contrast, the preterm labor group consisted of 41.70% primiparous and 58.30% multiparous women. There was no significant

difference in parity between the two groups ($p=0.275$). Khani et al. also reported similar results.

The current study revealed a relatively high rate of vitamin D deficiency among parturients in Sokoto, Nigeria. It also demonstrated a significant link between maternal hypovitaminosis D and preterm delivery. These findings could have future implications for preventing preterm birth among Nigerian women.

The study found a vitamin D deficiency prevalence of 76.7%, double the 29% reported by Gbadegesin A et al in 2017 in Lagos. This discrepancy may stem from the fact that the current research was conducted in Sokoto, Nigeria, a sunny region where many women wear full-coverage clothing, limiting sunlight exposure—the main natural source of vitamin D. Conversely, studies from the United States, Poland, and China reported prevalence rates of 70%, 69.6%, and 50%, respectively, demonstrating the global variation in vitamin D deficiency.

Numerous studies have indicated that women with darker skin are more prone to serum 25-hydroxy vitamin D deficiency than lighter-skinned women. (20,21) This disparity is linked to higher melanin levels in darker skin, which provide greater protection against ultraviolet B radiation than fair or white skin. In this study, vitamin D deficiency was notably more common in women who experienced preterm delivery than in those who had full-term births. This result supports a previous meta-analysis that identified vitamin D deficiency as a significant risk factor for preterm birth.⁶ Additionally, various other studies comparing preterm and term deliveries have found a higher rate of vitamin D deficiency among women who deliver preterm. (7,9,20)

It is important to note that different studies have reported contrasting findings. For example, Gbadegesin et al. (22) in Lagos, Nigeria, and Yang et al. (23) in Guangdong, China, found no association between vitamin D deficiency and pregnancy complications, including preterm delivery.

According to receiver operating characteristic (ROC) analysis, serum Vitamin D achieved an area under the curve (AUC) of 0.833. A threshold of 28.30 ng/mL was identified based on serum Vitamin D levels, with a sensitivity of 87.0% and a

specificity of 72.0%. This threshold also resulted in a positive predictive value (PPV) of 75.0% and a negative predictive value (NPV) of 80.0% for predicting preterm labour.

In a study by Kook et al. (24), Vitamin D-binding protein (VDBP) levels in cervicovaginal fluid (CVF) were assessed for their independent predictive value for intra-amniotic infection and imminent spontaneous preterm delivery in women with preterm labour (PTL) with intact membranes or preterm premature rupture of membranes (PPROM). Among women with PTL, the AUCs for CVF VDBP levels in predicting intra-amniotic infection and imminent preterm delivery were 0.66 and 0.71, respectively. The cutoff value for predicting intra-amniotic infection was 1.76 µg/mL (sensitivity: 64.3%, specificity: 78.4%), while the cutoff for imminent preterm delivery was 1.37 µg/mL (sensitivity: 65.4%, specificity: 72.6%). Notably, CVF VDBP levels were significantly higher in women with PPRM compared to those with PTL.

Conclusion

The present study demonstrated that serum vitamin D deficiency was more common among women with preterm delivery than those with full-term delivery. Although some predictive tests for preterm births are routinely used in developed countries, they still have low sensitivities and positive predictive values and are very costly. Furthermore, since this study observed that low serum vitamin D levels are linked to the onset of preterm labour, we can suggest that maternal hypovitaminosis D may serve as a predictor of preterm labour. It can be concluded that measuring serum vitamin D during pregnancy could be a useful tool in forecasting preterm labour. The findings of this study will contribute to the existing evidence that low serum vitamin D levels may be a risk factor for preterm labour.

Limitations

This research was hospital-based; the findings might not be representative of the broader population. Since the study population was drawn from a single hospital in Sokoto State, the results may not accurately reflect the situation in the entire state.

Recommendations

A randomised, multicentre study with a larger sample size should be conducted to increase the study's power and enable broader generalisation. Estimation of serum vitamin D levels may be a valuable parameter in pregnancy, particularly in women at high risk of preterm labour. Prophylactic oral vitamin D supplementation for women at increased risk of preterm labour may help prevent it.

Conflict of interest

There was no conflict of interest in this research work.

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