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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_3using 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 D_2 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 women[2] 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 2018[5] reported a prevalence rate of 84% and 88% respectively. Vitamin D naturally occurs in humans as cholecalciferol (vitamin D_3). Primary hydroxylation of vitamin D to 25(OH)D occurs in the liver, while secondary hydroxylation to the active form known as 1,25 $(OH)_2D$ occurs in the kidney, and is regulated by the circulating levels of calcium, phosphorus and parathyroid hormones[5,6]. Vitamin D receptors occur widespread in humans especially in endothelial and vascular smooth muscle cells, and infact in more than 30 different tissues including the pancrease, myocardium, lymphocytes, breast and prostrate.[7,8]Measurement of nutritional vitamin D level of an individual is in the form of 25 $(OH)D_3$ rather than $1,25(OH)_2D_3$. Circulating $25(OH)D_3$ 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[9,10,11]. It is therefore likely that maternal vitamin D levels affect fetal growth and bone development-explaining the low birth weight associated with low maternal vitamin D levels[12,13,14]. Mothers with low levels of vitamin D have been reported to give birth to offspring with reduced intrauterine and postnatal skeletal development[15,16]. Low level of maternal vitamin D has also been associated with poor Apgar score, increased risk of post-partum haemorrhage, increased risks for pre-eclampsia, and caesarean section due to uterine hypotonia.[17,18,19]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 as a 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 serumvitamin D levels of pregnant women in sub-Saharan Africa together with the influenceon pregnancy outcome. This study has been undertaken as a pilot,to determine the serum vitamin D levels

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 upto 6 out of 36 states of Nigeria.

Serum obtained from each maternal blood sample was labelled and stored at -80^0 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 thecomputer. 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 ≤0.05 providing 95% confidence interval.

3. Results

Of the 40 parturient women studied, 37 (92.5%) had normal/sufficient level of Vitamin D (≥32ng/ml or 80nmol/l), while only 3(7.5%) had abnormal/deficient levels of vitamin D (<32ng/ml or 80nmol/l)-table 1 a.

The prevalence accordingly for the classification of maternal serum vitamin D levels into deficiency (≤20.9ng/ml), insufficiency (21-29.9ng/ml) and sufficiency (≥30.0ng/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%) placentae 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

Table 2: Frequency distribution of the pregnancy outcomes

Pregnancy outcomes	*Frequency*	*Percentage (%)*
Birth weight		
<2.5	1	2.5
2.5-4.1	36	90
≥4.2	3	7.5
Total	40	100.0
Placental weight		
≤0.4	3	7.5
0.5-0.8	33	82.5
≥0.9	4	10.0
Apgar score (1-minute)		
≤4 (poor)	1	2.5
5-7 (good)	0	0
8-10 (very good)	39	97.5
Apgar scores (5-minutes)		
≤4 (poor)	0	0
5-7 (good)	0	0
8-10 (very good)	40	100
Uterine atony	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	df	p-value	Significant level
	Normal N (%)	Low N (%)				
<2.5	0 (0)	1(100)	18.378	4	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	Pearsons 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 paturient women of this study population when compared to previous studies carried out in ireland, 56.2%[2]; Iran 86% and 46% in both winter and summer respectively[3]; and India, 84%[4] and 88%[5].

This prevalence rate is even lower, 2.5% VDD when computed withthe 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 clothingsmay play a role in the overall availability of vitamin D in this study population.

This study further revealsa 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 macrosomic infants (≥4.2Kg). The findings in this study corroborate the report from two studies carried out by Marya et al.[12,21] 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,[9,10,11]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. [17,18,19] In this studythe only baby with poor one-minute Apgar score of 4 was due to fetal distress following events of labour. None of the paturient mothers haduterine 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 parturients studied 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

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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