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Association of Serum Vitamin D Level with Gestational Hypertension and Preeclampsia in Pregnant Women: A Case-Control Study

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Abstract
Background: Vitamin D status has been increasingly associated with wide-ranging clinical outcomes. There is now a wealth of observational studies reporting on its association with obstetric complications, including gestational hypertension, preeclampsia and gestational diabetes. So we did a case control study to see the Vitamin D Levels in pregnant Women with gestational HTN and preeclampsia which are compared to age and gestational age-matched healthy pregnant controls. This study was conducted at Department of Obstetrics and Gynaecology, Dinajpur medical college Hospital, Dinajpur.
Objectives: To see the association of serum vitamin D level with gestational HTN and pre eclampsia.
Material and methods : This was a Hospital- based observational case control study carried out in Dep. of Obstetrics and Dinajpur medical college Hospitalfor a period of 6 months. Consecutive, convenient sampling was done. 100 pregnant Women with gestational HTN and preeclampsiafulfilling inclusion and exclusion criteria was included in the study.100 age and gestational age matched healthy pregnant controls was included in the study attending at outpatient department. Serum vit D level was measured of all subjects and data was analyzed to find out the association of vit D level with gestational HTN and preeclamsia .
Results: Our study found significant relationship of serum vit D level with gestational HTN & preeclampsia. After doing statistical analysis we found P value was 0.043 which is statistically significant. Among all the subjects, Mean values of serum vitamin D levels in study group and control group were 13.83 ± 7.41 ng/ml and 18.86 ± 5.88 ng/ml respectively. Our study population had a very high prevalence of vitamin D deficiency (<20 ng/ml). Among all the subjects, 77.50 % had serum 25(OH)D levels <20 ng/ml reflecting widespread vit D deficiency in all pregnant women. We observed that 86% of the case and 69% of the control were vitamin D deficient with a odds ratio 2.76 (OR>1) which is a positive association.
Conclusion: Our study found very high prevalence of vitamin D deficiency (75.50 %). We found that. Risk of developing gestational HTN and preeclampsia rises with vitamin D deficiency.

Keywords: Vitamin D, Hypertension in pregnancy, Preeclampsia, Gestational hypertension, 25(OH)D

INTRODUCTION:

Vitamin D status has been increasingly associated with wide-ranging clinical outcomes. Vitamin D deficiency (<20 ng/ml)[1]has been associated with various poor maternal and fetal outcome and is proposed to be important in the pathogenesis of Hypertensive disorders of pregnancy.

Hypertensive disorders of pregnancy remains a major health issue for pregnant women and fetus. Hypertensive disorders of pregnancy include gestational hypertension, preeclampsia, eclampsia, preexisting essential hypertension. Gestational HTN is defined as pregnant women with systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg on two occasion at least four hours apart after 20 weeks of gestation with previous normal blood pressure in the absence of proteinuria [2]. Preeclampsia is defined as gestational HTN with Proteinuria and features of new onset organ dysfunction[2].

Hypertensive disorders of pregnancy affect about 10% of all pregnant women around the world. This group of diseases and conditions includes preeclampsia and eclampsia, gestational hypertension and chronic hypertension. Hypertensive disorders of pregnancy are important cause of severe acute morbidity, long-term disability and death among mothers and babies. In Asia and Africa, nearly one tenth of all maternal deaths are associated with hypertensive disorders of pregnancy, whereas one quarter of all maternal deaths in Latin America have been associated with hypertensive disorders of pregnancy[12].

Various epidemiological studies have emphasized the role of vitamin D deficiency in the development of gestation HTN and Preeclampsia[7,8]. The pathophysiology of gestational HTN and preeclampsia is complex. Many factors are thought to contribute to the development of the disorder including environmental, behavioral, immunological, and hereditary factors, advanced maternal age, and dark skin. It is currently thought that preeclampsia progresses in two stages. The first stage arises when a woman's uterine spiral arteries do not remodel normally during early pregnancy. The remodeling of these arteries usually occurs when the trophoblast invades the spiral arteries and dilates the vessels, which helps supply sufficient amounts of blood to the placenta and fetus. When uterine spiral arteries are not remodeled, there is decreased perfusion of the placenta and fetus and increased secretion of placental materials into the maternal circulation [2].

Vitamin D is thought to influence gene transcription, immune function, and blood pressure, some have suggested that 1,25dihydroxyvitamin D may play a role in the regulation of genes responsible for placental invasion and blood vessel formation. In addition, since preeclampsia may be due to an immunological intolerance to pregnancy, the role of vitamin D in modulating immune function may affect the immunological response to fetus. Lastly, vitamin D deficiency may exacerbate the hypertension that is clinically associated with preeclampsia through its potential effects on the renin-angiotensin system.

So we did a case control study to see the Vitamin D Levels in pregnant Women with gestational HTN and preeclampsia which are compared to age and gestational age matched healthy pregnant controls.

Objectives:

To see the association of serum 25(OH) D level with gestational HTN and pre eclampsia. Compare all the socio demographic data between case and control.

Materials and Methods:

This hospital-based observational case-control study was conducted at the Department of Obstetrics and Gynecology, Dinajpur Medical College Hospital, Dinajpur, Bangladesh, from November 2018 to April

2019, to investigate the association between serum vitamin D levels and gestational hypertension (HTN) and preeclampsia. A total of 100 pregnant women aged 18–35 years with a gestational age greater than 20 weeks, diagnosed with gestational HTN or preeclampsia, were enrolled as cases, alongside 100 age- and gestational age-matched healthy pregnant women as controls.

Participants were selected using consecutive, convenient sampling, with strict inclusion criteria ensuring no pre-existing essential hypertension, endocrine disorders, or other chronic conditions, and exclusion criteria eliminating factors such as vitamin D supplementation or smoking history that could confound results. Informed written consent was obtained from all participants in English and Bengali, and data were collected using a structured questionnaire.

Serum 25-OH vitamin D levels were measured via the ARCHITECT i2000sr Chemiluminescent Microparticle Immunoassay, with levels categorized as deficient (<20 ng/ml), insufficient (20–29 ng/ml), sufficient (30–100 ng/ml). Gestational HTN was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg after 20 weeks of gestation without proteinuria, while preeclampsia included proteinuria or other systemic complications.

Data were analyzed using SPSS version 22, with quantitative data expressed as mean ± standard deviation and categorical data as numbers and percentages. Statistical significance was set at a 95% confidence interval with a p-value <0.05, using unpaired t-tests, chi-squared tests, and Pearson correlation tests to compare socio-demographic data and vitamin D levels between groups. Logistic regression analyses were performed to estimate odds ratios, assessing the correlation between maternal serum vitamin D levels and the occurrence of gestational HTN and preeclampsia.

Results:

We found mean age was 26.51 ± 5.25years in case and 27.77 ± 4.16 years in control. Mean gestational age was 23.56 ± 2.75 weeks in case and 25.76 ± 1.75 weeks in control . Majority of the patients were multi gravida in both groups. BMI kg/m^2 was19.10 ± 1.25 in case and 20.50 ± 1.05 in control. Difference was not statically significant(p value >0.05) between case and control group regardingage,gestational age, parity& BMI. Among all the subjects, 77.50 % had serum 25(OH)D levels <20 ng/ml reflecting widespread vit D deficiency in all pregnant women.

Table 3.1: Distribution of the study patients by selected demographic and clinical characteristics (n=200)

Variables	Case (n=100)		Control (n=100)		P value
	n	%	n	%	
Age (yrs)					
≤20	20	20	25	25	
21-30	57	57	47	47	
≥31	23	23	28	28	
Mean ± SD	26.51 ± 5.25		27.77 ± 4.16		^{a}0.765 ^{ns}
Gestational age (weeks)					
21-30	76	76	81	81	
≥31	24	24	19	19	
Mean ± SD	23.56 ± 2.75		25.76 ± 1.75		^{a}0.585 ^{ns}

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Parity					
Primi	35	35	41	41	
Multi	65	65	59	59	
Mean ± SD	1.54 ± 2.01		1.75 ± 1.75		[a]0.665[ns]
BMI kg/m^2	19.10 ± 1.25		20.50 ± 1.05		[a]0.135[ns]

ns = non significant

[a] P value reached form unpaired t-test

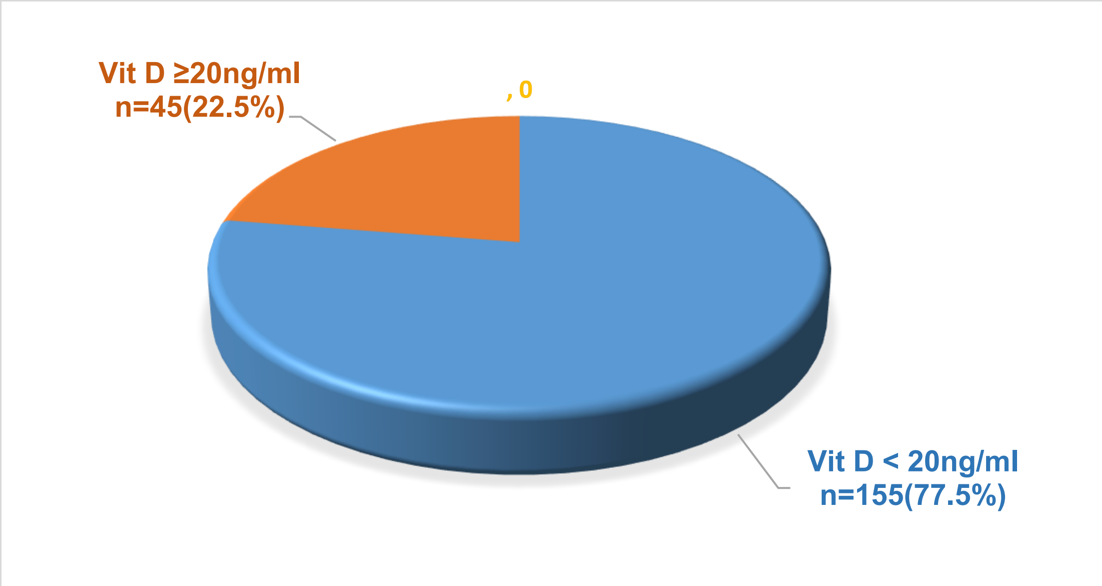

Fig. 3.2 Vitamin D deficiency (<20ng/ml) among all subjects(n=200) Pie chart showing 77.50% subjects were vitamin D deficient

Table 3.2: Comparison of serum vitamin D (ng/ml) level between case and control group.

Group	Vitamin D level (ng/ml)	P value
Case	13.83 ± 7.41	
Control	18.86 ± 5.88	[a]0.043

ns= non significant

[a]P value reached form unpaired t-test

Table 3.2 shows mean serum vitamin D (ng/ml) level between case and control group. It was found serum vitamin D level was13.83 ± 7.41 in case and 18.86 ± 5.88 in control. Difference was statically significant(p vale0.043) between case and control group regarding serum vitamin D level.

Table 3.3: Vitamin D deficiency in case and control group.

Vit D level	Case (n=100)		Control (n=100)		OR
	n	%	n	%	
Deficient(<20ng/ml)	**86**	**86**	**69**	**69**	

Not deficient(≥20ng)	**14**	**14**	**31**	**31**	**2.76**

Logistic regression analyses were conducted to estimate the odds ratio (OR)
Table4 shows high rate of vitamin D deficiency in patients. We observed that 86% of the case and 69% of the control were vitamin D deficient with a odds ratio 2.76 (OR>1) which is a positive association.

Discussion:
We did a case control study to see the Vitamin D Levels in pregnant Women with gestational HTN and preeclampsia which were compared to age and gestational age matched healthy pregnant controls. To simplify the study we only focused on gestational HTN and preeclampsia .
Among all the subjects, The Mean values of serum 25-hydroxyvitamin D levels in study group and control group were 13.83 ± 7.41ng/ml and 18.86 ± 5.88ng/ml respectively. Our study population had a very high prevalence of vitamin D deficiency. Among all the subjects, 75.50 % had serum 25(OH)D levels <20 ng/ml.We observed that 86% of the case and 69% of the control were vitamin D deficient with a odds ratio 2.76 (OR>1) which is a positive association.
Sahu M et al,[19] conducted a study in cuttaack, India atDepartment of Obstetrics and gynaecology, SCB Medical College and Hospital during 2017.Most pregnant females had vitamin D deficiency pointing towards universal prevalence. Only 10% had suboptimal to optimal vitamin D level while 90% had vitamin deficiency. The hypertensive group had lower mean serum vitamin D level (9.06±5.20 ng/ml) as compared to normotensive group (13.67±7.24 ng/ml). Our study was consistent with the study done by Sahu.In our study we found thatamong all the subjects, Mean values of serum viamin D levels in study group and control group were 13.83 ± 7.41ng/ml and 18.86 ± 5.88 ng/ml respectively.
DhillonMK et al,[18] conducted Hospital based observational comparative study in Department of Biochemistry, Rajindra Hospital, Patiala (2010) to find out significance of Vitamin D in Pregnancy Induced Hypertension. The Mean values of serum 25-hydroxyvitamin D levels in study group and control group were 9.83 ± 6.11 ng/ml and 17.86. ± 4.02 ng/ml respectively .There was decrease in Vitamin D levels in study group as compared to control group shows statistically significant association (p value< 0.04). Our study observed similar findings as compared to Dhillon M K et al.
Mehmood S et al,[17] conducted a study at Department of Gynaecology and Obstetrics, Abbasi Shaheed Hospital, Pakistan during 2016. They found significant relationship of Vitamin D Deficiency during Pregnancy with Pre-Eclampsia, Eclampsia and Gestational Hypertension. All participants had subnormal Vitamin D levels (<30 ng/ml) and 102(98%) had Vitamin D deficiency (<20 ng/ml). Of the total, 71(75.96%) had severe deficiency (<10 ng/ml). Mean Vitamin D level was 6.78 in cases and 9.43 in controls (p 0.002). Vitamin D deficiency was associated with Pre-eclampsia (p=0.045; OR 3.706) and Gestational Hypertension (p=0.025; OR 4.235). Our observation was similar(OR 2.76) to this study at South Asia region.
In North India (27ºN) Vit D deficiency was found in 91% of healthy school girls ,78% of healthy hospital staff and 84% of pregnant women[21] . our findings are consistent with the findings of North India[20]. In our study population we found that 77.50% of our subjects were vitamin D deficient.Vit D lvl may very with season, exposure to sun, clothing and other factors. Our patients were pregnant women who had lack of sun exposure. On the other hand clothing style of our country and winter season may contributed to lack of sun exposure. These factors may contributed to low level of vitamin D among study population.

Consistent with previous studies, our study showed increase in the risk of preeclampsia in vitamin D deficient mothers.Koch CA et al,[28] conducted a study on Vitamin D Deficiency and the Risk of Preeclampsia and Eclampsia in Bangladesh at 2010. In their study they found that prevalence of vitamin D insufficiency was very high with more than 3 quarters (78%) of all subjects having a serum 25(OH)D level<30 ng/ml. The mean serum 25(OH)D level was 27.86 ng/ml in controls, 23.96 ng/ml in preeclamptic women. Though our study consistent with the study, in our study we found very low vitamin D level among study subjects.

Conclusion:

Our study found significant relationship of serum vit D level with gestational HTN & pre-eclampsia. After doing statistical analysis we found P valuewas 0.043 which is statistically significant. Among all the subjects, Mean values of serum vitamin D levels in study group and control group were 13.83 ± 7.41ng/ml and 18.86 ± 5.88ng/ml respectively. Our study population had a very high prevalence of vitamin D deficiency. Among all the subjects, 77.50 % had serum 25(OH)D levels <20 ng/ml reflecting widespread vit D deficiency in all pregnant women. We observed that 86% of the case and 69% of the control were vitamin D deficient with a odds ratio 2.76 (OR>1) which is a positive association.

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