

# Association of Sunlight Exposure and Consumption of Vitamin D-Rich Foods During Pregnancy with Adverse Birth Outcomes in an African Population

Hamudat Balogun, MSc,<sup>1</sup> Jouni J. K. Jaakkola, PhD,<sup>1</sup> and  
A. Kofi Amegah, PhD<sup>2,3</sup>

<sup>1</sup>Center for Environmental and Respiratory Health Research (CERH), University of Oulu, Oulu, Finland

<sup>2</sup>Public Health Research Group, Department of Biomedical Sciences, University of Cape Coast, Cape Coast, Ghana

<sup>3</sup>Department of Clinical Nutrition and Dietetics, University of Cape Coast, Cape Coast, Ghana

Correspondence: A Kofi Amegah, Public Health Research Group, Department of Biomedical Sciences, University of Cape Coast, Cape Coast, Ghana. Tel: +233243032676. E-mail <aamegah@ucc.edu.gh>.

## ABSTRACT

**Background:** Our objective was to assess whether dietary vitamin D (vitD) intake and sunlight exposure during pregnancy is associated with birth outcomes in a healthy Ghanaian population.

**Methods:** A population-based cross-sectional study that included 703 mother-infant pairs accessing postnatal services at the five main health facilities in Cape Coast, Ghana was conducted in 2016. Information on sunlight exposure practices and consumption of vitD-rich foods during pregnancy was collected.

**Results:** A 1 µg increase in vitD intake resulted in a statistically significant 0.00505 weeks increase in gestational age (95% confidence interval [CI]: 0.00005, 0.01004). Mothers classified in the first quartile of vitD intake had 37% (prevalence ratio = 1.37, 95% CI: 1.10, 1.69) increased risk of preterm birth (PTB) compared to their counterparts classified in the fourth quartile. Decreased vitD intake was also associated with low-to-moderate Apgar score.

**Conclusion:** Nutrition education of mothers on the importance of screening for vitD deficiency during early months of pregnancy is recommended.

**KEYWORDS:** vitD, food, sunlight, preterm birth, Apgar score, birth weight

## BACKGROUND

Vitamin D (VitD) is a fat soluble vitamin which plays a key role in bone metabolism and fetal growth through its regulation of calcium and phosphorous homeostasis [1, 2]. VitD is naturally present in few foods such as fatty fishes, egg yolk and sun-exposed mushrooms. Another important source of vitD is ultraviolet rays from sunlight. VitD deficiency is a

major public health problem in many areas of the world [3–5], and it is more common among pregnant women in several populations [6, 7]. VitD deficiency is also a major public health problem in Africa in spite of the plentiful sunlight all year round [8]. High prevalence of vitD deficiency has been reported among women (including pregnant mothers) in Tunisia [9], Tanzania [10], Ethiopia [11] and Nigeria [12, 13].

Fifteen million neonates worldwide are born preterm annually [14]. Of these preterm births (PTBs), 1.1 million die as a result of complications of being born preterm with even more suffering from serious prematurity-related complications including learning disabilities [15]. Low birth weight (LBW) constitute 15% to 20% of all births worldwide, translating into >20 million births annually [16]. More than 95% of LBW babies are delivered in developing countries mostly in Asia and Africa [17]. A recent meta-analysis by Qin *et al.* [18] revealed a significant association between low vitD level and risk of PTB (OR: 1.29; 95% confidence interval [CI]: 1.16–1.45). Another recent systematic review and meta-analysis of longitudinal studies conducted by Amegah *et al.* [19], also found insufficient vitD levels to be associated with increased risk of both early and late PTB. Amegah *et al.* [19], however, reported the association of vitD insufficiency with Apgar score to be conflicting and controversial. Of the studies reviewed by Amegah and colleagues [19], none emanated from the African region. A systematic review and meta-analysis by Thorne-Lyman and Fawzi [20] found no significant association between maternal vitD status and LBW. A review conducted by Harvey *et al.* [21], reported conflicting results on the association between vitD status of mothers and LBW of infants. Again, none of these reviews included studies from Africa.

The only evidence from the African region associating vitD with pregnancy outcomes was a cross-sectional study conducted in Tanzania among 884 HIV-infected pregnant women who took part in a vitamin supplementation trial [10]. The authors found no association between vitD status of the study participants and LBW, PTB and small for gestational age (SGA). There is evidence linking HIV infection with unfavorable pregnancy outcomes including LBW and PTB [22], and hence the need to investigate a healthy population in the attempt to investigate the relationship between vitD intake and pregnancy outcomes in the Africa region so as to eliminate the issue of competing risk.

It is against this background that the objective of the present study is to ascertain whether dietary and non-dietary vitD intake is related with birth outcomes in a healthy Ghanaian population. Our

findings will add to the body of evidence on the importance of vitD during pregnancy in tropical countries.

## METHODOLOGY

Data from the Vitamin D and Pregnancy Outcomes (VDAP) study was analysed for this study. The study protocol has been described elsewhere [8]. In brief, VDAP was a population-based cross-sectional study conducted among mothers–infant pairs accessing postnatal services at the five main health facilities in the Cape Coast metropolitan area. The health facilities are the Cape Coast Teaching Hospital, Cape Coast Metropolitan Hospital, University Hospital, Ewim Polyclinic and Adisadel Urban Health Centre. Cape Coast, the smallest of the six metropolitan areas in Ghana is the capital of the Central Region of Ghana.

Simple random sampling technique was used to select 800 mothers who had singleton births and with no gross anatomical deformities from the five health facilities. The study population included 703 mother-infant pairs (response rate 87.9%).

### Assessment of sunlight exposure and vitamin D nutritional status

The protocols for assessing sunlight exposure and vitD nutritional status have been reported previously [8]. Information on the sunlight exposure practices of mothers were collected using a structured questionnaire. The information collected were the following: outdoor work or visits during pregnancy, trimester of pregnancy when most outdoor visits were made, frequency of outdoor work or visits and amount of time spent, and personal rating of sun exposure during these outdoor work/visits. A two-step procedure was used to summarize this information and define mothers' level of exposure to sunlight with scores ranging from 0 to 8.

A semi-quantitative food frequency questionnaire (FFQ) was used to determine the frequency at which eight vitD-rich foods were consumed by the study participants during pregnancy together with the usual portion size. The frequency of consumption of the selected foods was assessed on a

nine-level scale from 'never' to 'more than three times per day' in the FFQ. Color photographs of the selected food items was used to estimate the portion sizes (in grams) with the information used to estimate vitD intake (in micrograms) of the study participants using a four step procedure.

The selected vitD-rich foods were salmon, mackerel, tuna, sardine, herring, mushrooms (sun exposed), pork (raised outdoors) and egg yolk.

### Outcomes

The outcomes of interest were (1) birth weight (in grams) and LBW (birth weight less than 2500 grams), (2) gestational age (in weeks) and PTB (less than 37 completed weeks of gestation) and (3) low to moderate Apgar score (<7 on both the 1-min and 5-min Apgar score). The maternal health books were the source of the birth weight and gestational age data. A regularly calibrated weighing scale was used to measure birth weight of the newborns immediately after delivery. The last menstrual period (LMP) method was used to estimate gestational age. Apgar score was also estimated immediately after birth and comprises five components; color, heart rate, reflex irritability, muscle tone and respiration, each of which is given a score of 0, 1 or 2.

### Covariates

The potential confounders adjusted in the analysis were age, educational level, religion, ethnicity, occupation, monthly income level, parity and pre-pregnancy body mass index (BMI) of mothers, as well as nutritional supplementation, and malaria and sexually transmitted infections during pregnancy.

### Ethical consideration

The University of Cape Coast Institutional Review Board gave approval for the study (Ethical clearance ID No: UCCIRB/CANS/2015/03). We also sought approval from the management of the five selected facilities. Consent of all participants was sought before inclusion in the study using an informed consent form.

### Statistical analysis

Mean birth weight, gestational age and Apgar score were compared according to quartiles of vitD food

consumption and sunlight exposure using one-way ANOVA. The Tukey Post Hoc test was used to establish the group means that differ. We estimated the effect of vitD intake on birth weight, gestational age and Apgar score using linear regression modeling. Modified Poisson regression with logarithmic link function was used to estimate the effects of vitD intake and sunlight exposure on the occurrence of LBW, PTB and low to moderate Apgar score. The 95% CIs of the prevalence ratios estimated from the Modified Poisson regression were based on robust error variance [23]. All models were adjusted for potential confounders. Respondents in the highest quartile of vitD intake and sunlight exposure was the reference in the analysis. The analysis was performed using Stata version 13.

## RESULTS

The socio-demographic characteristics of the participants are presented in [Table 1](#). Over half (52%) of the participants were within the age group 20–29 years. Participants educated up to the university/tertiary level constituted 27%. Participants with no formal education constituted 8%. The proportion of participants who were employed was 76% with housewives and unemployed participants constituting 17%. About 87% of the participants were Christians with Muslims making up 12%. About 74% of the participants were Akans. About 74% of the participants were married. Participants earning a monthly income of more than GH¢1000 was 8%.

[Table 2](#) presents the obstetric history, and health, nutritional and lifestyle characteristics of the study participants. A very high proportion of the mothers took nutritional supplement (97.4%). About 23% of the mothers indicated being diagnosed of malaria during pregnancy. About 31% of the respondents were anemic during pregnancy. Only 3.4% of the mothers reported contracting sexually transmitted disease during pregnancy. About 52% of the mothers were either overweight or obese. Mothers who were classified as underweight was 6%.

[Tables 3](#) and [4](#) presents means of birth weight, gestation age, and 1-min and 5-min Apgar score according to quartiles of vitD intake and sunlight exposure of the respondents, respectively. Mean birth weight ranged from 3.127 kg (lowest quartile) to 3.266 kg (highest

**Table 1. Socio-demographic characteristics of respondents (N = 703)**

Characteristic	n (%)
<b>Age group (years)</b>	
<20	55 (7.8)
20–29	368 (52.3)
30–39 <sup>1</sup>	260 (37.0)
>39 <sup>1</sup>	17 (2.4)
Missing	3 (0.4)
<b>Education</b>	
None/Primary	55 (7.8)
Junior High School (JHS)	278 (39.5)
Senior High School (SHS)/Secondary/Technical	177 (25.2)
University/Tertiary <sup>2</sup>	191 (27.2)
Missing	2 (0.3)
<b>Occupation</b>	
Employed <sup>3</sup>	534 (76.0)
Hairdresser/Seamstress	138 (25.8)
Office worker	44 (8.2)
Trader/Street vendor/Fish monger	178 (33.3)
Other	174 (32.6)
Student	49 (7.0)
Housewife/Unemployed	119 (16.9)
Missing	1 (0.1)
<b>Religion</b>	
Christian <sup>4</sup>	612 (87.1)
Moslem	86 (12.2)
Other	2 (0.3)
Missing	1 (0.1)
<b>Ethnic group</b>	
Akan <sup>5</sup>	520 (74.0)
Ewe	41 (5.8)
Ga	11 (1.6)
Hausa and other northern tribe	80 (11.4)
Other southern tribe	47 (6.7)
Foreigner	4 (0.6)
<b>Marital status</b>	
Single	99 (14.1)
Married	522 (74.3)
Cohabitation	78 (11.1)
Divorced	3 (0.4)
Missing	1 (0.1)
<b>Monthly income (GH¢)</b>	
None	115 (16.4)

(continued)

**Table 1. (continued)**

Characteristic	n (%)
<200	210 (35.7)
201–500	208 (35.4)
501–1000	114 (19.4)
>1000 <sup>6</sup>	56 (8.0)
<b>Skin color</b>	
Dark	273 (38.8)
Light/Fair <sup>7</sup>	168 (23.9)
Intermediate/Chocolate	261 (37.1)
Missing	1 (0.1)

Covariates: <sup>1</sup>>30 years, <sup>2</sup>University/Tertiary, <sup>3</sup>Employed, <sup>4</sup>Christian, <sup>5</sup>Akan, <sup>6</sup>>GH¢1000, <sup>7</sup>Light/Fair served as reference.

quartile) with regards to maternal vitD intake ( $p = 0.1331$ ), and 3.095 kg (lowest quartile) to 3.247 kg (upper quartile) with regards to maternal sunlight exposure ( $p = 0.1405$ ). There was a difference in mean gestational age ( $p = 0.0178$ ), and 1-min ( $p = 0.0037$ ) and 5-min ( $p = 0.0293$ ) Apgar score with respect to maternal vitD intake. Respondents in the third quartile recorded the highest mean estimate. With respect to maternal sunlight exposure, there was no statistically significant differences in mean gestational age, and 1-min and 5-min Apgar score.

Mean vitD intake and sunlight exposure score was found to be 71.41 µg (SD: 50.74 µg) and 5.71 (SD: 2.36), respectively. Table 5 present the effect of maternal vitD intake on gestational age, birth weight and Apgar score. A 1 µg increase in vitD intake resulted in a statistically significant 0.00505 weeks increase in gestational age (95% CI: 0.00005, 0.01004). For the remaining outcomes, the results were not statistically significant. Tables 6 and 7 present the effect of maternal vitD intake and sunlight exposure on prevalence of adverse perinatal outcomes. Compared to participants classified in the fourth quartile of vitD intake, participants classified in the third quartile had 76% decreased risk of LBW (Prevalence ratio [PR]: 0.24, 95% CI: 0.07, 0.83). Participants classified in the first quartile of vitD intake had 37% (PR = 1.37, 95% CI: 1.10, 1.69) increased risk of PTB compared to their counterparts classified in the fourth quartile. Participants classified in the second quartile of vitD intake had

**Table 2. Obstetric history, and health, nutritional and lifestyle characteristics of respondents (N = 703)**

Characteristic	n (%)
<b>Parity</b>	
Primiparous	307 (43.7)
Multiparous	396 (56.3)
<b>Intake of prescribed nutritional supplements</b>	
Yes	685 (97.4)
No	18 (2.6)
<b>Pre-pregnancy BMI (kg/m<sup>2</sup>)</b>	
Underweight (<18.5)	40 (5.7)
Normal (18.5–24.9)	294 (41.8)
Overweight (25.0–29.9)	214 (30.4)
Obese (≥30.0)	151 (21.5)
Missing	4 (0.6)
<b>Malaria infection during pregnancy</b>	
Yes	158 (22.5)
No	545 (77.5)
<b>Anaemia episode during pregnancy</b>	
Yes	215 (30.6)
No	481 (68.4)
Missing	7 (1.0)
<b>Sexually transmitted infection during pregnancy</b>	
Yes	24 (3.4)
No	667 (94.9)
Missing	12 (1.7)
<b>Smoking status</b>	
Smoker	1 (0.1)
Non-smoker	702 (99.9)

53% (PR = 1.53, 95% CI: 1.12, 2.08) and 258% (PR = 3.58, 95% CI: 1.36, 9.39) increased risk of delivering babies with low to moderate 1-min and 5-min Apgar score, respectively. Participants classified in the first quartile of sunlight exposure had 71% (PR = 1.71, 95% CI: 0.86, 3.42) increased risk of LBW, compared to their counterparts classified in the fourth quartile. The CI, however, included the null value. Inadequate maternal sunlight exposure was not associated with the other outcomes studied.

## DISCUSSION

Low maternal vitD intake was associated with PTB and low to moderate Apgar score of newborns. Moderate maternal vitD intake was associated with decreased risk of LBW. A 1 µg increase in vitD intake resulted in a slight increase in gestational age. Sunlight exposure score was not associated with adverse perinatal outcomes in the study area.

### Validity of results

Selection bias was minimized in the study owing to the population-based nature of the study and the high response rate achieved (87.9%). The potential selection bias from the exclusion of mothers who do not access postnatal services was also minimized. In urban areas of Ghana including Cape Coast, there is high patronage of postnatal services as a result of the high level of awareness of Reproductive and Child Health (RCH) services and benefits among urban residents and the easy access to RCH services due to the short traveling distances [24]. The potential selection bias emanating from mothers delivering at home and not accessing postnatal services should not be a concern in the study. This is because, in urban areas of Ghana, only very few mothers deliver at home compared to rural areas [24]. In addition, the small number of home births in urban Ghana usually occurs by accident with majority of these mothers immediately taken to the nearest health facility as result of the wide distribution of health services in these areas.

The outcomes of interest were retrieved from maternal health books of the mothers and were not self-reported. The birth weight and Apgar score were taken and recorded immediately after delivery in the maternal health books and hence are quite reliable. Gestational age of the mothers was assessed using the LMP. Using the LMP method for determining gestational age has limitations and can obviously result in invalid estimates of gestational age but as pointed out by Lynch and Zhang [25] so does the ultrasound measurements. However, any potential misclassification bias in our study from the use of the LMP method is likely to be non-differential as assessment of gestational age was independent of our study.

Maternal sunlight exposure was assessed retrospectively using a structured questionnaire.

**Table 3. Birth weight, gestational age and Apgar score according to quartiles of vitD intake**

	Quartile			
	I (n = 175)	II (n = 176)	III (n = 176)	IV (n = 176)
<b>Birth weight</b>				
Mean	3.165	3.135	3.263	3.205
Standard deviation	0.582	0.559	0.481	0.512
	$F = 1.87, p = 0.1331$			
<b>Gestational age</b>				
Mean	35.66	36.53	36.62	36.61
Standard deviation	3.99	3.42	2.95	2.90
	$F = 3.38, p = 0.0178, \text{Post Hoc } p: 0.036^{\text{III vs I}}; 0.040^{\text{IV vs I}}$			
<b>1-min Apgar score</b>				
Mean	6.89	6.65	7.03	7.00
Standard deviation	0.96	1.26	1.04	0.97
	$F = 4.53, p = 0.0037, \text{Post Hoc } p: 0.005^{\text{III vs II}}; 0.012^{\text{IV vs II}}$			
<b>5-min Apgar score</b>				
Mean	8.06	7.89	8.27	8.16
Standard deviation	0.91	1.22	0.78	0.81
	$F = 3.02, p = 0.0293, \text{Post Hoc } p: 0.0022^{\text{III vs II}}; 0.045^{\text{IV vs II}}$			

**Table 4. Birth weight, gestational age and Apgar score differences in sunlight exposure of respondents**

	Quartile			
	I (n = 117)	II (n = 90)	III (n = 153)	IV (n = 338)
<b>Birth weight</b>				
Mean	3.095	3.212	3.247	3.193
Standard deviation	0.570	0.508	0.478	0.556
	$F = 1.83, p = 0.1405$			
<b>Gestational age</b>				
Mean	36.51	36.36	36.50	36.22
Standard deviation	3.37	3.90	3.10	3.33
	$F = 0.36, p = 0.7836$			
<b>1-min Apgar score</b>				
Mean	6.87	6.81	6.93	6.91
Standard deviation	1.30	0.94	0.92	1.08
	$F = 0.24, p = 0.8673$			
<b>5-min Apgar score</b>				
Mean	8.07	8.01	8.11	8.12
Standard deviation	1.09	0.98	0.97	0.89
	$F = 0.34, p = 0.7994$			

**Table 5. Effect of maternal vitD intake on gestational age, birth weight and Apgar score**

	Unadjusted $\beta$ (95% CI)	Adjusted $\beta$ (95% CI)
Gestational age	0.00495 (0.00005, 0.00986)	0.00505 (0.00005, 0.01004)
Birth weight	0.00026 (−0.00052, 0.00105)	0.00008 (−0.00072, 0.00088)
1-min Apgar score	0.00182 (0.00025, 0.00338)	0.00137 (−0.00021, 0.00296)
5-min Apgar score	0.00128 (−0.00011, 0.00268)	0.00108 (−0.00035, 0.00251)

Covariates were age, education, religion, ethnic group, employment status, monthly income, parity, nutritional supplementation, pre-pregnancy BMI, and malaria and sexually transmitted infection.

The reliability and validity of this method has previously been investigated [26–29]. According to Milen and Bodnar [26], population-based studies on vitD nutritional status should determine individual-specific sunlight exposure where possible because sunlight exposure can account for majority (approximately 90%) of circulatory vitD. However, studies [27–29] have reported weak correlation between vitD status and self-reported sunlight exposure. According to McCarthy [29], the weak correlations reported is not surprising. This is because cutaneous vitD synthesis is also influence by personal factors such as melanin content in skin and age. McCarthy [29] concluded that questionnaires used to assess sunlight exposure currently provide imprecise estimates of vitD status. King *et al.* [30] have also revealed that self-reported questionnaire provides a valid ranking in long-term sun exposure over other methods. We did, however, evaluate the potential confounding role of age and skin color in the analysis.

A semi-quantitative FFQ was used to assess the vitD nutritional status of the respondents. Use of FFQ for estimating the usual food and nutrient intake of study participants has limitations and we have documented these issues and the practical advantages it offers over other diet measurement methods in our previous report [8]. In this report, we have also justify the inclusion of mushroom and pork meat, and exclusion of milk and breakfast cereal in the determination of vitD intake.

Our study adjusted for a number of potential confounders in the analysis including age, educational level, religion, ethnicity, employment status, monthly income, parity, nutritional supplementation, pre-pregnancy BMI, skin color, malaria and STD.

However, we were unable to assess the potential confounding role of gestational hypertension and diabetes, bacterial vaginosis and history of preterm. This is as a result of our inability to collect information on these important risk factors. We did not also adjust for smoking status of the mothers. However, in Ghana, only 0.4% of women smoke [31] and so this cannot be considered to compromise the validity of our result.

In this study, we were able to address some of the limitations of previous studies. Most of the previous studies only considered diet in the assessment of vitD nutritional status, whereas our study considered both diet and sunlight exposure. As indicated earlier, sunlight is the main source of vitD and should be considered in the estimation of vitD intake in epidemiologic studies to better capture individuals' vitD status. We have documented the limitations with the approach used to assess sunlight exposure together with our inability to collect information on the clothing style of participants especially Muslims, and use of sunscreen in our previous report [8].

#### Synthesis with previous studies

Very limited number of studies provides information on vitD levels of pregnant women in African countries which experience sunlight all year round. We previously reported vitD intake of pregnant women in this population to be low ( $71.41 \pm 50.74 \mu\text{g}$ ) with vitD nutrition awareness during pregnancy also noted to be low [8]. Studies conducted in Ethiopia [11], Nigeria [12, 13] and East African populations [32] have also reported low vitD levels among women including pregnant mothers.

We found low levels of vitD intake to be associated with PTB. Mothers classified in the lowest quartile of vitD intake had 37% increased risk of PTB.

**Table 6. Modified poisson regression of adverse perinatal outcomes on maternal vitD intake (N = 703)**

Quartile	LBW (n = 43)		PTB (n = 332)		Low to moderate 1-min Apgar score (n = 207)		Low to moderate 5-min Apgar score (n = 30)	
	Unadjusted PR (95% CI)	Adjusted PR (95% CI)	Unadjusted PR (95% CI)	Adjusted PR (95% CI)	Unadjusted PR (95% CI)	Adjusted PR (95% CI)	Unadjusted PR (95% CI)	Adjusted PR (95% CI)
I	1.02 (0.47, 2.22)	0.96 (0.43, 2.12)	1.40 (1.13, 1.73)	1.37 (1.10, 1.69)	1.17 (0.83, 1.65)	1.10 (0.78, 1.54)	1.82 (0.62, 5.33)	1.92 (0.66, 5.55)
II	1.34 (0.65, 2.75)	1.36 (0.67, 2.76)	1.20 (0.95, 1.50)	1.15 (0.91, 1.45)	1.56 (1.14, 2.14)	1.53 (1.12, 2.08)	2.66 (0.97, 7.31)	3.58 (1.36, 9.39)
III	0.25 (0.07, 0.88)	0.24 (0.07, 0.83)	0.95 (0.74, 1.22)	0.91 (0.70, 1.17)	1.03 (0.72, 1.48)	0.96 (0.67, 1.37)	0.61 (0.15, 2.50)	0.70 (0.17, 2.95)
IV	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00

Covariates were age, education, religion, ethnic group, employment status, monthly income, parity, nutritional supplementation, pre-pregnancy BMI, and malaria and sexually transmitted infection.

**Table 7. Modified poisson regression of adverse perinatal outcomes on maternal sunlight exposure (N = 703)**

Quartile	LBW (n = 43)		PTB (n = 332)		Low to moderate 1-min Apgar score (n = 207)		Low to moderate 5-min Apgar score (n = 30)	
	Unadjusted PR (95% CI)	Adjusted PR (95% CI)	Unadjusted PR (95% CI)	Adjusted PR (95% CI)	Unadjusted PR (95% CI)	Adjusted PR (95% CI)	Unadjusted PR (95% CI)	Adjusted PR (95% CI)
I	1.78 (0.92, 3.45)	1.71 (0.86, 3.42)	0.78 (0.61, 1.00)	0.79 (0.61, 1.01)	0.81 (0.57, 1.15)	0.74 (0.52, 1.05)	1.24 (0.49, 3.16)	1.04 (0.41, 2.63)
II	0.54 (0.16, 1.77)	0.55 (0.18, 1.73)	0.90 (0.70, 1.15)	0.91 (0.71, 1.16)	1.13 (0.81, 1.57)	1.02 (0.73, 1.43)	1.12 (0.38, 3.31)	0.95 (0.31, 2.95)
III	0.64 (0.26, 1.56)	0.69 (0.28, 1.71)	0.92 (0.75, 1.12)	0.95 (0.78, 1.16)	0.90 (0.67, 1.22)	0.89 (0.66, 1.21)	0.96 (0.38, 2.45)	0.86 (0.32, 2.27)
IV	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00

Covariates were age, religion, ethnic group, employment status and skin color.



Our result is consistent with a study conducted in the Netherlands [33] that also reported mothers in the lowest quartile of vitD intake to have 72% increased risk of PTB (OR: 1.72; 95% CI: 1.14–2.60). The authors estimated the population attributable risk of low vitD level for PTB to be 17.3%. It must, however, be pointed out that this study relied on laboratory measurements in the estimation of vitD intake of their study population. A study conducted in Texas [34], however, found no statistically significant association between women classified in the lowest quartile of vitD intake and risk of PTB (OR: 1.33, 95% CI: 0.48–3.70).

The recent systematic review and meta-analysis conducted by Amegah *et al.* [19] reported that the association of vitD insufficiency with low Apgar score is controversial and conflicting. We found low levels of vitD intake to be associated with increased risk of delivering babies with low-to-moderate 1- and 5-min Apgar score and certainly sheds some light on the association. Our findings are similar to the findings a study conducted in Tehran [35] that also used FFQ in assessing vitD status. This study found 1-min Apgar score to be higher in infants whose mother had sufficient vitD level ( $p = 0.03$ ).

Regarding LBW, we found mothers in the third quartile of vitD intake to have 76% decreased risk of LBW compared to mothers classified in the fourth quartile. This is contrary to our expectation but consistent with the findings of the only previous study [10] conducted in the African region on the topic. This study found low levels of vitD to be associated with 16% decreased risk of LBW (RR: 0.84, 95% CI: 0.55–1.28). It must, however, be pointed out that this study was conducted among HIV infected mothers.

### Biological plausibility

The role of vitD in modulation of maternal and fetal calcium homeostasis cannot be over-emphasized. Insufficient vitD can lead to malabsorption of calcium, an essential nutrient in pregnancy for adequate fetal development and growth [36]. Mahon *et al.* [37] reported that insufficient vitD intake during pregnancy can affect fetal skeleton development and function. Poor fetal development and growth can result in PTB, LBW, low Apgar score and other adverse perinatal outcomes [38, 39].

VitD also has immunomodulatory properties that help in the formation of vitD3 in the placenta and is important for proper growth and development of both the mother and fetus [40]. Liu and Hewison [36] reported that vitD3 act as either an immunomodulator or as a regulator of implantation gene during the fetal-maternal interface. The authors further reported that VitD plays a significant role in boosting immune responses to reduce the risk of inflammation in the tissue at the fetal-maternal interface. VitD has also been found to increase tolerogenic immunity through the induction of immunosuppressive regulatory T cell (Treg) during pregnancy [41]. VitD's role in immune responses also helps in stimulating antimicrobial activity and aid intracellular killing of bacteria [42, 43]. Studies have revealed that VitD plays an important role in generating cathelicidin (an antimicrobial peptides) which is vital in the prevention of infection during pregnancy and also in early childhood [44, 45]. Romero *et al.* [46] reported that intrauterine infection is one of the possible risk factors of PTB which can be related to the stimulation of the innate immune system.

### CONCLUSION

In conclusion, the importance of vitD throughout the life-course of an individual cannot be over-emphasized. In spite of the fact that several studies have investigated the effect of vitD on pregnancy outcomes, they have mainly been conducted in developed countries. Studies from Africa are very rare despite the increasing occurrence of adverse pregnancy outcomes in the region. Our study is therefore timely and revealed that low intake of vitD-rich food can increase the risk of PTB and low Apgar score of the newborn. Inadequate sunlight exposure could also increase the risk of LBW. There is a need for more studies in Africa on the adverse health effects of low vitD intake to enhance the literature. Nutritional education of mothers on the importance of screening for vitD deficiency during the early months of pregnancy is also recommended.

### ACKNOWLEDGEMENTS

We would like to acknowledge all the mothers who participated in this study. We will also like to thank the field staff.

## REFERENCES

1. Ross AC, Manson JE, Abrams SA, *et al.* The 2011 Dietary Reference Intakes for Calcium and VitD: what dietetics practitioners need to know. *J Am Diet Assoc* 2011;111: 524–7.
2. Nair R, Maseeh A. VitD: the “sunshine” vitamin. *J Pharmacol Pharmacother* 2012;3:118–26.
3. Dror DK, Allen LH. VitD inadequacy in pregnancy: biology, outcomes, and interventions. *Nutr Rev* 2010;68:465–77.
4. Mithal A, Wahl DA, Bonjour JP, *et al.* Global vitD status and determinants of hypovitaminosis D. *Osteoporos Int* 2009;20:1807–20.
5. Holick MF. VitD deficiency. *N Engl J Med* 2007;357: 266–81.
6. Dawodu A, Wagner CL. Prevention of vitD deficiency in mothers and infants worldwide – a paradigm shift. *Paediatr Int Child Health* 2012;32:3–13.
7. Dawodu A, Akinbi H. VitD nutrition in pregnancy: current opinion. *Int J Womens Health*. 2013;5: 333–43.
8. Amegah AK, Nsoh M, Ashley-Amegah G, Anaman-Togbor J. What factors influences dietary and non-dietary vitD intake among pregnant women in an African population? *Nutrition* 2018;50:36–44.
9. Meddeb N, Sahli H, Chahed M, *et al.* VitD deficiency in Tunisia. *Osteoporos Int*. 2005;16:180–3.
10. Mehta S, Hunter DJ, Mugusi FM, *et al.* Perinatal outcomes, including mother-to-child transmission of HIV, and child mortality and their association with maternal vitD status in Tanzania. *J Infect Dis* 2009;200:1022–30.
11. Feleke Y, Abdulkadir J, Mshana R, *et al.* Low levels of serum calcidiol in an African population compared to a North European population. *Eur J Endocrinol* 1999;141: 358–60.
12. Okonofua FE, Calcium and vitD nutrition in Nigerian women and children. In: Thacher TD (ed). *Nutritional Rickets in Nigerian Children: The Way Forward*. Vevey, Switzerland: Nestle Nutrition, 2002, 17–21.
13. Okonofua F, Houlder S, Bell J, Dandona P. VitD nutrition in pregnant Nigerian women at term and their newborn infants. *J Clin Pathol* 1986;39:650–3.
14. WHO. Preterm birth Fact sheet. Reviewed November 2016. <http://www.who.int/mediacentre/factsheets/fs363/en/> (22 November 2017, date last accessed).
15. WHO. 15 Million babies born too soon. [http://www.who.int/mediacentre/news/releases/2012/preterm\\_20120502/en/](http://www.who.int/mediacentre/news/releases/2012/preterm_20120502/en/) (22 November 2017, date last accessed).
16. WHO. Global Nutrition Targets 2025: Low birth weight policy brief. [http://www.who.int/nutrition/publications/globaltargets2025\\_policybrief\\_lbwh/en/](http://www.who.int/nutrition/publications/globaltargets2025_policybrief_lbwh/en/) (22 November 2017, date last accessed).
17. Kiess W, Chernaus SD, Hokken-Koelega ACS (eds.). *Small for Gestational Age. Causes and Consequences*. Pediatric and Adolescent Medicine. vol. 13. Basel: Karger, 2009, pp 148–62.
18. Qin LL, Lu FG, Yang SH, *et al.* Does maternal vitD deficiency increase the risk of preterm birth: a meta-analysis of observational studies. *Nutrients* 2016;8:pii: E301.
19. Amegah AK, Klevor MK, Wagner CL. Maternal vitD insufficiency and risk of adverse pregnancy and birth outcomes: a systematic review and meta-analysis of longitudinal studies. *PLoS One* 2017;12:e0173605.
20. Thorne-Lyman A, Fawzi WW. VitD during pregnancy and maternal, neonatal and infant health outcomes: a systematic review and meta-analysis. *Paediatr Perinat Epidemiol* 2012;26(Suppl. 1):75–90.
21. Harvey NC, Holroyd C, Ntani G, *et al.* VitD supplementation in pregnancy: a systematic review. *Health Technol Assess* 2014;18:1–190.
22. Xiao P, Zhou Y, Chen Y, *et al.* Association between maternal HIV infection and low birth weight and prematurity: a meta-analysis of cohort studies. *BMC Pregnancy and Childbirth* 2015;15:246.
23. Zou G. A modified poisson regression approach to prospective studies with binary data. *Am J Epidemiol* 2004;159:702–6.
24. Amegah AK, Damptey OK, Sarpong GA, *et al.* Malaria infection, poor nutrition and indoor air pollution mediate socioeconomic differences in adverse pregnancy outcomes in Cape Coast, Ghana. *Plos One* 2013;8:10.
25. Lynch CD, Zhang J. The research implications of the selection of a gestational age estimation method. *Paediatr Perinat Epidemiol* 2007;21(Suppl. 2):86–96.
26. Millen AE, Bodnar LM. VitD assessment in population-based studies: a review of the issues1– 4. *Am J Clin Nutr* 2008;87(Suppl):1102S–5S.
27. Brot C, Vestergaard P, Kolthoff N, *et al.* VitD status and its adequacy in healthy Danish perimenopausal women: relationships to dietary intake, sun exposure and serum parathyroid hormone. *Br J Nutr* 2001;86(Suppl. 1):S97–103.
28. van der Mei IA, Blizzard L, Ponsonby AL, Dwyer T. Validity and reliability of adult recall of past sun exposure in a case-control study of multiple sclerosis. *Cancer Epidemiol Biomarkers Prev* 2006;15:1538–44.
29. McCarty CA. Sunlight exposure assessment: can we accurately assess vitD exposure from sunlight questionnaires? *Am J Clin Nutr* 2008;87:1097S–1S.
30. King L, Dear K, Harrison SL, *et al.* Investigating the patterns and determinants of seasonal variation in vitD status in Australian adults: the Seasonal D Cohort Study. *BMC Public Health BMC series – open, inclusive and trusted* 2016;16:892.
31. Ghana Statistical Service (GSS), Ghana Health Service (GHS), and ICF Macro. *Ghana Demographic and Health Survey 2008*. Accra, Ghana: GSS, GHS, and ICF Macro, 2009.
32. Luxwolda MF, Kuipers RS, Kema IP, *et al.* VitD status indicators in indigenous populations in East Africa. *Eur J Nutr* 2013;52:1115–25.

33. Miliku K, Vinkhuyzen A, Blanken LM, *et al.* Maternal vitD concentrations during pregnancy, fetal growth patterns, and risks of adverse birth outcomes. *Am J Clin Nutr* 2016; 103:1514–22.
34. Thorp JM, Camargo CA, McGee PL, *et al.* VitD status and recurrent preterm birth: a nested case-control study in high-risk women. *BJOG* 2012;119:1617–23.
35. Sabour H, Hossein-Nezhad A, Maghbooli Z, *et al.* Relationship between pregnancy outcomes and maternal vitD and calcium intake: a cross-sectional study. *Gynecol Endocrinol* 2006;22:585–9.
36. Liu NQ, Hewison M. VitD, the placenta and pregnancy. *Arch Biochem Biophys* 2012;523:37–47.
37. Mahon P, Harvey N, Crozier S, Study Group SWS, *et al.* Low maternal vitD status and fetal bone development: cohort study. *J Bone Miner Res* 2010;25:14–9.
38. Coutinho PR, Cecatti JG, Surita FG, *et al.* Perinatal outcomes associated with low birth weight in a historical cohort. *Reprod Health* 2011;8:18.
39. Cosmi E, Fanelli T, Visentin S, *et al.* Consequences in Infants That Were Intrauterine Growth Restricted. *J Pregnancy* 2011;2011:364381.
40. Rebut-Bonneton C, Demignon J. Effects of 1, 25-dihydroxyvitD3 on in vitro lymphocyte reactions: arguments for a role at the maternofetal interface. *Gynecol Obstet Invest* 1991;32:134–8. PMID: 1836774.
41. Barrat FJ, Cua DJ, Boonstra A, *et al.* In vitro generation of interleukin 10-producing regulatory CD4(+) T cells is induced by immunosuppressive drugs and inhibited by T helper type 1 (Th1)- and Th2-inducing cytokines. *J Exp Med* 2002;195:603–16.
42. Adams JS, Hewison M. Unexpected actions of vitD: new perspectives on the regulation of innate and adaptive immunity. *Nat Clin Pract Endocrinol Metab* 2008;4:80–90.
43. Hewison M. VitD and immune function: an overview. *Proc Nutr Soc* 2012;71:50–61.
44. Liu PT, Stenger S, Li H, *et al.* Toll-like receptor triggering of a vitD-mediated human antimicrobial response. *Science* 2006;311:1770–3.
45. Walker VP, Modlin RL. The vitD connection to pediatric infections and immune function. *Pediatr Res* 2009;65:106R–13R.
46. Romero R, Espinoza J, Kusanovic JP, *et al.* The preterm parturition syndrome. *Br J Obstet Gynaecol* 2006;113:17–42.