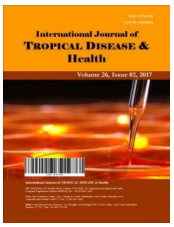

International Journal of TROPICAL DISEASE & Health

38(1): 1-10, 2019; Article no.IJTDH.50589
ISSN: 2278–1005, NLM ID: 101632866

Maternal Vitamin D Status and Risk of Preeclampsia in Abuja, Nigeria

Kate Ifeoma Omonua[1,2*], Olutunde Onafowokan[2], Nathaniel Adewole[1,2], Maxwell Nwegbu[3,4], Aliyu Yabaji Isah[1,2] and Odiase Special Omonua[5]

[1]College of Health Sciences, Department of Obstetrics and Gynaecology, University of Abuja, Nigeria.
[2]Department of Obstetrics and Gynaecology, University of Abuja Teaching Hospital, Abuja, Nigeria.
[3]Department of Chemical Pathology, University of Abuja, Abuja, Nigeria.
[4]Department of Chemical Pathology, University of Abuja Teaching Hospital, Abuja, Nigeria.
[5]Endocrinology Unit, Department of Internal Medicine, University of Abuja Teaching Hospital, Abuja, Nigeria.

Authors' contributions

This work was carried out in collaboration among all authors. Author KIO designed the study, collected the data and wrote the first draft of the manuscript. Authors KIO and OSO performed the literature searches and managed the analyses of the study. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/IJTDH/2019/v38i130179
Editor(s):
(1) Dr. Payala Vijayalakshmi, Department of Microbiology, Gitam Institute of Medical Sciences and Research, GITAM University, India.
Reviewers:
(1) S. Sreelatha, International Medical University, Malaysia.
(2) Ayfer Pazarbasi, Çukurova University, Turkey.
(3) Apeksha Niraula, B. P. Koirala Institute of Health Sciences, India.
Complete Peer review History: http://www.sdiarticle3.com/review-history/50589

Original Research Article

Received 09 June 2019
Accepted 14 August 2019
Published 21 August 2019

ABSTRACT

Aim: To determine the relationship between maternal serum 25(OH) D concentrations and development of preeclampsia.
Study Design: A cross sectional comparative study.
Place and Duration of Study: Department of Obstetrics and Gynaecology, University of Abuja Teaching Hospital, Abuja, between March 2016 and February 2017.
Methodology: We included 55 women with preeclampsia and 55 healthy women. Data obtained included sociodemographic characteristics, clothing style and duration of exposure to sun light. ELISA method was used for evaluation of serum vitamin D levels.

**Corresponding author: Email: kateodogwu@yahoo.com;*

Results: The prevalence of VD deficiency in the population was 15%, while 16.8% and 73% of the participants had insufficient and normal levels respectively. The prevalence of VD deficiency in women with preeclampsia was 20.4% while that in healthy pregnant women was 9.4% (*P*=.19). The mean serum 25-OH-D level of women with pre-eclampsia was significantly lower than that of healthy women (34.5±14.9 vs. 43.5±15.1, *P* = .003). Preeclamptic women with vitamin D insufficiency delivered at a higher gestational age than those with vitamin D deficiency (37.67(2.77) weeks vs. 33.55(2.38) weeks respectively, *P* = .007). In the adjusted analysis of cases with vitamin D defficiency, the odds of developing preeclampsia was not statistically significant [odds ratio (OR) = 3.27, CI = 0.99-10.83, *P* =.05]. However, the odds of developing preeclampsia in women with Vitamin D insufficiency was statistically significant (OR = 3.20, CI = 1.02–10.06, = 0.046).
Conclusion: In conclusion, an association between vitamin D deficiency and preeclampsia was not demonstrated in this study. The results however suggest that maternal vitamin D insufficiency in late pregnancy is an independent risk factor for preeclampsia.

Keywords: Vitamin D; Vitamin D status; preeclampsia; Abuja; Nigeria.

1. INTRODUCTION

Hypertensive disorders complicate 5 to 10 percent of all pregnancies. The World Health Organisation (WHO) estimates the incidence of preeclampsia to be seven times higher in developing countries (2.8% of live births) than in developed countries (0.4%) and 10-25% of these cases will result in maternal death [1,2]. In Nigeria, it's a major cause of maternal morbidity and mortality with incidence rates of about 1-9% and accounting for up to 40 percent of maternal deaths [3]. The fact that preeclampsia has remained a significant contributor to maternal morbidity and mortality [1,2] has led to active research in its primary prevention. With regard to this, efforts have been directed on the use of anti-inflammatory agents and micronutrients, including vitamin D [4].

An emerging area of study that has attracted significant attention is the role of vitamin D and its active metabolite, 1,25-dihydroxyvitamin D. Increased production of inflammatory cytokines, such as TNF-α, have been reported in pregnancies complicated by vitamin D deficiency. Furthermore, 1,25-dihydroxyvitamin D stimulates the activity of T-regulatory cells, which are vital in supporting placental implantation through immune tolerance. Also, in preeclampsia, the metabolism of vitamin D in placental tissue is altered, and these differences may play a role in the abnormal trophoblastic invasion found in these pregnancies [5]. It is also possible that in preeclampsia, insufficiency in the production of vitamin D by the placenta causes a reduction in the gastrointestinal absorption of calcium. With a decrease in the serum level of calcium, synthesis of parathyroid hormone is increased and this may cause hypertension [6].

Vitamin D deficiency has been found in up to 50% of pregnant women and it has also been noted to have increased incidence among persons of African American race. [7] Other factors that have been suggested to affect vitamin D levels include use of sunscreen, decreased sun exposure, insufficient dietary intake, covering dressing style, effect of northern latitude and seasonal changes [8,9].

Data from similar geographical region and population like ours appear to be sparse and results obtained from those identified appear to be conflicting. For example, Feleke et al. [10] compared vitamin D status in people living in Ethiopia (10ºN) with people living in Oslo (60ºN) and found that the Ethiopians had significantly lower serum levels of s-calcidiol than the Norwegians (25 (17–46) nmol/l vs 36 (27–57) nmol/l, P < 0.02). Possible explanation for this surprising result was the clothing style of the population of pregnant women studied which coupled with skin colour, reduced the capacity for vitamin D production. Conversely, another study by Okonofua et al. [11] had found that the mean serum levels of Vitamin D in all Nigerian women(including those practising Purdah) was higher than that of caucasian women living in London. With an increased incidence of vitamin D deficiency documented in these populations, there is heightened awareness of the potential impact on pregnancy outcome [12]. Also, the known racial disparity in preeclampsia, with black women being more likely to develop severe preeclampsia and suffer greater morbidity associated with the disorder than white women, suggests vitamin D may be relevant [13].

Data from studies suggesting an association between preeclampsia and vitamin D deficiency

is also now developing although these results remain inconsistent. In a recent investigation of 25-OH-D levels in pregnancy prior to the onset of preeclampsia, vitamin D levels assessed in early pregnancy were found to be lower among women who eventually developed preeclampsia. In this study, investigators noted a two-fold increased risk for preeclampsia when serum vitamin D levels decreased by 20 ng/mL after adjusting for confounders. [13] Findings from case-control studies have revealed that serum vitamin D concentrations in preeclamptic women were lower than non-preeclamptic women. [5,12-15] However, some other studies failed to reach such associations but rather concluded that low levels of vitamin D were not associated with adverse maternal outcome. [16,17] One prospective cohort study also reported no association between vitamin D deficiency and risk of developing preeclampsia [18] but a in larger Canadian cohort study, it was shown that low serum 25(OH)D concentrations (<50 nmol/L or <20 ng/mL) at weeks 24–26 of gestation was associated with 3.2 times greater risk of preeclampsia [19].

Despite these inconsistencies, a systematic review and meta-analysis of published observational studies conducted by Tabesh et al, [20] summarised the evidence on the association between maternal serum vitamin D levels and risk of pre-eclampsia and concluded that there was a significant relationship between vitamin D deficiency and increased risk of preeclampsia. They however reiterated that further studies were required, particularly in developing countries.

There is therefore the need to determine concentrations of serum 25(OH)D in pregnancy and examine the association between maternal 25(OH)D and risk of adverse pregnancy outcomes like preeclampsia in low income countries like ours where vitamin D deficiency may be a growing problem. This may be due to factors like lower dietary intake, higher disease burden, many prevalent social and cultural practices that preclude adequate exposure of adolescent girls and young women to sunshine and urbanization.

Because pre-eclampsia is one of the major causes of maternal mortality, the prevention, timely diagnosis and effective treatment could help to reduce maternal mortality particularly in our environment and given the few effective preventive strategies for severe preeclampsia, studies establishing this link are needed so that effective interventions can be developed.

2. METHODOLOGY

2.1 Study Design

The study was a cross sectional comparative study involving 55 preeclamptic and 55 normotensive women attending antenatal clinic or admitted for delivery in the maternity and labour wards of the University of Abuja Teaching Hospital, Abuja.

2.2 Study Location

University of Abuja Teaching Hospital is a government owned tertiary institution situated in Gwagwalada, a high population density area in Abuja, Nigeria's Federal capital territory. Abuja is located between latitudes 8º25′and 9º25′north of the equator and experiences three weather conditions annually. This includes a warm, humid rainy season an intense dry season and a short harmattan season which comes in between. The rainy season begins from April and ends in October, with daytime temperatures reaching 28ºC (82.4ºF) to 30ºC (86.0ºF). In the dry season, daytime temperatures can reach as high as 40ºC (104.0ºF).

2.3 Study Subjects

Cases were women with a diagnosis of preeclampsia in the third trimester and admitted for delivery. Exclusion Criteria included those with pre-gestational hypertension, renal disease, diabetes mellitus, multiple gestation, patients on anticonvulsants, antiretroviral therapy or those with weight greater than 90kg. The control patients were excluded by the same criteria and comprised of normal healthy pregnant women who had given consent. They were matched according to parity (nulliparous vs multiparous) and gestational age (within 1 week).

2.4 Data Collection

Data was collected with the aid of a proforma and included information on sociodemographic characteristics, parity and gestational age. Information on duration of sun exposure and clothing style to reflect percentage body surface area exposed and was also obtained. Examination and investigations carried out were weight, blood pressure, urinalysis and serum vitamin D levels.

Preeclampsia was defined as systolic blood pressure persistently 140 mm Hg or higher and/or diastolic blood pressure persistently 90 mm Hg or higher for the first time after 20 weeks gestation with proteinuria.

Proteinuria was defined as a urine sample of 1+ protein or more. 1+ of protein was confirmed by a catheter specimen.

Sun exposure was considered adequate when a person is exposed for more than 15min while the type of clothing worn reflected the body surface area exposed. According to the rule of nines, the head and neck sun skin exposure accounts for 9%, each arm for 9%, each leg for 18%, and the front and back torso for 18% each.

2.5 Categorization of Serum Vitamin D Levels

Vitamin D deficiency was defined by levels less than 20 ng/ml, vitamin D insufficiency as levels between 20 ng/ml and 29 ng/ml while normal levels were defined as levels greater than or equal to 30 ng/ml [17,18].

2.5.1 Blood collection and serum measurement of vitamin D

A trained phlebotomist collected non-fasting blood samples by venipuncture, separated serum, and stored at −20ºC until analysis. Serum vitamin D levels was measured with the Calibiotech, Inc. 25-hydroxy (25-OH) Vitamin D enzyme linked immunosorbent assay (ELISA) kit, a solid phase ELISA which is based `on the principle of competitive binding. Microtitre wells coated with anti-Vitamin D antibody were incubated with Vitamin D standards, controls, patient samples (serum), and vitamin D-Biotin conjugate (biotin-labeled vitamin D) at room temperature for 90 minutes. During this incubation, a fixed amount of the biotin-labeled vitamin D competes with the endogenous Vitamin D in the patient's sample, standard, or quality control serum for a fixed number of binding sites on the anti-Vitamin D antibody impregnated wells. A wash step was then undertaken and bound Vitamin D-Biotin is detected with Streptavidin-HRP (Horseradish Peroxidase) by the addition of the latter. Streptavidin-HRP conjugate immunologically bound to the well progressively decreases as the concentration of Vitamin D in the specimen increases and vice versa. Unbound SA-HRP conjugate was then removed by decanting the contents of the wells and the wells are washed. Next, a solution of Tetramethylbenzidine (TMB) Reagent was added and incubated at room temperature for 30 minutes, leading to the generation of a blue color. The color development was stopped with the addition of a stop solution, and the absorbance measured spectrophotometrically at a wavelength of 450 nm using a microplate reader. The concentration of the standard against the absorbance was plotted, to produce a standard curve and the values of the sample were read off the curve. The color intensity is inversely proportional to the concentration of 25(OH)D in a patient's sample. The assay measured both Vitamin D2 and D3.

The sensitivity of the test kit was 0.67ng/ml while its intra-assay mean according to the guideline of the kit for high and low human standards was 8.1ng/ml with CV = 3.87%, 25.3 ng/ml with CV = 6.36% and 35.9 ng/ml with CV = 4.62%. The inter-assay mean was 7.9ng/ml with CV = 4.55%, 23.4ng/ml with CV = 6.95% and 37.6ng/ml with CV = 5.38%.

Vitamin D deficiency was defined by levels less than 20 ng/ml, while levels between 20 ng/ml and 29 ng/ml were regarded as insufficient and greater than or equal to 30 ng/ml were normal 25-OH-D concentrations [17,18].

2.5.2 Outcome measures

The primary outcome measure was vitamin D deficiency in both groups while secondary outcome was gestational age at delivery among patients with preeclampsia and vitamin D deficiency.

2.6 Data Analyses

Data analysis was done using Statistical Package for the Social Sciences (spss) version 20 (SPSS Inc., Chicago, IL, USA) software. Continuous variables were presented as mean (SD) while categorical variables were presented as proportions. The analysis of categorical variables was done using the Pearsons chi-square test and Fishers exact test while the independent samples *t*-test and ANOVA test were used for comparing continuous variables between groups. Logistic regression was used to determine the relationship between vitamin D status and risk of preeclampsia after adjusting for potential confounders like age, parity and weight. P value less than 0.05 was

considered statistically significant in all of the analysis.

3. RESULTS

Out of the 110 samples obtained, 54 cases and 53 controls were successfully analyzed. Three cases were excluded because the results were below the detectable range. Overall, the mean serum 25-OH-D level in the study population was 38.98 ng/ml with a range of 14.10 ng/ml -83.50 ng/ml. Also, the overall prevalence of vitamin D deficiency was 15%, while 16.8% and 68.2% of the participants had insufficient and normal levels respectively.

The characteristics of the study population are shown in Table 1. Women with preeclampsia had significantly higher blood pressures compared to the healthy women, (P < .001). In addition to age and body weight, other baseline characteristics like gestational age, educational status, religion and occupation were similar between the two groups.

Table 2 compares the vitamin D status of the two groups. The prevalence of vitamin D deficiency among women with preeclampsia was 20.4% while that of healthy women was 9.4%. This however was not statistically significant (P = .19). The prevalence of Vitamin D insufficiency was also similar in both groups (22.2% vs. 11.3%, P = .21 respectively). Conversely, the proportion of healthy women with normal serum vitamin D was significantly higher than in women with preeclampsia (79.2% vs. 57.4%, P = .03).

Table 3 compares serum vitamin D levels and other associated factors in the study subjects. It shows that the mean serum 25-OH-D levels of women with preeclampsia was significantly lower when compared to that of the healthy women (34.5(14.9) vs. 43.5(15.1), P = .003). Other factors related to vitamin D status like time of exposure to sunlight and mean body surface area exposed were similar in both groups, P = .99 and P = .19 respectively. Within the study population, none of the women were taking vitamin D supplements and so this was not included in the table.

Within the categories of vitamin status of women with preeclampsia, there was a statistically significant difference in gestational age (GA) at

Table 1. Sociodemographic characteristics of study subjects

Characteristics	Pre-eclampsia n=54 Mean (SD) or n (%)	Healthy women n=53 Mean (SD) or n (%)	*P*-value
Age(yrs)	30.0(4.9)	29.0(4.9)	.27
Parity	2.8(2.1)	2.2(1.3)	.08
1st preg	21(38.9)	20(37.7)	.90
>1 preg	33(61.1)	33(62.3)	.90
Gestational age (weeks)	35.4(3.4)	35.5(3.5)	.90
Education			
Illiterate	2(3.7)	0(0.0)	.495
Primary	6(11.1)	3(5.7)	.49
Secondary	16(29.6)	13(24.5)	.67
Tertiary	30(55.6)	37(69.8)	.16
Religion			
Christian	41(75.9)	38(71.7)	.62
Muslim	13(24.1)	15(28.3)	.62
Occupation			
civil servant	18(33.3)	18(34.0)	.95
Trader	15(27.8)	11(20.8)	.40
Artisan	2(3.7)	1(1.9)	.57
House wife	13(24.1)	15(28.3)	.62
Unemployed	1(1.9)	2(3.8)	.62
Student	5(9.3)	6(11.3)	.73
Weight (kg)	73.9(9.9)	74.5(9.2)	.78
Systolic blood pressure (mmHg)	170.2(16.8)	108.7(10.0)	<.001
Diastolic blood pressure (mmHg)	107.2(13.8)	64.5(8.0)	<.001

Table 2. Comparison of vitamin D status of study subjects

Vitamin D status	Pre-eclampsia n=54 n (%)	Healthy women n=53 n (%)	*P*-value
Deficient (<20.0 ng/mL)	11(20.4)	5(9.4)	.19
Insufficient (20.0–29.9 ng/mL)	12(22.2)	6(11.3)	.22
Normal levels(≥30 ng/mL)	31(57.4)	42(79.2)	.03

Table 3. Comparison of serum vitamin D levels and other associated factors in study subjects

Characteristics	Pre-eclampsia n=54 Mean (SD) or n (%)	Healthy women n=53 Mean (SD) or n (%)	*P*-value
Serum Vit D(ng/ml)	34.5(14.9)	43.5(15.1)	.003
Sufficient exposure to sunlight			
<15 mins day^{-1}	2(3.7)	2(3.8)	.99
>15 mins day^{-1}	52(96.3)	51(96.2)	
%Body surface area exposed	30.1(12.0)	27.1(11.3)	.19

delivery as determined by one-way ANOVA ((*F* (2,51) = 5.153, *P* = .009). A Tukey post hoc test revealed that women with vitamin D insufficiency delivered at a statistically significant mean higher gestational age than those with vitamin D deficiency (37.67(2.77) weeks vs. 33.55(2.38) weeks respectively, *P* = .007). There was no statistical significant difference in GA at delivery between the deficient and normal groups (*P* = .85). Other characteristics like age, parity, weight and body surface area exposed were similar within these groups (Table 4).

Following adjustment for age, parity and body weight in a bivariate logistic regression analysis, maternal vitamin D deficiency was not associated with the development of preeclampsia [odds ratio (OR) = 3.27, CI = 0.99-10.83, *P* = .05]. On the other hand however, women with vitamin D insufficiency had about a three-fold odd of developing preeclampsia and this was statistically significant (OR = 3.20, CI = 1.02–10.06, *P* = .046) (Table 5). Age, parity and weight were not significantly associated with the development of preeclampsia in this study.

Table 4. Comparison of maternal characteristics by vitamin D status in pregnant women with preeclampsia

Characteristics	25(OH)D deficiency (<20.0 ng/mL) n=11	25(OH)D insufficiency (20.0–29.9 ng/mL) n=12	25(OH)D normal (≥30 ng/mL) n=31	p-value
Age(yrs)	30.1(5.4)	30.7(4.7)	29.7(4.9)	.86
Parity	2.6(2.5)	2.3(1.8)	3.0(2.0)	.53
Gestational age at delivery (weeks)	33.6(2.4)	37.7(2.8)	35.2(3.4)	.009
Weight (kg)	72.6(6.5)	72.5(10.7)	74.9(10.8)	.82
% BSA exposed	31.1(11.9)	28.2(14.43)	30.5(11.5)	.31

Table 5. Unadjusted and adjusted ORs for preeclampsia according to vitamin D status

Serum 25(OH)D level (ng/ml)	Pre-eclampsia n=54 n (%)	Healthy women n=53 n (%)	Unadjusted OR(CI)	p-value	Adjusted[a] OR(CI)	*P*-value
Deficient <20	11(20.4)	5(9.4)	2.98 (0.94-9.46)	0.064	3.27 (0.99-10.83)	.05
Insufficient 20–29.9	12(22.2)	6(11.3)	2.71 (0.92-8.01)	0.072	3.20 (1.02-10.06)	.046

[a]*Adjusted for Age, Parity, Weight*

4. DISCUSSION

In this study, vitamin D deficiency was defined by a 25-hydroxy vitamin D level of less than 20 ng per milliliter (50 nmol per liter) [21] and using this set point, a prevalence rate of 15% was recorded. This value is low compared to reports of vitamin D deficiency among pregnant women in literature and one possible explanation for this could be the different cut off points which have been used by various researchers. Rates of 42%, 61%, 80% and 60–84% have been reported in northern India [22], New Zealand [23], Iran [24] and Netherlands [25] using a threshold of 10ng/ml while rates of about 69-80% have been reported in black pregnant women in studies done in the US [26] and Ethiopia [10] using higher cut off points.

With regard to the factors determining amount of serum vitamin D, it seems that effect of latitude, sun exposure and dietary supplementation all have a role to play. This may explain the comparatively low prevalence rate of vitamin D defficiency recorded in this study, and this is despite the total lack of multivitamin use among the participants. Another factor that may have contributed to this result was their adequate exposure to sunshine which is in abundance in the area the study was undertaken i.e Abuja, Nigeria. This suggestion may seem plausible because the mean serum level of vitamin D in our study was similar to that of the study done in North Carolina [14] (34.5ng /ml vs. 30 ng/ml). This study was conducted in an area of higher altitude but reported regular intake of supplements by the subjects while our study was conducted in a low altitude region, among women who did not take supplements but were adequately exposed to sunshine. On the other hand, a study which was conducted in the middle-east [27], where about two thirds of the population had insufficient sun exposure and also reported low supplement intake recorded significantly lower serum vitamin D levels (18.1ng/ml) among women with preeclampsia. This highlights the role of vitamin D supplementation. To further support this, Hypponen et al. [28] conducted a systematic review and meta-analysis of observational studies and randomized control trials with focus on on vitamin D supplementation and risk of preeclampsia. These analysis had included data from 2 large-scale epidemiological studies to results from observational studies and found that the odds of developing pre-eclampsia was lower in mothers receiving vitamin D supplementation (pooled OR 0.81; 95% CI: 0.75-0.87). Results from randomized controlled trials were suggestive of a protective association (pooled OR 0.66; 95% CI 0.52-0.83). A small number of studies were however included in these analyses and the authors agreed that evidence was insufficient to show a causal relationship. This could be achieved by larger adequately powered clinical trials.

In order to determine the relationship between vitamin D deficiency and preeclampsia at the point of delivery, the women were categorized based on their serum vitamin D levels. Our findings revealed that there was no relationship between vitamin D deficiency and preeclampsia. However, vitamin D insufficiency was found to be a risk factor for preeclampsia. Various studies have correlated the association of preeclampsia with hypovitaminosis but the results are inconclusive. For example, our results were not consistent with the findings of some published epidemiological studies [5,13,14,27,29,30] and reasons for this may not be so clear. The study by Abedi et al. [5] in Iran had a similar sample size with this study and also had samples taken at delivery but pertinent differences with this study are the fact that it was done in an area of greater latitude and in a population where less than half of the women had sufficient exposure to sunshine. These differences seem to be reflected in their mean serum vitamin D levels which were much lower than what was obtained in this study (17.48 vs. 34.5 ng/ml respectively), they had however reported a higher risk of PE at 25(OH)D concentrations <25 nmol/L (OR 24.04, 95% CI: 2.1, 274.8). Bodner et al. [13] conducted a nested case-control study of nulliparous pregnant women. Serum samples at less than 22 weeks gestation were analysed and their results revealed a monotonic dose-response relation between serum 25(OH)D concentrations at less than 22 wk and risk of preeclampsia. After confounder adjustment, a 50-nmol/liter decline in 25(OH)D concentration doubled the risk of preeclampsia (adjusted odds ratio, 2.4; 95% CI, 1.1–5.4). On the other hand however, another large cohort study undertaken by the same author had looked at the relationship between Vit D levels and various categories of preeclampsia at late midggestation and after adjusting for relevant cofounders, they reported a significant increased risk of severe preeclampsia with vitamin D levels less than 50nmol/l. This effect was not seen with mild preeclampsia and preeelampsia overall [31].

Our findings revealed that the odds of developing preeclampsia in women with vitamin D levels less than 20ng/ml was not statistically significant. Vitamin D insufficiency was however more suggestive of a risk factor for preeclampsia. Similar report as ours were reported in other epidemiological studies [15,17,18]. Goel et al. [32] in a prospective case control study measured vitamin D levels in preeclamptic and normal women. They reported that even though all women in the preeclamptic group had vitamin D deficiency (<20 ng/ml) as compared to 92% in the healthy group, this was not statistically significant. The limitations in this study lie in the small sample size and the failure to calculate the odds ratio. Other nested case-control studies have also failed to show significant association between vitamin D status in pregnancy and development of PE [17,33,34] and findings of cross-sectional studies [35,36] were also found to be conflicting.

A recent systematic review by Purswani et al. [37] on the role of vitamin D in preeclampsia still highlighted the inconsistences in available evidence and the fact that clinical trials to date have failed to demonstrate the effect of vitamin d supplementation on the development of preeclampsia. This view was supported by O'Callaghan et al. [38] in their systematic review but they had on the other hand found evidence from clinical trials that a combined supplemntation of Vitamin D and calcium was protective against preeclampsia. Reasons for these inconsistencies may be due to differences in study design, methodology data analysis, use of different cut off points to define vitamin D deficiency and lack of adjustment of key confounding variables.

This study showed that preeclamptic women who had vitamin D deficiency delivered at a lower gestational age than those who were not. This result may be explained by reports of increased production of inflammatory cytokines in pregnancies complicated by vitamin D deficiency thereby suggesting a possible role for vitamin D in preventing spontaneous preterm birth through anti-inflammatory and immunomodulatory effects [39]. Baker et al. [14] tested but failed to prove this hypothesis, but this may have been due to the fact that they had used first trimester samples. There were no differences in other maternal characteristics demonstrated between preeclamptic women with and without vitamin D deficiency in our study and this may have been due to the fact that the two groups were matched by parity and gestational age and women above 90kg were also excluded. Studies that did not match their groups were able to establish significant relationship between serum vitamin D levels and BMI [5,15], age [5,27] and socioecomomic status [27].

5. CONCLUSION

Our study showed that maternal vitamin D deficiency in the third trimester was not associated with preeclampsia. The results however suggest that maternal vitamin D insufficiency in late pregnancy is an independent risk factor for preeclampsia. I recommend that further large, well designed studies and trials on vitamin D supplementation to reduce preeclampsia be carried out, including in environments like ours.

CONSENT

As per university standard guideline written informed consent has been collected and preserved by the authors.

ETHICAL APPROVAL

Ethical approval was obtained from the University of Abuja Teaching Hospital ethical board (Approval no. UAH/HREC/480).

ACKNOWLEDGEMENT

I would like to acknowledge the entire staff of the Departments of Obstetrics and Gynaecology and Chemical Pathology, University of Abuja Teaching Hospital for their support and involvement with data collection. This research had no external source of funding.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. World Health Organisation. WHO recommendations for prevention and treatment of pre-eclampsia and eclampsia, World Health Organization, Geneva, Switzerland; 2011.
Available:http://whqlibdoc.who.int/publications/2011/9789241548335_eng: (Accessed 27/03/2015)

2. World Health Organisation. Make every mother and child count. In: The world health report, World Health Organization, Geneva, Switzerland; 2005.
Available:http://www.who.int/whr/whr 2005_eng.
(Accessed- 2/04/2015)
3. Attahir A, Dikko AAU, Sufiyan MB, Salihu A, Rabiu AM. Association between maternal socio–economic status, polygamy and risk of pre–eclampsia in rural areas of Northern Nigeria. JFRH. 2010;4(1):47-52.
4. Royal College of Obstetricians and Gynaecologists (RCOG). The management of hypertensive disorders during pregnancy. NICE Clinical Guideline No107. London: RCOG Press; 2010.
5. Abedi P, Mohaghegh P, Afshary P, Latifi M. The relationship of serum vitamin D with pre-eclampsia in the Iranian women. Matern Child Nutri. 2014;10:206–212.
6. Hamilton SA, McNeil R, Hollis BW, Davis DJ, Winkler J, Cook C, et al. Profound vitamin D deficiency in a diverse group of women during pregnancy living in a sun-rich environment at latitude 32°N. Int J Endocrinol. 2010; 2010:917428.
7. Robinson CJ, Wagner CL, Hollis BW, Baatz JE, Johnson DD. Maternal vitamin D and fetal growth in early-onset severe preeclampsia. Am J Obstet Gynecol. 2011; 204(6):556–4.
8. Parlak M, Kalay S, Kalay Z, Kirecci A, Guney O, Koklu E. Severe vitamin D deficiency among pregnant women and their newborns in Turkey. J Matern Fetal Neonatal Med. 2014;30:1-4.
9. Yu CK, Ertl R, Skyfta E, Akolekar R, Nicolaides KH. Maternal serum vitamin D levels at 11-13 weeks of gestation in preeclampsia. Hum Hypertens 2013; 27:115-8.
10. Feleke Y, Abdulkadir J, Mshana R, Mekbib T, Brunvand L, Berg JP, et al. Low levels of serum calcidiol in an African population compared to a North European population. Eur J Endocrinol. 1999;141:358–360.
11. Okonofua F, Houlder S, Bell J, Dandona P. Vitamin D nutrition in pregnant Nigerian women at term and their newborn infants. J Clin Path. 1986;39:650–653.
12. Robinson CJ, Wagner CL, Hollis BW, Baatz JE, Johnson DD. Maternal vitamin D and fetal growth in early-onset severe preeclampsia. Am J Obstet Gynecol. 2011; 204(6):556–4.
13. Bodnar LM, Catov JM, Simhan HN, Holick MF, Powers RW, Roberts JM. Maternal vitamin D deficiency increases the risk of preeclampsia. J Clin Endocrinol Metab. 2007;92:3517–3522.
14. Baker AM, Haeri S, Camargo CA Jr, Espinola JA, Stuebe AM. A nested case-control study of midgestation vitamin D deficiency and risk of severe preeclampsia. J Clin Endocrinol Metab. 2010;95:5105-9.
15. Ringrose JS, PausJenssen AM, Wilson M, Blanco L, Ward H, Wilson IW. Vitamin D and hypertension in pregnancy. Clin Invest Med. 2011;34(3):E147-E154.
16. Powe CE, Seely EW, Rana S, Bhan I, Ecker J, Karumanchi SA, et al. First trimester vitamin D, vitamin D binding protein, and subsequent preeclampsia. Hypertension. 2010;56:758-63.
17. Schneuer FJ, Roberts CL, Guilbert C, Simpson JM, Algert CS, Khambalia AZ. Effects of maternal serum 25-hydroxyvitamin D concentrations in the first trimester on subsequent pregnancy outcomes in an Australian population. Am J Clin Nutr. 2014;99(2):287-295.
18. Shand AW, Nassar N, Von Dadelszen P, Innis SM, Green TJ. Maternal vitamin D status in pregnancy and adverse pregnancy outcomes in a group at high risk for pre-eclampsia. BJOG. 2010;117:1593–1598.
19. Wei SQ, Audibert F, Hidiroglou N, Sarafin K, Julien P, Wu Y, et al. Longitudinal vitamin D status in pregnancy and the risk of pre-eclampsia. BJOG. 2012;119:832-9.
20. Tabesh M, Salehi-Abargouei A, Esmaillzadeh A: Maternal vitamin D status and risk of pre-eclampsia: A systematic review and meta-analysis. J Clin Endocrinol Metabol. 2013;98:3165-3173.
21. Vitamin D: Screening and supplementation during pregnancy. Committee opinion No. 495. American College of obstetricians and gynecologists. Obstet Gynecol. 2011; 118:197–8.
22. Sachan A, Gupta R, Das V, Agarwal A, Awasthi PK, Bhatia V. High prevalence of vitamin D deficiency among pregnant women and their newborns in northern India. Am J Clin Nutr. 2005;81(5):1060–1064.
23. Judkins A, Eagleton C. Vitamin D deficiency in pregnant New Zealand women. N Z Med J. 2006;119(1241): U2144.

24. Bassir M, Laborie S, Lapillonne A,Claris O, Chappuis MC, Salle BL. Vitamin D deficiency in Iranian mothers and their neonates: A pilot study. Acta Paediatr 2001;90577–579.
25. Van Der Meer IM, Karamali NS, Boeke AJP, Lips P, Middelkoop BJ, Verhoeven I et al. High prevalence of vitamin D deficiency in pregnant non-Western women in The Hague, Netherlands. Am J Clin Nutr. 2006;84:350–353.
26. Ginde AA, Sullivan AF, Mansbach JM, Camargo CA. Jr. Vitamin D insufficiency in pregnant and non-pregnant women of childbearing age in the United States. Am J Obstet Gynecol. 2010;202(5):436–438.
27. Bener A, Al-Hamaq AO, Saleh NM. Association between vitamin D insufficiency and adverse pregnancy outcome: Global comparisons. Int J Womens Health. 2013;5:523–31.
28. Hyppönen E, Cavadino A, Williams D, Fraser A, Vereczkey A, Fraser WD, et al. Vitamin D and pre-eclampsia: Original data, systematic review and meta-analysis. *Ann.* Nutr. Metab. 2013;63:331–340.
29. Zhou J, Su L, Liu M, Liu Y, Cao X, Wang Z et al.. Associations between 25-hydroxyvitamin D levels and pregnancy outcomes: A prospective observational study in southern China. Eur J Clin Nutr 2014;68(8):925–30.
30. Buchanan AS, Ebeling MD, Mateus JF, Wagner CL. Maternal vitamin d deficiency and the risk of preeclampsia. AJOG. 2018;218(1):S488.
31. Bodnar LM, Simhan HN, Catov JM, Roberts JM, Platt RW, Diesel JC, et al. Maternal vitamin D status and the risk of mild and severe preeclampsia. Epidemiology. 2014;25(2):207–14.
32. Goel P, Garg G, Kaur J, Mehra R, Tandon R, Huria A. Association of vitamin D deficiency during pregnancy with preeclampsia and eclampsia. Int J Reprod Contracept Obstet Gynecol. 2016;5:3046-50.
33. Wetta LA, Biggio JR, Cliver S, Abramovici A, Barnes S, Tita AT. Is midtrimester vitamin D status associated with spontaneous preterm birth and preeclampsia*?* Am J Perinatol. 2014;31(6): 541–6.
34. Gidlof S, Silva AT, Gustafsson S, Lindqvist PG. Vitamin D and the risk of preeclampsia - A nested case-control study. Acta Obstet Gynecol Scand. 2015;94(8):904–8.
35. Pena HR, de Lima MC, Brandt KG, de Antunes MM, da Silva GA. Influence of preeclampsia and gestational obesity in maternal and newborn levels of vitamin D. BMC Pregnancy Childbirth. 2015;15:112.
36. Al-Shaikh GK, Ibrahim GH, Fayed AA, Al-Mandeel H. Impact of vitamin D deficiency on maternal and birth outcomes in the Saudi population: A cross-sectional study. BMC Pregnancy Childbirth. 2016;16:119.
37. Purswani JM, Gala P, Dwarkanath P, Larkin HM, Kurpad A, Mehta S. The role of vitamin D in pre-eclampsia: A systematic review. BMC Pregnancy and Childbirth 2017;17:231.
38. O'Callaghan KM, Kiely M. Systematic review of vitamin D and hypertensive disorders of pregnancy. Nutrients. 2018; 10:E294.
39. Luk J, Torrealday S, Neal Perry G, Pal L. Relevance of vitamin D in reproduction. Hum Reprod. 2012;27:3015–27.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle3.com/review-history/50589