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Maternal Serum Hypovitaminosis-d and Adverse Pregnancy Outcome: Any Correlation?

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ABSTRACT

To determine the association between maternal hypovitaminosis D and adverse pregnancy outcomes among Nigerian parturients at the Lagos University Teaching Hospital (LUTH), Lagos. A descriptive cross-sectional study carried out between December 2015 and October 2016. Total maternal 25-hydroxyvitamin D level was measured using a solid-phase competitive ELISA. Low serum vitamin D was defined as below 30ng/mL. Univariate analysis was used to show association between the baseline variables and adverse pregnancy outcomes and multivariate analyses using binary logistic regression models. $P < 0.05$ was considered statistically significant. The prevalence of vitamin D deficiency was 14.1%. Maternal vitamin D level was positively associated with gestational age at delivery ($P = 0.012$), low birth weight neonates ($P = 0.004$) and primary PPH ($P = 0.021$). No association shown between serum vitamin D levels and perinatal asphyxia (low 5-minute Apgar, $P = 0.174$). After controlling for gestational age at delivery, level of education, and booking status, low maternal vitamin D levels was not independently associated low birth weight (LBW) babies (adjusted OR-0.76, 95%CI-0.24-2.41) primary PPH (adjusted OR-2.42, 95%CI-0.79-7.42). A lower overall prevalence of serum vitamin D deficiency is noted among the study participants. Maternal serum hypovitaminosis D was not associated with primary PPH and perinatal asphyxia. Large, well designed, multi-center RCTs are therefore required to determine if supplementation in pregnant women with low vitamin D status will reduce the risk of these adverse pregnancy outcomes.

Keywords: LBW, Preterm Birth, PPH, perinatal asphyxia, Serum vitamin D levels.

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Introduction

Interest in the diverse functions of vitamin D in the human body keeps on trending in the medical world. Vitamin D, a fat-soluble vitamin has both classical and non-classical effects.^{1,2} The classical effects involve maintaining the skeleton, by regulating calcium and phosphate homeostasis, while its non-classical effects involve mainly its anti-bacterial effects, chief of which is the intricate interactions between vitamin D and the immune system.¹ Vitamin D supplementation enhances the production of anti-bacterial proteins Cathelicidin, occurring after activation of monocytes.³ Vitamin D conversion from 25-hydroxyvitamin D (its most widely available form in the body) to 1, 25-dihydroxy vitamin D (its metabolically active form) within the placenta, in response to maternal vitamin D status exerts immunomodulatory properties.^{1,2} Vitamin D level in humans is influenced by various factors such as duration of exposure of vital skin surfaces to sunlight, skin type, type of clothing, dietary availability of vitamin D rich diet, body mass index, the presence of chronic disease and so on.^{1,3}

There has been expanding research on the role of vitamin D in pregnancy and the implications of its deficiency on maternal and perinatal outcomes. Meta-analysis of several observational studies has demonstrated positive associations between low maternal vitamin D status and adverse pregnancy outcomes such as preeclampsia, gestational diabetes mellitus, preterm births, low birth weight, and others.⁴⁻⁶ Although several randomized controlled clinical trials of Vitamin D supplementation during pregnancy have been conducted with varying effects on pregnancy outcomes,^{4,5,10} many health organizations have recommended vitamin D supplementation in pregnancy and lactation to improve maternal vitamin D status during pregnancy and thus protects against adverse gestational outcomes.^{7,8} The potential underlying mechanisms of vitamin D in regulating each of the outcomes have not been extensively studied and there is limited data on the association among African obstetric population. This current study, therefore, sought to determine the association

between low maternal vitamin D levels and adverse pregnancy outcomes among Nigerian parturients at the Lagos University Teaching Hospital, Lagos.

Materials and Methods

- Study design

This was a descriptive cross-sectional study carried out among parturients at the labour ward unit of the Lagos University Teaching Hospital (LUTH) between December 2015 and October 2016. Ethical approval for the study was obtained from the hospital's research and ethics committee (HREC number: ADM/DCST/HREC/APP/170).

- Study population and eligibility criteria

Participants enrolled in the study were established parturients with a singleton fetus from 28 completed weeks of gestation. Criteria for inclusion were women with no known medical condition, no history of vitamin D supplement intake, and those who gave informed written consent to participate upon an explanation of the nature and purpose of the study. Established parturients were women who had at least one uterine contraction in a 10 minutes duration with at least 4cm cervical dilatation.

- Sample size estimate and data collection

The sample size is estimated using preliminary data from our pilot study with the rate of maternal serum vitamin D deficiency being 14.1%. A minimum sample size of 206 women is required to ensure at least 80% power and to compensate for the expected attrition or non-response rate of 10%. A structured interviewer-administered questionnaire was used for the data collection. Gestational age was based on the participants' last normal menstrual period confirmed or modified by ultrasound. Maternal socio-demographic data and characteristics such as skin colour and clothing type among others were obtained at presentation and from the participants' case records. A venous blood sample (5ml) was

collected from each participant immediately after delivery and sent to the laboratory where the samples were centrifuged, and serum obtained and stored at -20°C until assayed. Total 25-hydroxyvitamin D level in the serum was measured using a solid-phase competitive enzyme-linked immunosorbent assay (ELISA) according to the manufacturer's instructions (CALBIOTECH® USA Catalog Number VD 2208). Low serum vitamin D was defined as a level below 30ng/mL.

Statistical analyses

Relevant data were collected and analyzed using SPSS version 22.0 for Windows (IBM, Armonk, NY, USA). Descriptive statistics were then computed for all relevant data. Quantitative data were tested for normality with the Kolmogorov-Smirnov test. The independent sample t-test or Mann-Whitney U test was used to compare continuous variables. Univariate analysis was used to test for the association between the baseline variables and adverse pregnancy outcomes and this was followed by multivariate analyses using binary logistic regression models to study the effects of age and other variables that had bivariate P -value < 0.2 , to adjust for confounders in the relationship between low serum vitamin D levels and adverse pregnancy outcomes such as low birth weight and primary postpartum haemorrhage. $P < 0.05$ was considered statistically significant.

Results

The prevalence of vitamin D deficiency in this study was 14.1%. As shown in Table 1, maternal vitamin D levels was not significantly associated with the parturients' age ($P=0.162$), parity ($P=0.102$), BMI ($P=0.821$), educational level ($P=0.612$), religion ($P=0.158$), booking status ($P=0.072$), dressing style ($P=0.439$), alcohol use ($P=0.901$), and skin color ($P=0.170$). Maternal vitamin D level was, however, positively associated with gestational age at delivery ($P=0.012$), delivery of low birth weight neonates ($P=0.004$)

and the occurrence of primary postpartum haemorrhage (PPH) ($P=0.021$). There was no relationship between serum vitamin D levels and perinatal asphyxia (low 5-minute Apgar, $P=0.174$).

The median vitamin D levels in women who delivered babies with low birth weight was 49.5 (30.0-57.0) ng/mL while that of women with normal birth weight babies was 57.0 (42.5-64.5) ng/mL [Figure 1]. In Table 2, after controlling for gestational age at delivery, level of education, and booking status, low maternal vitamin D levels was not independently associated with the delivery of low birth weight babies (adjusted OR-0.76, 95%CI-0.24-2.41). A further multivariate analyses, did not reveal any independent association between low maternal serum vitamin D levels and the occurrence of primary PPH (adjusted OR-2.42, 95%CI-0.79-7.42).

Discussion

Our study revealed an overall prevalence of 14.1% (29/177) for low maternal serum vitamin D, and this is almost one-half of the 29.0% prevalence reported in a study conducted by Gbadegesin et al in similar settings in Lagos.⁹ Despite this disparity, the population of participants recruited in these two studies are mostly well educated and are likely to take diets that are rich in vitamin D and other nutrients compared to women who delivered outside of the health facilities. However, in studies conducted in the United States,¹⁰⁻¹¹ Iran¹² and China¹³ the reported prevalence rates of vitamin D deficiency ranged between 50% and 75.5%. Several studies have shown serum 25(OH)vitamin D deficiency to be higher among dark-skinned women compared to lighter skin women,¹⁴⁻¹⁶ despite dark-complexioned women possessing more melanin that protects their skin against damage from too much Ultraviolet B exposure compared to the fair skinned and Caucasian women. Subsequently, with less Ultraviolet B getting through the skin, less vitamin D is produced each minute.¹⁷ The variation of our study from these other studies may be due to the fact that our study was conducted in Lagos, Nigeria, which is a largely

sunny region all year round and which also has a considerable proportion of women not wearing fully covered clothing as reflected in the findings from this study. This thus exposes them to more sunlight, which has been documented as the major source of naturally occurring vitamin D.^{18,19}

Our study showed that maternal hypovitaminosis D did not have any independent relationship between neonatal LBW. This is similar to the finding by Gbadegesin et al⁹ in Lagos, Nigeria that also reported no association between vitamin D deficiency and pregnancy complications including LBW but in variation to the findings from previous studies conducted in Tehran, Iran by Khalessi et al¹¹ and in Pittsburgh, Pennsylvania by Bodnar et al²⁰ that showed a positive correlation between the two variables. Lee et al in a study carried out in Ann Arbor, Michigan also reported that among 354 newborns, the prevalence of LBW was higher in vitamin D deficient mothers.¹¹ These differences may, however, be as a result of the racial differences in the categories of participants used in these studies compared to ours. Similar studies among predominantly black population of participants especially in the African continents may allow for data synthesis that may be used in arriving at a far-reaching conclusion.

Serum vitamin D deficiency which causes decrease in serum calcium, thereby affecting uterine smooth muscle contractility may result in uterine atony uterus and postpartum hemorrhage. In this study, we assessed the association of Vitamin D deficiency with primary postpartum haemorrhage, a life-threatening condition, which may lead to increased maternal morbidity and mortality, and the likelihood of emergency peripartum hysterectomy. We did not record any independent association unlike previous studies by Khan et al that reported an association between maternal hypovitaminosis D and uterine atony which is a direct cause of primary PPH.²¹ Uterine

atony accounts for 80% of postpartum hemorrhage.²² This may, however, be explained partially by the large proportion of participants with vitamin D deficiency who delivered before term compared to those who delivered at term in this study. A major limitation of this study is the extreme difficulty in extracting reliable information on the intake of vitamin D-rich diets among the women, and this factor could have had some direct or indirect influence on the observed association noted in the initial analyses. The hospital-based setting of the study will also not allow for the extrapolation of any observed association noted in the study to the general population of pregnant women in Lagos.

Conclusion

This study showed that maternal serum hypovitaminosis D did not have any independent relationship with low birth weight, primary PPH and perinatal asphyxia.

Large, well designed, multi-center RCTs are therefore required to determine whether vitamin D supplementation in pregnant women with low vitamin D status will reduce the risk of these adverse pregnancy outcomes.

Conflicts of Interest

The authors report no conflict of interest

Author Contributions

AAO contributed to the conception and design of the study, data collection, analysis, and interpretation, and writing and revising the manuscript. KSO contributed to the conception and design of the study, data collection, and revising the manuscript. OEO contributed to the conception, data collection, writing and revising the manuscript. All authors read and approved the final version of the manuscript.

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