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Ratio between Low Serum Maternal 25-Hydroxy vitamin D Concentration and the Risk of Preeclampsia

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ABSTRACT

Background: Vitamin D may play a role in the etiology of preeclampsia by regulating the transcription and function of genes associated with placental function, including placental invasion, normal implantation, and angiogenesis. Vitamin D also, modulates immune function and inflammatory response. Maternal vitamin D concentration may be influenced by several factors, including diet, supplementation, sun exposure, skin pigmentation, and genetics. Therefore, vitamin D deficiency is a potentially modifiable risk factor for preeclampsia.

Objective: To find out if lower levels of vitamin D is more prevalent in preeclamptic women.

Patients and Methods: This study carried out on 50 pregnant women recruited at pre labour room. They divided into preeclamptic group and non-preeclamptic group, 25 cases in each group. Current study was conducted as a case-control study to compare vitamin D level between preeclamptic and non-preeclamptic women at Al-Hussein University Hospital as current study recruited 50 primigravida. Women after 36 weeks of gestation without any other medical disorders. They were classified into preeclamptic case group and normotensive control group.

Results: The current study found that vitamin D levels were lower in preeclamptic group than normotensive control group but these differences were not statistically significant.

Keywords: Pregnancy, Preeclampsia, Hypertension, Vitamin D deficiency, 25-Hydroxyvitamin D

INTRODUCTION

Preeclampsia is a multisystem pregnancy disorder defined by new-onset hypertension and proteinuria after 20 weeks of gestation. Preeclampsia affects 2%–8% of all pregnancies and remains a leading cause of maternal and perinatal mortality and morbidity, including preterm birth and small for gestation age [(1,2)].

Multiple factors, such as maternal constitutional factors, angiogenetic factors, endothelial dysfunction, syncytio trophoblastic microparticles (STMP) and inflammatory activation, play a role in the development and progression of preeclampsia. The maternal diet is among the factors related to the etiology of preeclampsia; an insufficient diet, especially in terms of calcium, magnesium, selenium and vitamin A and C, is a contributing factor to preeclampsia [(3)].

The etiology of preeclampsia is poorly understood a leading theory is insufficient spiral artery remodeling in the placenta may result in a hypoxic environment with reperfusion injury and up–regulation of oxidative stress. The pre-eclamptic placenta secrete factors such as inflammatory cytokines and reactive oxygen species into maternal circulation to induce hypertension through local production of vasoconstriction, notably endothelin -1[(4)].

Vitamin D as a fat-soluble steroid hormone is mainly synthesized by the skin on exposure to ultraviolet light and to a lesser extent can be ingested in the diet. It undergoes hydroxylation in the liver to produce an inactive supply form of 25-hydroxyvitamin D, 25(OH)D. Circulating 25(OH)D gets converted by renal 1-alpha-hydroxylase to the active form 1,25-dihydroxyvitamin (vitamin D3) which is the hormonally active form of vitamin D [(5)].

Vitamin D plays pivotal role in bone and mineral metabolism. During pregnancy, vitamin D plays important role in implantation and placental function due to angiogenic, immunomodulatory, and anti-inflammatory effects. While, the pathophysiology of hypertensive disorders in pregnancy (HDP) involving abnormal placentation and angiogenesis still incompletely understood. Several studies have demonstrated an association between higher 25(OH) D levels and reduced risk of HDP especially in preeclampsia [(6)].

AIM OF THE WORK

To find out if lower levels of vitamin D is more prevalent in preeclamptic women.

PATIENTS AND METHODS

Study Settings: After obtaining approval from the Research Ethical Committee of AL-Azhar University. This study was conducted pre labour room Al-Hussein University Hospital. **Study Design:** Case control study.

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Inclusion criteria:

Parity: primigravida and multipara. Age: 18 - 35 years old. Single pregnancy. Gestational age: 36-40 weeks. No past history of any medical disorder and with no other medical complications during pregnancy.

Exclusion criteria:

Women with preexisting medical conditions like rheumatoid arthritis, thyroid, hepatic or renal failure, metabolic bone disease, diabetes mellitus. History of intake of medications influencing bone, vitamin D or calcium metabolism e.g. antiepileptic, anti-tubercular drugs in the last 6 months.

Sample Size: Total of 50 pregnant patients were recruited in this study. They were divided into two groups: group of patients with preeclampsia (n=25) and controls group (n=25. They were screened at time of presentation to the delivery ward in Al-Hussein University Maternity Hospital for serum vitamin D assay. Data of all patients in both groups were collected and scheduled.

Statistical analysis

Data were analyzed using Statistical Program for Social Science (SPSS) version 20.0. Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

RESULTS

Table (1): Comparison between cases and control according to demographic data.

Demographic Data	Cases (N=25)	Control (N=25)	t-test	p-value	Sig.
Age (years)					
Mean ± SD	19.88 ± 1.39	19.92 ± 1.22	0.012	0.915	NS
Range	18-22	18-22			
GA (wks)					
Mean ± SD	38.46 ± 0.82	38.86 ± 0.59	3.865	0.055	NS
Range	36.3-40	37.7-39.9			

This table showed no statistically significant difference between groups concerning demographic data.

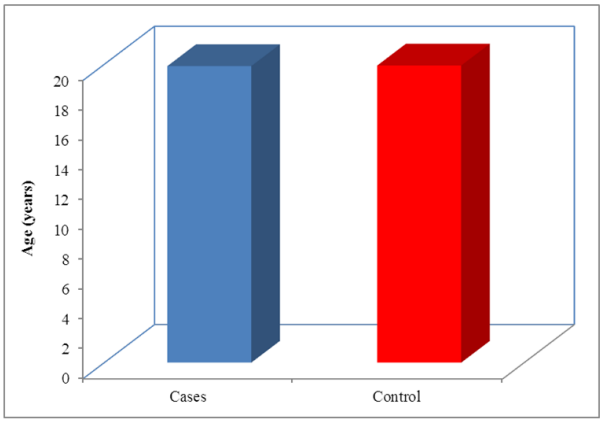

Figure (1): Bar chart between cases and control in regard to Age (years).

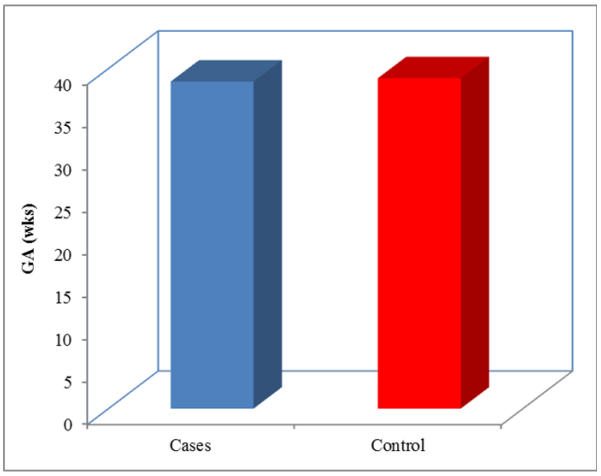

Figure (2): Bar chart between cases and control in regard to GA (wks).

Table (2): Comparison between cases and control concerning systolic and diastolic bl P.

Clinical Data	Cases (N=25)	Control (N=25)	t-test	p-value	Sig.
Systolic pr					
Mean ± SD	148.40 ± 7.46	110.80 ± 8.12	290.499	<0.001	HS
Range	140-160	100-120			
Diastolic pr					
Mean ± SD	99.60 ± 8.89	72.00 ± 7.07	147.628	<0.001	HS
Range	90-110	60-80			

This table showed highly statistically significant difference between groups as regards systolic and diastolic bl P.

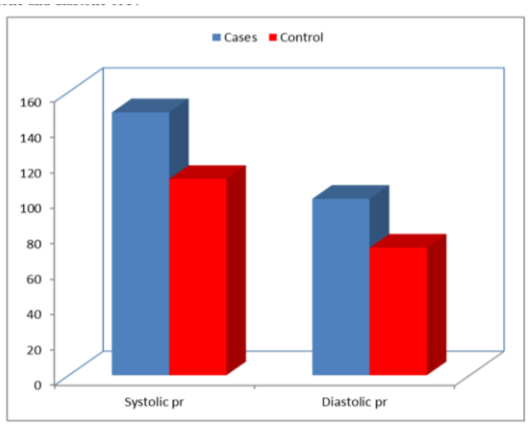

Figure (3): Bar chart between case and control regarding systolic & diastolic bl P.

Table (3): Comparison between cases and control according to mode of delivery.

Mode of delivery	Cases (N=25)		Control (N=25)		Chi-square test		Sig.
	No.	%	No.	%	x2	p-value	
LSCS	6	24%	4	16%	0.500	0.480	NS
NVD	19	76%	21	84%			

This table showed no statistically significant difference between groups regarding mode of delivery.

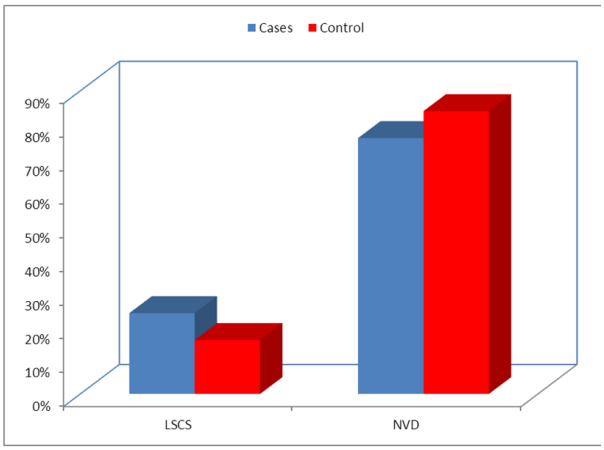

Figure (4): Bar chart between cases and control regarding mode of delivery.

Table (4): Comparison between cases and control according to laboratory data.

Laboratory Data	Cases (N=25)	Control (N=25)	t-test	p-value	Sig.
Creatinine					
Mean ± SD	0.82 ± 0.12	0.8 ± 0.10	2.847	0.036	S
Range	0.7-1	0.7-1			
Alt					
Mean ± SD	16.96 ± 4.24	16.64 ± 4.16	0.051	0.823	NS
Range	9-32	9-27			
Ast					
Mean ± SD	15.76 ± 3.94	16.36 ± 4.09	0.172	0.680	NS
Range	7-33	9-27			
Plt					
Mean ± SD	228.28 ± 57.07	280.72 ± 58.40	9.335	0.004	S
Range	150-345	165-390			
HB					
Mean ± SD	10.71 ± 0.66	10.55 ± 0.63	0.806	0.374	NS
Range	9.8-12.5	9-11.7			

This table showed statistically significant difference between groups concerning creatinine and platelet.

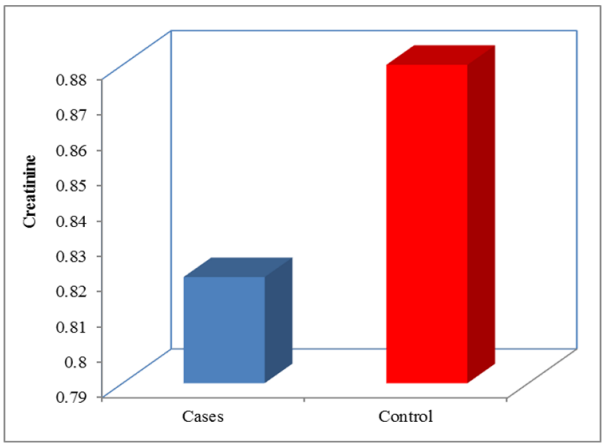

Figure (5): Bar chart between cases and control concerning creatinine.

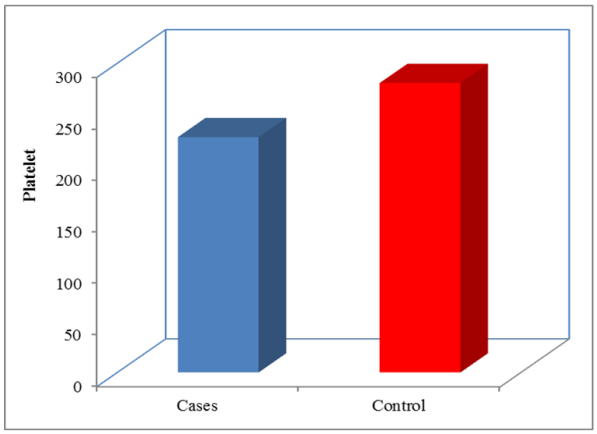

Figure (6): Bar chart between cases and control concerning platelet.

Table (5): Comparison between cases and control in regard to vit. D (ng/ml).

Vit d (ng/ml	Cases (N=25)	Control (N=25)	t-test	p-value	Sig.
Mean ± SD	5.40 ± 1.35	5.02 ± 1.25	0.083	0.775	NS
Range	1-26	1-13			

This table showed no statistically significant difference between groups in regard to vit. D (ng/ml).

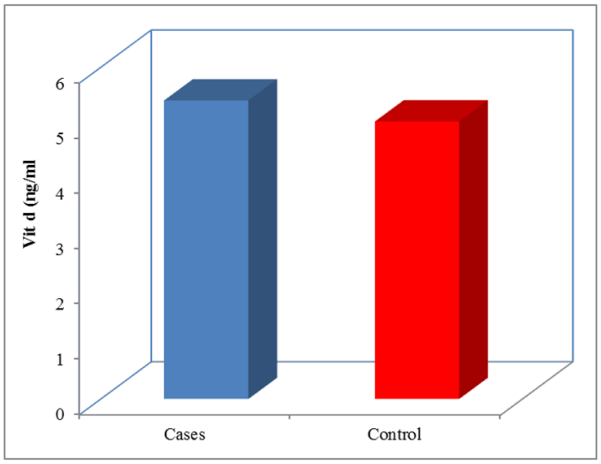

Figure (7): Bar chart between cases and control in regard to Vit. D (ng/ml).

Table (6): Correlation between Vit. D (ng/ml) and other parameters, using Pearson Correlation Coefficient in cases group.

	Vit d (ng/ml		Sig.
	r	p-value	
Age (years)	0.227	0.274	NS
GA (wks)	-0.078	0.591	NS
Systolic pr	-0.039	0.790	NS
Diastolic pr	-0.059	0.686	NS
Creatinine	0.274	0.054	NS
ALT	-0.093	0.523	NS
AST	0.027	0.850	NS
Plt	0.172	0.234	NS
HB	0.111	0.444	NS

r- Pearson Correlation Coefficient

No statistically significant correlation between Vit D. (ng/ml) and other parameters.

Table (7): Correlation between Vit. D (ng/ml) level and severity of preeclampsia.

Vit d (ng/ml	Bl Pr groups		t-test	p-value	Sig.
	Mild Preeclampsia (N=11)	Severe Preeclampsia (N=14)			
Mean ± SD	5.91 ± 1.47	6.43 ± 1.60	3.626	0.069	NS
Range	2-26	1-13			

No statistically significant relation between Vit. D (ng/ml) level and severity of preeclampsia.

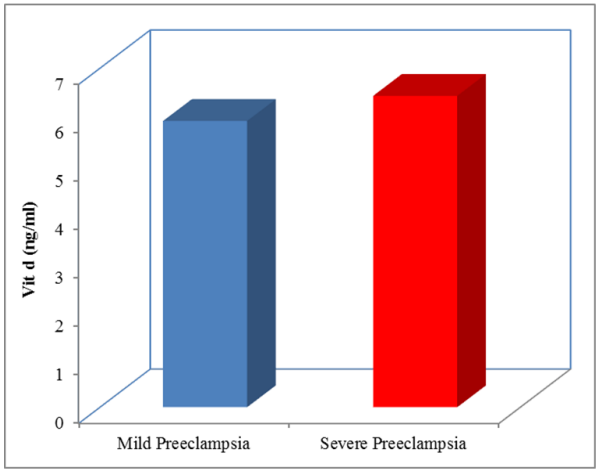

Figure (8): Correlation between Vit. D (ng/ml) level and severity of preeclampsia.

DISCUSSION

The current study found that vitamin D levels were lower in preeclamptic group than normotensive control group but these differences were not statistically significant. Two studies confirmed current findings was performed by ***Wetta et al.*** [7] and ***Burris et al.*** [8] but at different gestational ages as ***Wetta et al.*** [7] performed a nested case-control study at 15-21 weeks of gestation and found that mean 25 (OH) D levels did not differ in preeclamptic cases (68 nmol/L) and controls (71 nmol/L). Also, ***Burris et al.*** [8] studied associations of 25 (OH) D levels obtained at 16.4-36.9 weeks of gestation (mean 27.9 weeks) with preeclampsia and found no association between plasma 25 (OH) D concentration and preeclampsia. While, In contrary with current findings, ***Baker et al.*** [9] conducted a nested case-control study at United States to assess relationship between mid-gestation vitamin D deficiency and preeclampsia between 43 cases and 198 controls. They found that maternal midgestation vitamin D deficiency was associated with increased risk of preeclampsia. Besides, ***Xu et al.*** [10] conducted a large cohort study on 100 preeclamptic and 100 normotensive pregnant women. Both were screened for Vitamin D and IL-6 concentrations. They found that the mean concentration of 25 (OH) D was 49.4 ± 22.6 nmol/L in normotensives and 42.3 ± 17.3 nmol/L in preeclamptic women (p = 0.01). Therefore, it was hypothesized that the plasma concentrations of maternal 25 (OH) D measured at an average of 35 week gestational age were statistically significantly lower in women with preeclampsia compared to non-preeclamptic controls. The current study evaluated

vitamin D level at end of third trimester (36–40) weeks of pregnancy as near term assessment might lead to real association between vitamin D deficiency and preeclampsia. Calcium and vitamin D demand reach the peak in the last trimester of pregnancy as viewed in literature. These different ages in previous studies may lead to different results. Using several different assays to measure vitamin D may lead to the discrepant findings as ***Wei et al.*** [(11)] used chemiluminescence immunoassay in assessment of maternal serum 25-hydroxyvitamin D concentrations at 12–18 and 24–26 weeks of gestation and found a strong positive correlation that was observed in maternal 25 (OH) D concentrations between the two gestational ages. Mean maternal 25 (OH) D concentrations at 24–26 weeks of gestation were significantly lower in women who subsequently developed preeclampsia compared with those who did not (mean ± SD: 48.9 ± 16.8 versus 57.0 ± 19.1 nmol/l, P = 0.03). Whereas, the association was not statistically significant for maternal 25 (OH) D level at 12–18 weeks of gestation. While, ***Wetta et al.*** [(7)] used liquid chromatography-tandem mass spectrometry and found no association between vitamin D deficiency and preeclampsia.

Halhali et al. [(12)] found significant association between vitamin D deficiency and preeclampsia using radioimmunoassay (RIA) in vitamin D assay. Using RIA is difficult because such technique works best in aqeuous environment and vitamin D is poorly solube in water. ***Singla et al.*** [(13)] used ELISA technique in comparing serum vitamin D concentration between two groups (74 nulliparous preeclamptic women with singleton pregnancy and without any known medical disorder versus 100 healthy nulliparous controls of same age). They found that mean serum 25 hydroxy vitamin D was significantly lower among cases as compared to controls. So, hypothesized that women with preeclampsia had significantly lower vitamin D level as compared to normal women. The current study used ELISA for testing as it was available, sensitive, rapid and more accurate than other assays which may need radioisotope or costly radiation counter (radiation-counting apparatus). The majority of prior studies done by ***Yu et al.*** [(14)], ***Bodnar et al.*** [(15)] **and** ***Bakacak et al.*** [(16)] evaluated women of Caucasian background and found a significant association between vitamin D deficiency and preeclampsia. No previous studies evaluated women of African-American race, who because of melanin inhibition of UVB-mediated synthesis of vitamin D, are at increased risk for insufficiency or deficiency. This may give possible explanation for different studies' findings. ***Singla et al.*** [(13)] also compared the vitamin D level of women with mild and severe preeclampsia. Severity of the disease was not related to vitamin D level. There was no correlation between vitamin D and severity of preeclampsia in the current study as well. All the differences in ethnicity, geographic location, and gestational age at vitamin D measurement and different assays made it difficult to generalize across different studies with any high degree of accuracy. It is likely that different latitude, different skin color, and different multivitamin intake can explain the different results between different countries.

Limitations of current study included the small sample size and the small number of women with pre-eclampsia compared to the other studies. This dissimilarity in study size and population characteristics may explain the null results and potential differences in study findings. In addition, currently there was no consensus on a cutoff for vitamin D deficiency in the pregnant population, as most studies extrapolate cutoffs from the non-pregnant population. The cause of preeclampsia is still unknown.

CONCLUSION

Vitamin D deficiency in the pregnant women has been associated with adverse pregnancy outcomes, such as gestational diabetes mellitus (GDM), small for gestational age (SGA). Maternal vitamin D concentration might be influenced by several factors, including diet, supplementation, sun exposure, skin pigmentation, and genetics. Therefore, vitamin D deficiency is a potentially modifiable risk factor for preeclampsia risk (1). From this study it could be concluded that vitamin D assay cannot be used for prediction of preeclampsia and vitamin D supplementation cannot be routinely used in prevention of preeclampsia. So, no association between vitamin D and preeclampsia.

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