Vitamin D Status of Pregnant Women and the Association between Vitamin D Levels and Selected Pregnancy Outcomes

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Abstract: Background: High prevalence of vitamin D deficiency is recognized to be widespread amongst pregnant women, especially in the temperate regions of the world, and has been associated with adverse pregnancy outcomes. There is paucity of data on studies evaluating vitamin D status, and its effect on pregnancy in African population. Study objectives: This study was conducted to determine the vitamin D status of parturient women, and its relationship with selected pregnancy outcomes-fetal birth weight, placental weight, and Apgar scores at Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi, Nigeria. Methods: This is a pilot cross-sectional study involving 40 consecutive consenting parturient women at NAUTH, Nnewi. The subject were recruited through a convenience sampling technique. The serum of maternal blood samples collected before delivery was assayed for 25 hydroxyvitamin D using HPLC system. The neonatal characteristics and placental weights were recorded in an attached proforma form. Statistical analysis of data was perform using SPSS version 21. Relationship of variables was done with Chi-square test. A p-value of 0.05 was considered to be statistically significant at 95% confidence interval. Result: The mean maternal serum 25-hydroxyvitamin D₂ was 53.2 ± 11.3ng/ml. The prevalence of vitamin D deficiency was 7.5%, while 92.5% of the parturient women had normal maternal levels of vitamin D. The mean fetal birth weight was 3.3 ± 0.5kg, and there was a significant positive correlation between maternal serum vitamin D status and fetal birth weight (p=0.01, r=0.560). Conclusion: Prevalence of vitamin D amongst pregnant women of southeast Nigeria is low. There is positive correlation between maternal vitamin D status and fetal birth weight. Recommendation: There is probably no need for maternal supplementation of vitamin D in pregnancy in this environment. Further research with wider and larger population may be necessary to corroborate this findings.

1. Introduction

Vitamin D deficiency is believed to be widespread globally and is currently recognized to be one of the most untreated nutritional deficiencies worldwide.¹ Vitamin D deficiency in pregnancy has high prevalence in several part of the world where it has been studied. An Irish study reported a prevalence rate of 52.6% amongst Irish pregnant women² while Kazemi et al.³ reported a prevalence rate of 86% and 46% amongst pregnant Iranian women in winter and summer respectively. Studies conducted in India in 2005,⁴ and another in 2018⁵ reported a prevalence rate of 84% and 88% respectively. Vitamin D naturally occurs in humans as cholecalciferol (vitamin D₃). Primary hydroxylation of vitamin D to 25(OH)D occurs in the liver, while secondary hydroxylation to the active form as 1,25 (OH)₂D occurs in the kidney, and is regulated by the circulating levels of calcium, phosphorus and parathyroid hormones.⁶ Vitamin D receptors occur widespread in humans especially in endothelial and vascular smooth muscle cells, and infect in more than 30 different tissues including the pancreas, myocardium, lymphocytes, breast and prostate.⁷ Measurement of nutritional vitamin D level of an individual is in the form of 25 (OH)D₂ rather than 1,25(OH)₂D₃. Circulating 25(OH)D₂ relates directly to ultraviolet B light. On the contrary, circulating 1, 25 (OH)₂D₃ is controlled mainly by calcium homeostasis and is directly unrelated to one’s nutritional vitamin D status. Several studies have reported that infants of mothers with low vitamin D levels have low cord blood serum levels of calcium buttressing the relationship between calcium and vitamin D.⁹ Vitamin D deficiency has also been associated with poor Apgar score, increased risk of postpartum haemorrhage, increased risks for pre-eclampsia, and caesarean section due to uterine hypotonia.¹⁰ Although vitamin D is obtainable from various types of foods, such as oily fish and fortified margarines, the major source is the skin’s synthesis of the vitamin through exposure to solar ultraviolet light. Sunshine is abundant in Africa. The thickly pigmented dark skin of the black people of Africa usually act sunscreen preventing the penetration of ultraviolet light expected to produce vitamin D. Vitamin D levels are therefore expected to be low amongst the black African population inspite of the abundant sunshine. The literature is deplete of studies investigating serum vitamin D levels of pregnant women in sub-Saharan Africa together with the influence on pregnancy outcome. This study has been undertaken as a pilot, to determine the serum vitamin D levels

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of pregnant parturient women in South eastern Nigeria and the relationship if any with fetal birth weight, placental weight, Apgar scores and uterine atony. The findings from this study will constitute a framework for the design of a more comprehensive study on vitamin D levels involving a larger group of pregnant women from this important segment of the world population.

2. Subject and method

This is a pilot cross-sectional, prospective study designed to determine the vitamin D status of pregnant parturient women at Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi, and its influence on selected pregnancy outcomes—Fetal Apgar scores, fetal birth weight, and placental weight.

Ethical approval for this study was obtained from the ethical committee of NAUTH and appropriate participatory consent elicited and obtained from the parturient women following appropriate explanation and counselling on the nature of the study. Relevant consultations were held with the head of department of Obstetrics and Gynaecology and other supervising consultants of the departments, together with the chemical pathologists, laboratory scientists, resident doctors, and nurse-midwives involved in the study. The study was carried out at the labour ward of NAUTH, Nnewi. NAUTH is located in Nnewi, a semi-urban town and second largest city in Anambra state, south eastern Nigeria. NAUTH is a tertiary referral hospital with 23 clinical departments with patient catchment covering up to 6 out of 36 states of Nigeria.

Serum obtained from each maternal blood sample was labelled and stored at -80\(^\circ\) centigrade, and ultimately assayed for 25 hydroxyvitamin D\(_2\) and D\(_3\) using High Pressure Liquid Chromatography (HPLC).\(^{20}\) The proforma containing the fetal Apgar Scores, fetal birth and placental weight was completed. The data obtained (i.e. assay and proforma) were appropriately coded and keyed into the computer. Data analysis was performed using SPSS version 21. Crosstabulation was done to explore relationship between variables. The level of statistical significance was set at p-value of \(\leq 0.05\) providing 95% confidence interval.

3. Results

Of the 40 parturient women studied, 37 (92.5%) had normal/sufficient level of Vitamin D (\(\geq32\text{ng/ml or 80nmol/l}\)), while only 3 (7.5%) had abnormal/deficient levels of vitamin D (<32ng/ml or 80nmol/l)—Table 1a.

The prevalence accordingly for the classification of maternal serum vitamin D levels into deficiency (\(\leq20.9\text{ng/ml}\)), insufficiency (21-29.9ng/ml) and sufficiency (\(\geq30.0\text{ng/ml}\)) were 1(2.5%), 2(5.0%), and 37(92.5%) respectively - Table 1b.

The mean maternal serum vitamin D concentration was 53.2 ±11.3 ng/ml—Table 1b

Table 2 summarizes the frequency distribution of the pregnancy outcomes. The mean fetal birth weight was 3.3 ± 0.5kg. Only one (2.5%) fetus weighed below 2.5kg (premature) while 3(7.5%) weighed >4.2kg (postmature). The remaining 36(90%) weighed within the range of maturity (2.5kg-4.1kg).

Three (7.5%) placenta weighed less than 0.4kg while 4(10.0%) weighed greater than 0.9kg. The remaining 33 (82.5%) weighed between 0.5kg and 0.8kg. One minute Apgar score of 0-4 occurred in only one (2.5%) fetus; while that of 8-10 occurred in 39 (97.5%) fetuses. No fetus had an Apgar score between 5 and 7 (0%). All the fetuses 40(100%) had a 5-minute Apgar score of 8-10. Uterine atony did not occur in any of the parturient women-0%.

Table 3 shows the distribution by fetal birth weight for normal and low level of vitamin D. Normal vitamin D levels occurred with increasing range of fetal birth weight -0(0%) for fetal birth weight <2.5kg and 34(89.5%) for fetal birth weight from 2.5 to 4.1; and 3 (100%) for fetal birth weight >4.2kg. Conversely, low vitamin D levels were associated with decreasing fetal birth weight- 0(0%) for birth weight >4.2kg; 2(5.4%) for birth weight 2.5 to 4.1 and 1(100%) for fetal birth weight <2.5kg. The relationship was statistically significant (pearson chi-square value=18.378; df=4; P-value=0.001).

Table 4 shows the distribution by pregnancy outcomes for maternal serum vitamin D level correlation. Only fetal birth with showed significant correlation with maternal serum vitamin D (rho=0.560, P= 0.01).placental weight and Apgar scores at 1-minute and 5minutes show no significant correlation with maternal serum vitamin D levels-rho=0.288, P=0.158; Rho=0.040, p=0.806; rho=0.140, p=0.388 for placental weight, Apgar score at 1-minute and Apgar scores at 5-minutes respectively.

Table 5 summarizes the descriptive statistics of vitamin D status and pregnancy outcomes -fetal birth weight, placental weight, one-minute Apgar score and Five minute Apgar scores with respect to number, minimum and maximum values, mean and standard deviation.

Table 1 (a): Frequency distribution of vitamin D status according to normal and abnormal/deficient levels

| Vitamin D status (ng/ml) | Frequency | Percentage |
|-------------------------|-----------|------------|
| Normal/sufficient level (≥32) | 37 | 92.5 |
| Abnormal/deficient level (<32) | 3 | 7.5 |
| **Total** | **40** | **100.0** |

Table 1(b): Frequency distribution of vitamin D status according to deficient, insufficient and normal/sufficient levels

| Vitamin D status (ng/ml) | Frequency | Percentage |
|-------------------------|-----------|------------|
| Normal/sufficient level (≥30) | 37 | 92.5 |
| Insufficient level (21-29.9) | 2 | 5.0 |
| Deficient level (<20.9) | 1 | 2.5 |
| **Mean vitamin (ng/ml)** | **53.2 ±11.3** | **%** |
| **Total** | **40** | **100.0** |
The prevalence rate is even lower, 2.5% VDD when computed with the older definition of VDD of <20ng/ml as shown in table 1b of the result. In general, this very low levels of maternal serum vitamin D observed amongst this homogenous black population compared to the relatively very high figures reported from studies from predominantly white Caucasian and Asian population, appears paradoxical seeing in the light of the fact that the dark pigmented skin of the women in this study would have constituted sunscreen sufficient enough to prevent the availability of the needed ultraviolet sunrays for the endogenous production of vitamin D. Sunshine in Africa is abundant and it is tempting to suggest that the intensity of sunshine might be playing a superiority role than the degree of skin pigmentation with respect to the availability of the necessary rays for the production of vitamin D. It is also possible that other unconfirmed variables such as place of domicile, local diet, occupation, and clothings may play a role in the overall availability of vitamin D in this study population.

This study further reveals a significant positive correlation (P=0.01) between maternal serum vitamin D status and fetal birth weight. The newborns of mothers with normal and high levels of serum vitamin D had higher birth weights than those of low levels. Maternal serum vitamin D values were therefore lowest in low birth weight infants (<2.5kg) and highest in macromomeric infants (≥4.2Kg). The findings in this study corroborate the report from two studies carried out by Marya et al.,21 which clearly revealed the beneficial effect of maternal vitamin D supplementation on fetal birth weight, although another report from Zhila et al,22 did not show any significant correlation between maternal serum vitamin D status and fetal birth weight. Studies have reported the link between low maternal vitamin D levels and low cord blood calcium, as a plausible explanation of the relationship between low maternal serum vitamin D levels and low infant birth weight. Mothers with low levels of serum vitamin D invariably give birth to offspring with reduced intrauterine skeletal development that ultimately result in low fetal birth weight.15

In contradistinction to studies that have reported a correlation between low levels of maternal serum vitamin D and low Apgar scores, there is no significant correlation between maternal serum vitamin D and the other variables of pregnancy outcomes, Apgar score inclusive. In this study, the only baby with poor one-minute Apgar score of 4 was due to fetal distress following events of labour. None of the puerperal mothers had uterine atony or primary postpartum haemorrhage, irrespective of vitamin D status –low or normal as opposed to previous report. In this study, the only baby with poor one-minute Apgar score of 4 was due to fetal distress following events of labour. None of the puerperal mothers had uterine atony or primary postpartum haemorrhage, irrespective of vitamin D status –low or normal as opposed to previous report.17,18,19 It is possible that the low number of parturient studies may be responsible for this difference. The low prevalence of Vitamin D deficiency observed in this study obviously indicate that maternal vitamin D supplementation in pregnancy as practiced in some countries may not be necessary in the pregnant women in this

### Table 2: Frequency distribution of the pregnancy outcomes

| Birth weight | Frequency | Percentage (%) |
|--------------|-----------|----------------|
| <2.5         | 1         | 2.5            |
| 2.5-4.1      | 36        | 90             |
| ≥4.2         | 3         | 7.5            |
| Total        | 40        | 100.0          |

| Placental weight | Frequency | Percentage (%) |
|------------------|-----------|----------------|
| ≤0.4             | 3         | 7.5            |
| 0.5-0.8          | 33        | 82.5           |
| ≥0.9             | 4         | 10.0           |
| Total            | 40        | 100.0          |

| Apgar score (1-minute) | Frequency | Percentage (%) |
|-----------------------|-----------|----------------|
| ≤4 (poor)             | 1         | 2.5            |
| 5-7 (good)            | 0         | 0              |
| 8-10 (very good)      | 39        | 97.5           |
| Total                 | 40        | 100.0          |

| Apgar scores (5-minutes) | Frequency | Percentage (%) |
|--------------------------|-----------|----------------|
| ≤4 (poor)                | 0         | 0              |
| 5-7 (good)               | 0         | 0              |
| 8-10 (very good)         | 0         | 0              |
| Total                    | 0         | 0              |

| Uterine atony | Frequency | Percentage (%) |
|---------------|-----------|----------------|
|               | 0         | 0              |

### Table 3: Distribution by the association of fetal birth weight for normal and low levels of vitamin D

| Birth Weight (kg) | Vitamin D (ng/ml) | Pearson Chi-square | p-value | Significant level |
|------------------|-------------------|--------------------|---------|------------------|
| ≤2.5             | 0 (0)             | 1(100)             | 18.378  | 0.001 Significant |
| 2.5-4.1          | 34 (89.5)         | 2 (5.2)            |         |                  |
| ≥4.2             | 3 (100)           | 0 (0)              |         |                  |
| Total            | 37 (92.5)         | 3 (7.5)            |         |                  |

DF= degree of freedom

### Table 4: Distribution by pregnancy outcomes for maternal serum vitamin D level correlation

| Pregnancy outcomes | Pearson correlations | P-value | Level of significance |
|--------------------|----------------------|---------|----------------------|
| Birth weight       | 0.560                | 0.001   | Significant          |
| Placental weight   | 0.288                | 0.158   | Not significant      |
| Apgar score (1-minute) | -0.040             | 0.806   | Not significant      |
| Apgar scores (5-minutes) | -0.140        | 0.388   | Not significant      |

**Correlation is significant at 0.01**

### Table 5: Descriptive statistics of vitamin D status and pregnancy outcomes-fetal birth weight, placental weight, one-minute Apgar score and Five minute Apgar scores

| Pregnancy outcomes | N | Minimum | Maximum | Mean | Std. Deviation |
|--------------------|---|---------|---------|------|----------------|
| Vit. D. Status     | 40| 19.2    | 68.1    | 53.195 | 11.3400       |
| Fetal birth wt.    | 40| 1.8     | 4.4     | 3.267 | 0.4875         |
| Placental wt.      | 40| 0.4     | 1.1     | 0.640 | 0.1516         |
| One minute Apgar   | 40| 4       | 10      | 9.08  | 1.141          |
| Five minutes Apgar | 40| 6       | 10      | 9.90  | 0.632          |

### 4. Discussion

This study reveals a relatively low prevalence rate (7.5%) of maternal vitamin D deficiency (VDD) amongst the puerperal women of this study population when compared to previous studies carried out in Ireland, 56.2%; Iran 86% and 46% in both winter and summer respectively; and India, 84% and 88%. This study reveals a relatively low prevalence rate (7.5%) of maternal vitamin D deficiency (VDD) amongst the puerperal women of this study population when compared to previous studies carried out in Ireland, 56.2%; Iran 86% and 46% in both winter and summer respectively; and India, 84% and 88%. This study reveals a relatively low prevalence rate (7.5%) of maternal vitamin D deficiency (VDD) amongst the puerperal women of this study population when compared to previous studies carried out in Ireland, 56.2%; Iran 86% and 46% in both winter and summer respectively; and India, 84% and 88%.
study area. Pregnant women may instead benefit from advice and encouragement on adequate exposure of their body (skin) to sunlight, especially for those holding indoor occupation.

However, further research may be necessary to study the influence of social, environmental and dietary factors on vitamin D status during pregnancy in this study environment.

Apart from the positive correlation that exist between vitamin D levels and infant birth weight, none of the other delivery outcome variables showed any correlation with low vitamin D levels. There may therefore be no need for maternal supplementation of vitamin D during pregnancy in this study environment.

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