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ASSOCIATION OF MATERNAL SERUM VITAMIN D LEVEL WITH PREECLAMPSIA

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ABSTRACT

Pre-eclampsia is a pregnancy specific syndrome, often resulting in several maternal and fetal morbidities. It is a disease of theories. The main causes for this disorder have not been specifically determined so far vitamin-D deficiency is proposed to be an important element in the pathogenesis of pre-eclampsia. The aim of the study is to evaluate the association of maternal serum vitamin-D level with pre-eclampsia. A case control study carried out in the department of Obstetrics and Gynecology, Institute of Child and Mother Health (ICMH), Matuail, Dhaka, from July 2018 to June 2019. A total 60 singleton pregnant women between 18-35 years of age were included in this study in their 24-40 weeks of gestation. Among them, 30 diagnosed women with pre-eclampsia as cases and the rest of the 30 matched healthy pregnant women were selected as controls their serum vitamin-D level was measured in the laboratory of the department of Biochemistry in BSMMU, Dhaka. Proteinuria was measured by the dip-stick method. Descriptive analysis was done using the analytic software SPSS V-270, were required vitamin D deficient state was more pronounced in pre-eclamptic women than the healthy controls which was 19.13±10.85 and 41.18±18.61 respectively considering serum vitamin-D level of 30 as a cut-off value, odd's ratio calculation showed pre-eclampsia incidence was 8.63 times more likely in pregnant women with vitamin-D <30ng/ml than those with <30ng/ml (OR=8.63, 95% CI=2.57-29.07). There was significant negative Pearson's (r= -.532, p<0.001) between serum vitamin-D level with systolic blood pressure and diastolic blood pressure (r=-.460, p<0.001). The study concluded low maternal serum vitamin-D level was found strongly associated with GDM.

INTRODUCTION

Pre-eclampsia is a serious pregnancy specific multisystem disorder that affects upto 8% of pregnant women. Its prevalence is 2-10% of all pregnancies and this may be higher in low resource settings (Kiondo et al 2014).[1] Worldwide the incidence of pre-eclampsia ranges between 2% and 10% of pregnancies (Osungbade et al.2011).[2] Its incidence is seven times higher in developing countries (2.8% of live births) than in developed countries (0.4%).(WHO, 2005).[3]

Preeclampsia is a multisystem disorder that is primarily characterized by systolic blood pressure of 140 mm Hg or more or diastolic blood pressure of 90 mm Hg or more on two occasions at least 4 hours apart 20 weeks of gestation in a woman with a previously normal blood pressure and proteinuria, 300mg or more per 24 hours urine collection (or this amount extrapolated from a timed collection (or this amount extrapolated from a timed collection) or protein/creatinine ratio of 0.3 mg/dl or more or dipstick reading of 2+ (used only if other quantitative methods not available) or in the absence of proteinuria, new-onset hypertension with the new onset of any of the following: thrombocytopenia (platelet<100,00x10^9/L), renal insufficiency (serum creatinine concentrations>1.1 mg/dl or a doubling of the serum creatinine concentration in the absence of other renal disease), impaired liver function (elevated blood concentrations of liver transaminases to twice normal concentration), pulmonary edema, new-onset headache unresponsive to medicine and not accounted by alternative diagnosis of visual symptom (ACOG, 2019).[4]

The complications of Preeclampsia include eclampsia, HELLP syndrome, pulmonary oedema, disseminated intravascular coagulation and renal and hepatic failure (Duley, 2009).[5] Risks to the fetus include intrauterine growth restriction(IUGR), small for gestational age (SGA), low birth weight, premature birth,

oligohydramnios, placental abruption, low APGAR score, still birth and neonatal death (Harmon et al., 2015).[6] The pathophysiological mechanism of preeclampsia in pregnancy is characterized by failure of the trophoblastic invasion of the spiral arteries, leading to maladaptation of maternal spiral arterioles, which may be associated with an increased vascular resistance of the uterine artery and a decreased perfusion of the placenta (orhan et al., 2003, osmanagaoglu et al., 2005).[7,8]

Many possible mechanisms have been proposed to explain why vitamin D status may impact preeclampsia risk. Because vitamin D is thought to influence gene transcription, immune function and blood pressure, some have suggested that 1, 25-dihydroxy vitamin D may play role in the regulation of genes responsible for placental invasion and blood vessel formation (Evans et al., 2004).[10]

Earlier studies have shown that maternal vitamin D deficiency during pregnancy may be an independent risk factor for preeclampsia (Achkar et al., 2015).[11] Vitamin D deficiency is associated with physiologic changes such as altered endothelium function and increased cytokine levels (Cardus et al., 2006)[12] that are similar to pathogenesis of preeclampsia. Several previous studies had reported a positive association of Vitamin D deficiency with preeclampsia (Tabesh et al., 2013)[13] whilst other study shown no association (Yu et al., 2013).[14] Present study aimed to investigate the relationship of maternal serum vitamin D level with preeclampsia.

METHODS

This is a case control study was conducted in the department of Obstetrics & Gynaecology of the institute of child and mother health (ICMH), Matuail, Dhaka from July 2018 to June 2019. A total of 60 pregnant women between 24 to 40 weeks of gestation (age 18 to 35 years) attending the inpatient & outpatient department of Obstetrics & Gynecology, ICMH, were enrolled in this study. Among them, 30 pregnant women diagnosed with preeclampsia considered the cases and the rest of the 30 matched healthy pregnant women were selected as controls criteria for exclusion were diagnosed case of chronic hypertension, chronic renal disease, gestational diabetes mellitus/ pregestational diabetes, autoimmune disease, multiple pregnancy, previous history of preeclampsia patient, patient who are taking vitamin D supplementation. After taking informed consent and matching eligibility criteria, data were collected from patients using the predesigned structured questionnaire measurement of serum vitamin D in the department of Biochemistry and Molecular Biology, BSMMU, Dhaka. For quantitative determination of total 25-OH vitamin D concentrations expressed in ng/ml with the reference value corresponding to low/inadequate level: Deficient:≤20.00ng/ml; Insufficient: 21.00-29.00ng/ml; Adequate/normal level:≥30.00ng/ml.(Holick et al., 2011).[15] For this study serum vitamin D level was categorized based on the cut off value as normal (≥30) and low (<30). After 10 minutes rest BP was measured following the standard procedure. Korotkoff phase-1(first beat heard) and phase V (disappearance of sound) was used to determine systolic (SBP) and diastolic blood pressure (DBP). Data were analysed using SPSS (version 27.0) and presented as table. P- value <0.05 was considered significant.

RESULTS

Table 1: Distribution of the study subjects by demographic variables (N=60)

Demographic variable	Case (n=30) No. (%)	Control (n=30) No. (%)	P value
Age (in years)			
20-25	11(36.7%)	7(23.3%)	
26-30	14(46.7%)	16(53.3%)	
>30	5(16.7%)	7(23.3%)	
Mean±SD Range (min-max)	26.13±3.51 20-32	27.73±3.16 21-35	[a]0.169[ns]
Occupation			
Housewife	24(80.0%)	20(66.7%)	
Service	6(20.0%)	8(26.7%)	[b]0.266[ns]
Heavy worker	0(0.0%)	2(6.7%)	
Monthly income (Tk)			
5000-10000 Tk.	3(10.0%)	2(6.7%)	[b]0.322[ns]
10000-20000 Tk.	5(16.7%)	1(3.3%)	
20000-30000 Tk.	12(40.0%)	14(46.7%)	
>30000 Tk.	10(33.3%)	13(43.3%)	

Data were expressed as frequency and percentage and mean±SD

[a]Unpaired student t-test and [b]Chi-square test
ns = not significant

Case: Pregnant women with preeclampsia
Control: Pregnant women without preeclampsia

Table-1 shows that maximum patients (46.7%) in case group age 26-30 years and 53.3% in control group. Majority of the patients were housewife (80.0%) in case group and 66.7% patients in control group. Maximum patients 40.0% and 46.7% had monthly income 20000-30000 Tk. in case and control group respectively. No significant difference was found between case and control group regarding age, occupation and monthly income (p>0.05).

Table-2: Distribution of the respondents according to obstetric history in two groups (N=60).

Obstetric history	Case (n=30)	Control (n=30)	P value
Gestational age (weeks) Mean±SD	37.13±1.87	36.61±1.94	[a]0.283[ns]
Gravida			
Primigravida	16(53.3%)	17(56.7%)	[b]0.795[ns]
Multigravida	14(46.7%)	13(43.3%)	

Data were expressed as frequency and percentage and mean±SD

[a]Unpaired student t-test and [b]Chi-square test
ns = not significant
Case: Pregnant women with preeclampsia
Control: Pregnant women without preeclampsia

Respondents gestational age were matched according to selection criteria and there was no statistically significant difference of gravida between case and control group (p=0.795).

Table 3: Comparison of mean serum 25-hydroxy vitamin D between two groups (N=60).

Serum 25-hydroxy vitamin D (nmol/L)	Case (n=30)	Control (n=30)	P value
Mean±SD	19.13±10.85	41.18±18.61	<0.001[s]
Median	15.0	39.15	
Range	7.14-47.60	16.39-84.82	

Data were expressed as frequency and percentage and mean±SD.

Mann-Whitney U test
s = significant
Case: Pregnant women with preeclampsia
Control: Pregnant women without preeclampsia

Table-3 shows that the mean serum 25-hydroxy vitamin D was significantly lower in case group compare to control (p<0.001).

Table 4: Status of serum 25-hydroxy vitamin D level at cut of value 30 nmol/L in two groups (N=60).

Serum 25-hydroxy vitamin D (nmol/L)	Case (n=30) No. (%)	Control (n=30) No. (%)	OR 95%CI	P value
<30 ng/ml	25(83.3%)	11(36.7%)	8.63 (2.57-29.07)	0.0002[s]
≥30 ng/ml	5(16.7%)	19(63.3%)		
Total	30(100.0%)	30(100.0%)		

Data were expressed as frequency and percentage

Chi-square
s = significant
Case: Pregnant women with preeclampsia
Control: Pregnant women without preeclampsia

According to Table-4, serum 25-hydroxy vitamin D deficiency (<30 ng/ml) was observed to be significantly associated with cases than that of their control counterpart (83.3% vs 36.7%), p=0.0002). The risk of developing severe preeclampsia was 8.63 times higher in pregnant women with serum 25(OH)D <30ng/ml than those pregnant women with serum 25(OH) D ≥ 30 ng/ml.

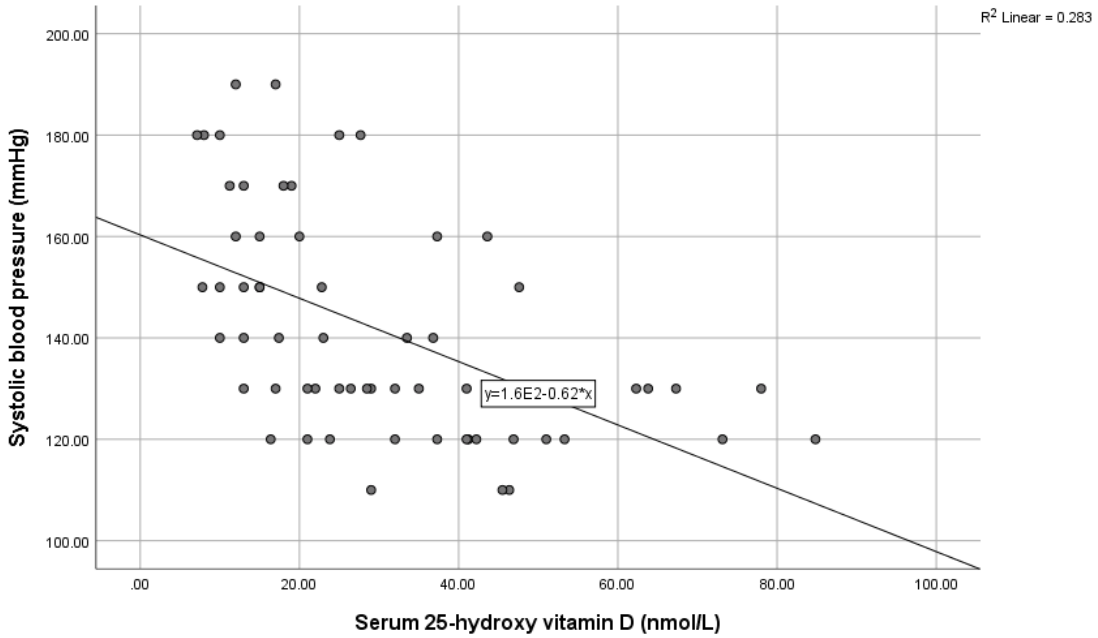

Figure 1: Scatter diagram shows the significant negative correlation of serum Vitamin D with systolic blood pressure (r=-.532, p<0.001).

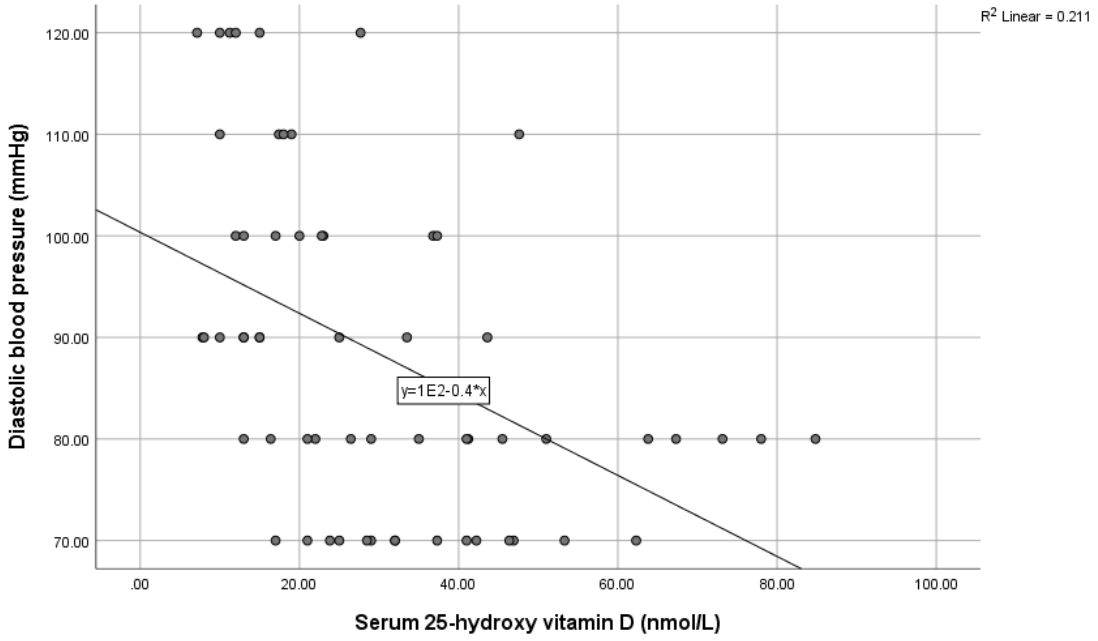

Figure-2: Scatter diagram shows the significant negative correlation of serum Vitamin D with diastolic blood pressure (r= -.460, p<0.001)

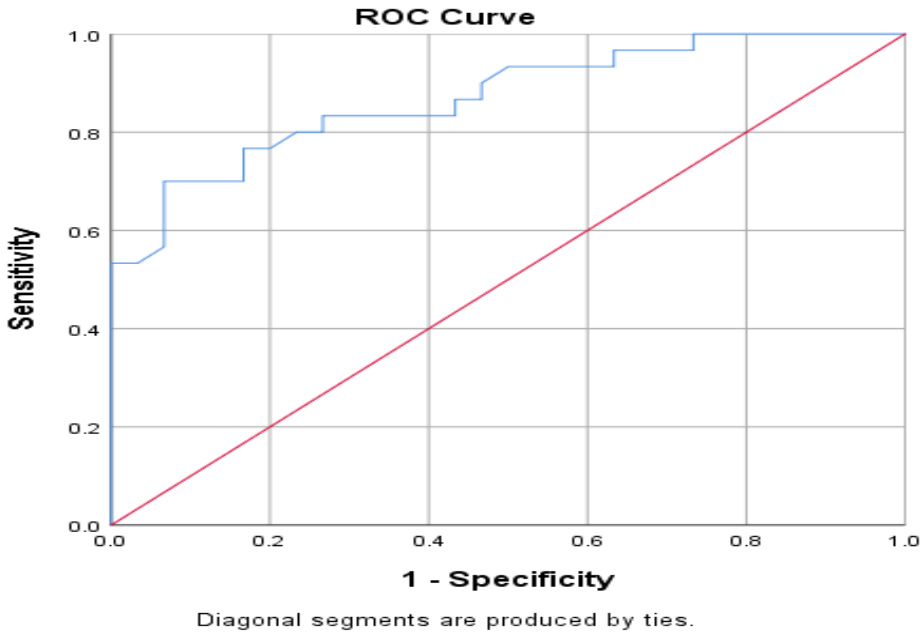

Figure-3: ROC curve analysis of serum Vitamin D and its relation with preeclampsia.

AUC	=	0.871
Cut of value	=	30.0
Sensitivity	=	80.0%
Specificity	=	70.0%

The ROC curves were used to calculate the threshold values having the best sensitivity and specificity for the prediction of preeclampsia. The areas under the curve (AUC) was to 0.871 (95% CI (0.782–0.595)), (P = 0.001) and the best cut of value of vitamin D value was 30.0 ng/mL with sensitivity 80% and specificity 70%.

DISCUSSION

This case control study was conducted to compare the serum vitamin D level in pregnant women with preeclampsia and without GDM for risk estimation and evaluate any association between maternal serum vitamin D and preeclampsia. A total of 30 pregnant women with preeclampsia and 30 pregnant women without Preeclampsia were taken according to the selection criteria.

In this study their mean age distribution was almost similar (case:26.13±3.51 years and control: 27.73±3.16 years) which was quite similar to finding of the study conducted by Mehmood and Karim (2016).[16]

In this current study occupation of women with preeclampsia was not significantly different from healthy pregnant women (Nugteren et al.2012).[17] Study did not found consistent association between any types of work associated with preeclampsia.

In this study there is no significant difference in the mean gestational age of cases (37.13±1.87) & controls (36.61±1.94) respectively which is quite similar to the study by Ullah et al. (2013).[18]

In this study 53.3% patients were primigravida in case and 56.7% in control .The difference was statistically not significant between two groups (Yelikar et al.,2016, and Wadhwani et al., 2015) which are consistent with the current study.

In this study mean serum vitamin D level among the case was much lower (19.13±10.85) than that of the controls (41.18±18.61) this result was statistically significant($p<0.001$).

Low level of vitamin D <30 ng/mi was more (83.3%) in the case compared to the control group (36.7%) which was statistically significant (p=0.0002), the respondents with vitamin D<30ng/ml had 8.63 times more chance to develop preeclampsia compared to that of the control group(OR=8.63; 95%CI=2.57-29.07).

Dabbagh manesh and his co researcher obtained in their study that vitamin D level was found to be 12.7±5 ng/ml and 15±51ng/ml in preeclampsia & healthy pregnant women respectively.

According to Sadin et al.(2015) 60% of the preeclamptic women were vitamin D deficient, and 40% were vitamin D insufficient therefore maternal 25(OH)D concentration less than 10ng/ml was associated with a 15 fold increase in the odds ratio of preeclampsia (adjusted OR,14.98; 95% CI, 4.01-55.95), compared to 25(OH)D concentration ≥10ng/ml.[22]

Abedi et al (2014) showed that on multiple logistic regression analysis vitamin D deficiency was found significantly higher in the preeclampsia group (Odds ratio, OR=24.04, CI=2.10-277.8, P=0.01).[23]

A negative correlation between the respondents blood pressure (both SBP & DBP) with their serum vitamin D level was observed (r= -0.532, p<0.001; and r= -0.460, p<0.001 respectively) among the the preeclamptic cases, which backs our hypothesis that low vitamin D level is closely related to preeclampsia similar observation was also observed in studies conducted by Sadin et al. (2015) where vitamin D concentration showed negative correlation with both systolic (r =-0.370; P= 0.001) and diastolic blood pressure (r=0.387; P=0.001).[22]

Therefore, in current study all the findings showed the association of low vitamin D level among the Preeclamptic women.

Coonclusion: The findings of this study suggest that low maternal serum vitamin D level is significantly associated with an elevated risk for the development of preeclampsia.

Limitations

1. The study was conducted in a single hospital. So, the study population might not represent the whole community.
2. Limited resources and facilities.
3. Sample size was small.

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