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Association of Maternal Serum Vitamin D with Preeclampsia

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Abstract

Preeclampsia is a pregnancy specific disorder in which hypertension and proteinuria occurs after 20 weeks of gestation. Preeclampsia and other hypertensive disorders of pregnancy are a leading cause of maternal and infant illness and death. But the exact pathophysiology is yet to be explored. Maternal vitamin D deficiency during pregnancy may be an independent risk factor for preeclampsia. The objective of this study is to explore the association of maternal serum vitamin D with preeclampsia. The aim of the study is to evaluate the association of maternal serum vitamin D level with preeclampsia. A cross sectional comparative study carried out in the Department of Obstetrics and Gynecology at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka for a period of twelve months. A total of 60 women between 28 to 37 complicated weeks of gestation were included in this study. Among them, 30 pregnant women with preeclampsia were included as group-I and rest 30 pregnant women without preeclampsia were served as group-II. After all aseptic precaution, 6 ml of fasting blood sample were collected from all the study subjects for estimation of serum vitamin D. Containers of urine samples were collected for estimation of urinary protein. All data were recorded, processed and plotted in tabular and figure form. Statistical analyses of the results were obtained by using window based computer software devised with Statistical Packages for Social Sciences (SPSS-22). The mean age was 27.00 ± 3.54 years in group I and 26.23 ± 3.5 years in group II. The mean BMI was 26.09 ± 6.05 kg/m² in group I and 24.12 ± 2.81 kg/m² in group II. The difference of BMI was statistically significant ($p < 0.05$) between two groups. More than half (53.3%) patients belonged to vitamin D level < 10 ng/ml in group I and 5(16.7%) in group II. The mean vitamin D level was 9.77 ± 1.98 ng/ml in group I and 12.78 ± 3.01 ng/ml in group II. The difference was statistically significant ($p < 0.05$) between two groups. A negative significant Pearson's ($r = -0.384$; $p = 0.002$) between serum vitamin D level with systolic blood pressure. Another negative significant Pearson's ($r = -0.366$; $p = 0.004$) between serum vitamin D level with diastolic blood pressure. The study concluded low maternal serum Vitamin D level increases the risk of preeclampsia.

Keywords: Maternal Serum, Vitamin D, Preeclampsia.

Introduction

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 after 20 weeks of gestation in a woman with a previously normal blood pressure and proteinuria, 300 mg or more per 24 hours urine 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 $< 100,000 \times 10^9$ /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 diagnoses of visual symptom [1]. Preeclampsia, defined by hypertension and proteinuria occurring after 20 weeks of gestation, is a multifactorial disorder that is associated with maternal and perinatal morbidity and mortality worldwide [2]. Its prevalence is 2-10% of all pregnancies and this may be higher in low resource settings [2]. It contributes 20.0% of maternal death in our country. Incidence of preeclampsia worldwide is around 2-10% of all pregnancies [3] and in developing countries around 4-18% [4]. According to the World Health Organization (WHO) its incidence is seven times higher in

developing countries (2.8% of live births) than in developed countries (0.4%) [5]. Some investigators Berhe *et al.* [6], Sebastian *et al.* [7] and Adane *et al.* [8] reported that in less-developed countries the incidence varied from 4.0% to 12.3%. These estimates are based on facility-based cross-sectional cohort studies, which are likely to overestimate rates compared with population-based data. Thus, the true incidence is unknown. Some studies have shown that changes in the levels of blood trace elements in preeclamptic patients may implicate in its pathogenesis [9, 10] while others have failed to show an association of blood levels of trace elements and prevalence of preeclampsia [11]. Preeclampsia sometimes develops without any symptoms and detected incidentally by health care providers on routine prenatal check up on maternal blood pressure and urine dipstick test. During pregnancy a rise in the diastolic blood pressure of 15 mmHg or systolic blood pressure of 30 mmHg or more than in normal, on at least two occasions are considered to be a cause of concern [12]. Others signs and symptoms of preeclampsia may include- weight gain of more than 3- 5 pound in a week, excess protein in urine (proteinuria) or additional signs of kidney problems, sudden appearance of nausea or vomiting after mid pregnancy, decreased urine output, decreased levels of platelets in the blood (thrombocytopenia,) hyperreflexia, and in severe cases upper abdominal pain, usually in the right upper quadrant area, impaired liver function, dull or severe throbbing headaches, changes in the vision, including sensation of flashing lights, auras, light sensitivity or blurry vision or spots and shortness of breath [13]. Previous studies have reported that preeclampsia may increase the prevalence of various cardiovascular disease risk factors, including metabolic syndrome, impaired insulin metabolism, micro albuminuria, endothelial dysfunction [14], inflammatory factors and oxidative stress [15]. Effective management of preeclampsia may be divided into three categories including the prevention of preeclampsia, early detection and treatment [16]. Approximately 10% to 15% of maternal death is directly associated with preeclampsia or eclampsia in low and middle income countries [17]. It is also related to unfavourable outcomes in both mother (e.g., placental abruption, preterm birth and haemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome, etc.) and foetus (e.g., stillbirth, low birth weight, and small for gestational age, etc. [18, 19] Recent epidemiological studies have emphasized the role of vitamin D deficiency in the development of preeclampsia [20]. There are Vitamin D receptors in placenta that justify the autocrine role of vitamin D in regulation of placental functions [21]. Vitamin D deficiency is prevalent among pregnant women especially in developing countries. Earlier studies have shown that maternal vitamin D deficiency during pregnancy may be an independent risk factor for pre-eclampsia [22, 23]. Recent evidence suggested that combined vitamin D and calcium intake may be associated with better metabolic health [24, 25]. The favourable effects of combined cholecalciferol and calcium intake on metabolic status and pregnancy outcomes might be result of their effects on the activation of antioxidant enzymes [26], and suppression of parathyroid hormone [27], influencing skeletal composition and smooth muscle strength [28]. There are several studies that have shown a positive association of vitamin D deficiency with preeclampsia [29], whilst other study shown no association [30]. This study aimed to investigate the maternal serum vitamin D levels in, pregnant woman with preeclampsia and pregnant woman without preeclampsia and to compare the value between the two groups.

Materials and Methods

Study design: Cross sectional comparative study.

Place of Study: This study was carried out in the Department of Obstetrics and Gynaecology, BSMMU, Dhaka, Bangladesh.

Duration of study: One year from the day of IRB approval.

Study Population: Pregnant woman with preeclampsia and pregnant woman without preeclampsia between 28 to 37 completed weeks of gestation were taken according to the selection criteria who was attending the inpatient and outpatient department of Obstetrics and Gynaecology of BSMMU, Dhaka, Bangladesh.

Sample size: Comparison of two means (Sample size of each group)

$\mu_1 - \mu_2 =$ difference between the means

$\sigma_1, \sigma_2 =$ standard deviations

$Z_{\alpha} Z_{\beta} =$ as bellow

$$\text{Sample size } (n) = \frac{(Z_{\alpha} + Z_{\beta})^2 \times (d_1^2 + d_2^2)}{(\mu_1 - \mu_2)^2} \quad [31]$$

Sample size=30 (each group).

Sampling method: Purposive and convenience sampling (non-randomized) according to availability of the patients and strictly considering the inclusion and exclusion criteria.

Inclusion criteria for Group 1: Pregnant woman aged between 20-35 years with singleton pregnancy with preeclampsia.

Inclusion criteria for Group 2: Pregnant woman aged between 20-35 years with singleton pregnancy without preeclampsia.

Exclusion criteria

- Pregnancy with chronic hypertension
- Pregnancy with GDM
- Pregnancy with chronic renal disease
- Multiple pregnancy
- Past history of preeclampsia
- Pregnant woman who have not given consent to participate in the study
- Intrauterine fetal death
- Pregnancy with acute or chronic infection

Study procedure

This cross-sectional comparative study was conducted on 60 pregnant women in 28 to 37 completed weeks of pregnancy. Among them, 30 pregnant woman with preeclampsia was included as group-I. Another 30 pregnant woman without preeclampsia was served as group-II according to the selection criteria who was attending the inpatient and out-patient department of Obstetrics and Gynecology of BSMMU.

After selection of the study subject according to inclusion and exclusion criteria and objectives, nature, purpose and potential risk of all procedures was used for the study explained in details and written informed consent from preeclampsia and woman without preeclampsia was taken. A detailed general, systematic, obstetric examination and medical history was taken. Data was collected from the patients on variables of interest using the structured pretested questionnaire designed for interview,

observation, clinical examination, hematological investigations of the patients. For each and every subject a separate data sheet was used.

Measurement of blood pressure

After 10 minutes rest, BP was measured following the standard procedure. Korotkoff phase I (first beat heard) and phase V (disappearance of sound) was used to determine systolic (SBP) and diastolic blood pressure (DBP). The BP was measured on the right arm, with the patient sitting comfortably, legs uncrossed and back and arm supported or lying on her back 45 degree to horizontal. In both cases, the occluded brachial artery was kept at the level of the heart. When BP found elevated on initial assessment, the measurement was repeated at least 4 to 6 hours apart to confirm hypertension.

Laboratory procedure (Blood collection technique)

With all aseptic precaution 5 ml fasting venous blood was collected from the subject. Sitting comfortably in a chair in a quiet room, by using sterile disposable syringe. Blood was poured in a test tube, which is covered by aluminum foil paper and immediately sent to the Biochemistry Department of BSMMU. After 10-15 minutes of collection, blood sample was centrifuged for 10-15 minutes at 3000 rpm in a dark room to obtain serum. Then sample was analyzed for serum 25 (OH) D. Competent laboratory personnel in the Department of Biochemistry and Molecular Biology, BSMMU, Dhaka, did this procedure.

Safety precaution: Universal precaution was taken. Gloves, lab

coats, and safety glasses were worn when handling all human blood products. All disposable things, which came in contact with blood was placed in a biohazard bag. Non-disposable materials at the end of the working day were disinfected. Hands were washed thoroughly after removal of personal protective devices used in handling specimens and kit reagents. Laboratory parameters Value of Vitamin D was analyzed in all blood samples collected from the study subjects.

Data collection Technique

Data was collected on variables of interest by interview, observation, clinical examination and necessary investigations. Data was collected by developing structured questionnaire which included respondent's personal information, demographic information, clinical examination and laboratory investigation.

Data Analysis

Statistical analyses was carried out by using the Statistical Package for Social Sciences version 22.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Quantitative variables was found with parametric distribution, presented as means standard deviations and tested by the Student t-test. The quantitative observations were indicated by frequencies, percentages and Chi-Square test with Yates correction was used to analyze, shown with cross tabulation. The statistical tests were conducted with the 95% confidence interval, Odds ratio and $p < 0.05$ was consider as statistically significant difference.

Results

Table 1: Distribution of the study subjects by demographic variable (n=60)

Demographic variable	Group I (n-30)		Group II (n-30)		p value
	n	%	n	%	
Age (in years)					
20-25	11	36.7	11	36.7	
26-30	14	46.6	15	50.0	
>30	5	16.7	4	13.3	
Mean \pm SD	27.00 \pm 3.54		26.23 \pm 3.5		^a 0.406 ^{ns}
Rang (min, max)	21,34		20,35		
Area of residence					
Urban	23	76.7	25	83.3	^b 0.519 ^{ns}
Rural	7	23.3	5	16.7	
Education					
Primary	4	13.3	4	13.3	^b 0.867 ^{ns}
Secondary	10	33.3	10	33.3	
Higher secondary	9	30.0	9	30.0	
Graduate	7	23.3	7	23.3	
Occupation					
House wife	23	76.7	22	73.3	^b 0.350 ^{ns}
Service	7	23.3	6	20.0	
Heavy Worker	0	0.0	2	6.7	
Monthly Income (Taka)					
5000-10000	2	6.7	1	3.3	^b 0.920 ^{ns}
10000-20000	7	23.3	8	26.7	
20000-30000	11	36.7	10	33.3	
>30000	10	33.3	11	36.7	

ns=not significant, ^ap-value reached from Unpaired t-test, ^bp value reached from Chi-square test

Group I: Pregnant woman with preeclampsia

Group II: Pregnant woman without preeclampsia

Table 1 shows the distribution of the study subjects by demographic variable. It was observed that almost half (46.6%) patients belonged to age 26-30 years in group I and 15(50.0%) in group II. The mean age was 27.00 \pm 3.54 years in group I and

26.23 \pm 3.5 years group II. More than three fourth (76.7%) patients come from urban area in group I and 22(83.3%) in group II. One third (33.3%) Patients education level were secondary in group I and group II. More than three fourth (76.7%) patients occupations were house wife in group I and 22 (73.3%) in group II. More than one third (36.7%) patients

belonged to monthly income 20000-30000 taka in group I and 10(33.3%) in group II. The difference was statistically not significant ($p>0.05$) between two groups.

Table 2: Distribution of responds by Gravida (n=60)

Gravida	Group I (n-30)		Group II (n-30)		p-value
	n	%	n	%	
Primigravida	10	33.3	11	36.7	0.787 ^{ns}
Multigravida	20	66.7	19	63.3	

ns=not significant

p-value reached from Chi-square test

Table 2 shows the distribution of responds by gravida. It was observed that more than two third (66.7%) patients were multigravida in group I and 19(63.3%) in group II. The difference was statistically not significant ($p>0.05$) between two groups.

Table 3: Distribution of responds by physical examination (n=60)

Physical examination	Group I (n-30)	Group II (n-30)	p-value
	Mean±SD	Mean±SD	
Height (cm)	153.43±5.50	153.97± 5.61	0.711 ^{ns}
Range (min-max)	144-167	148-167	
Weight (kg)	61.13±6.05	56.77±7.32	0.015 ^s
Range (min-max)	48-75	48-78	
BMI (kg/m ²)	26.09 ±6.05	24.12±2.81	0.005 ^s
Range (min-max)	22.0-31.30	18.80-30.60	

s=significant

ns=not significant

p value reached from Unpaired t-test

Table 6: Distribution of respondents by serum vitamin D level (n=60)

Serum vitamin D level ng/ml	Group I (n-30)		Group II (n-30)		OR (95% CI)	p value
	n	%	n	%		
<10 ng/ml	16	53.3	5	16.7	5.71(1.51-22.84)	0.001 ^s
>10 ng/ml	14	46.7	25	83.3		

s=significant

p value reached from Chi-square test

Table 6 shows the distribution of respondents by serum vitamin D level. It was observed that more than half (53.3%) patients belonged to vitamin D level <10 ng/ml in group I and 5(16.7%) in group II. The difference was statistically significant ($p<0.05$) between two groups

Table 7: Distribution of the study patients by severity in group I (n=30)

Severe preeclampsia	Serum vitamin D level ng/ml		p value
	Number	Mean±SD	
Mild preeclampsia	18	10.14±1.29	0.115 ^{ns}
Severe preeclampsia	12	9.17±1.99	

ns=not significant

p value reached from Unpaired t-test

The mean serum vitamin D level for mild preeclampsia was 10.14±1.29 ng/ml and 9.17±1.99 ng/ml for severe preeclampsia. The deference was statistically not significant ($p>0.05$) in severity of preeclampsia (table-7).

Table 8: Distribution of the study patients by urine protein in group I (n=30)

Urine protein	Number	Percentage
Null	0	0.0
++	27	90.0
+++	3	10.0

The mean height was 153.43±5.50 cm in group I and 153.97±5.61 cm in group II. The mean weight was 61.13±6.05 kg in group I and 56.77±7.32 kg in group II. The mean BMI was 26.09±6.05 kg/m² in group I and 24.12±2.81 kg/m² in group II. The difference of weight and BMI were statistically significant ($p<0.05$) between two groups.

Table 4: Distribution of the study subjects by blood pressure in group I (n-30)

Blood pressure	Mean±SD	Range (min-max)
Systolic blood pressure (mmHg)	152.33± 6.53	140-160
Diastolic blood pressure (mmHg)	97.83± 4.85	90-110

The mean systolic blood pressure was 152.33±6.53 mmHg. The mean Diastolic blood pressure was 97.83±4.85 mmHg.

Table 5: Comparison of vitamin D level between two groups (n-60)

Serum vitamin D level ng/ml	Group I (n-30)		Group II (n-30)		p value
	n	%	n	%	
<10 ng/ml	16	53.3	5	16.7	0.001 ^s
10-20 ng/ml	14	46.7	25	83.3	
Meant± SD	9.77± 1.98		12.78± 3.01		
Range(min-max)	5.6-13.0		8.5-20.0		

s=significant

p value reached from Unpaired t-test

Table 5 shows the distribution of responds by serum vitamin D level. It was observed that more than half (53.3%) patients belonged to vitamin D level <10 ng/ml in group I and 5(16.7%) in group II. The mean serum vitamin D was 9.77±1.98 ng/ml in group I and 12.78 ±3.01 ng/ml in group II. The difference was statistically significant ($p<0.05$) between two groups.

Table 8 shows the distribution of the study patients by urine protein in group I. It was observed that majority (90.0%) patients had ++ urine protein and 3(10.0%) in +++ urine protein.

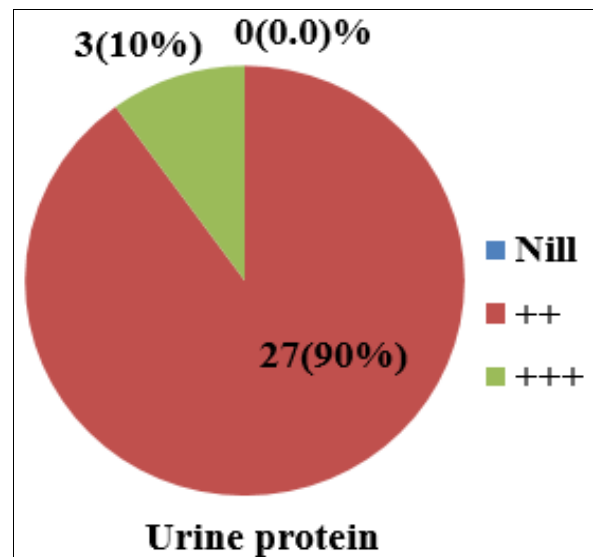


Fig 1: Pie chart showing urine protein of the study patients in group I.

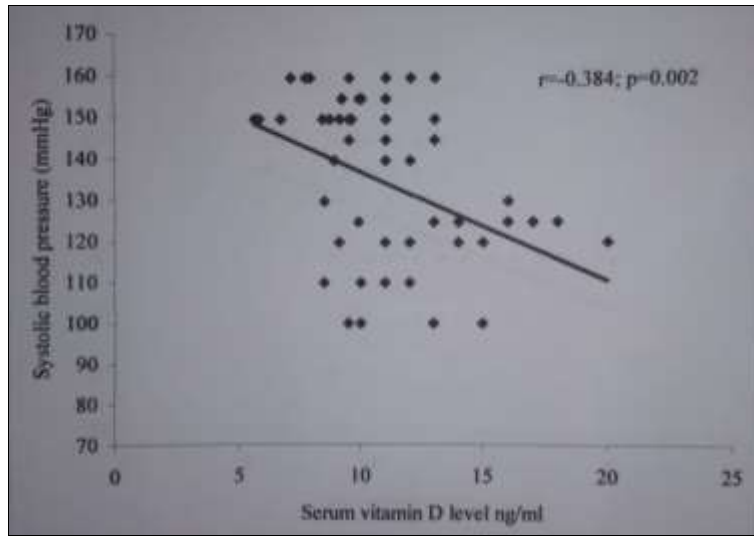


Fig 2: Scatter diagram showing negative significant Pearson's correlation ($r=-0.384$; $p=0.002$) between serum vitamin D level with systolic blood pressure.

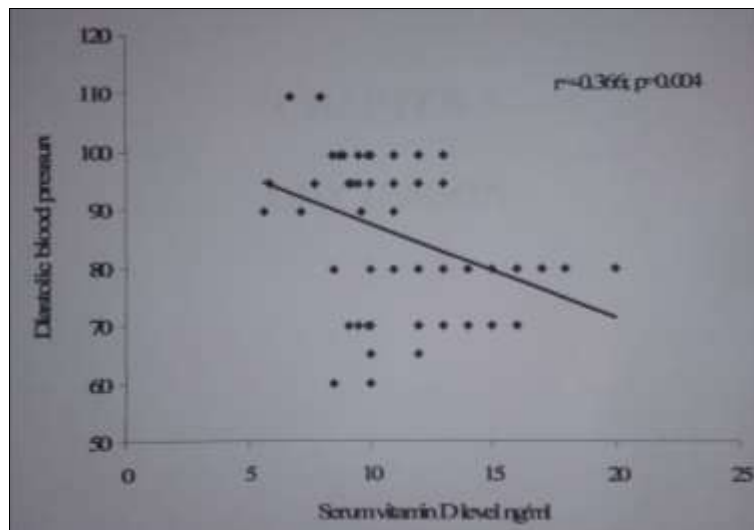


Fig 3: Scatter diagram showing negative significant Pearson's correlation ($r=-0.366$; $p=0.004$) between serum vitamin D level with diastolic blood pressure.

Discussion

This cross sectional study was carried out with an aim to estimate serum vitamin D in diagnosed case of preeclampsia and normal healthy pregnant woman as well as to compare serum vitamin D level between preeclamptic patients and serum vitamin D level in normal pregnant woman. A total of 30 pregnant woman with preeclampsia and 30 pregnant woman without preeclampsia between 28 to 37 completed weeks of gestation were taken according to the selection criteria who attended inpatient department of Obstetrics and Gynaecology of Bangabandhu Sheikh Mujib Medical University, Dhaka, during November 2019 to October 2020, were included in this study. Diagnosed case of preeclampsia with gestational age 28 to 37 completed weeks and aged between 20 to 35 years were enrolled as preeclampsia considered as Group-1. Healthy pregnant woman of 28 to 37 completed weeks of gestation and who gave consent to participate were enrolled as preeclampsia considered as Group-II. Pregnancy with chronic hypertension, GDM, chronic renal disease, multiple pregnancy, past history of preeclampsia, pregnant woman who didn't given consent, intrauterine fetal death and pregnancy with acute or chronic infection were excluded from the study. The present study findings were discussed and compared with previously

published relevant studies. In this present study, it was observed that 46.6% patients belonged to age 26-30 years in group I and 50.0% in group II. The mean age was 27.00 ± 3.54 years in group I and 26.23 ± 13.5 years in group II. The difference was statistically not significant ($p > 0.05$) between two groups. Paul *et al.* [32] study observed that the mean age was 25.15 ± 4.47 years in group I and 25.68 ± 3.55 years in group II. The difference was statistically not significant ($p > 0.05$) between two groups. However, 80.0% patient's age belonged to 21-30 years in group I and 87.5% in group II, which support with the present study. Similarly, Aghade and Bavikar *et al.* [33] showed the mean age was 24.40 ± 3.8 years in mild preeclampsia, 25.0 ± 4.3 years in severe preeclampsia and 25.50 ± 2.9 years in controls. In another study Bakacak *et al.* [34] found the mean age was 29.2 ± 8.40 in preeclampsia and 28.9 ± 5.80 in healthy pregnant. The difference was statistically not significant ($p > 0.05$), which are comparable with the current study. Again this observation indicates that there may be some unique genetic or environmental factors responsible for the disease in our country. Osman *et al.* [35] study showed the mean age was 27.50 ± 4.65 years in group I and 26.64 ± 5.49 years in group II. The difference was statistically not significant ($p > 0.05$) between two groups, which are consistent with the current study. Similar observations regarding the age

distribution were also observed by Fatima *et al.* [36] and Siddiqui *et al.* [37]. In this current study, it was observed that 76.7% patients came from urban area in group I and 83.3% in group II. The difference was statistically not significant ($p>0.05$) between two groups. Urban predominance may be due to the study place adjacent to urban area. Education is an important determinant of employment and economic circumstances and thus reflects material resources but also non-economic social characteristics, such as general and health-related knowledge which influences health behavior, literacy, problem-solving skills and prestige. Women with low educational level more likely to develop preeclampsia than women with high educational level [38]. In this present study, it was observed that 33.3% patients education level were secondary in group I and group II. The difference was statistically not significant ($p>0.05$) between two groups. Paul *et al.* [32] study found 42.5% patients education level were primary in group I and 32.5% in group II. The difference was statistically not significant ($p>0.05$) between two groups, which is similar with the present study. Silva *et al.* [38] observed after adjusted for the confounding effects of age. Gravidity and multiple pregnancy, women with low educational level were more likely to develop preeclampsia OR-5.12; 95% confidence interval: 2.20, 11.93 than women with high educational level, which support the present study. The most frequently used indicators of socioeconomic status are income level, occupational class and educational level. In this current study, it was observed that 76.7% patient's occupations were house wife in group I and 73.3% in group II. The difference was statistically not significant ($p>0.05$) between two groups. Nugteren *et al.* [39] study didn't found consistent associations between any types of work associated with preeclampsia, such as long periods of standing, walking, heavy lifting, night shifts, and working hours, nor exposure to chemicals with hypertensive disorders during pregnancy. A low maternal socioeconomic status at time of pregnancy has been shown to increase the risk for low birth weight, prematurity and perinatal mortality as well as a risk factor of hypertensive disorders in pregnancy. Low maternal socioeconomic status is a strong risk factor for preeclampsia [40]. Only a small part of this association can be explained by the mediating effects of established risk factors for preeclampsia. In this present study, it was observed that 36.7% patients belonged to monthly income 20000-30000 taka in group I and 33.3% in group II. The difference was statistically not significant ($p>0.05$) between two groups. English *et al.* [16] mentioned in their study that preeclampsia is more common in primigravida women and the risk of preeclampsia increases the greater the interval between pregnancies. In this current study, it was observed that 66.7% patients were multigravida in group I and 63.3% in group II. The difference was statistically not significant ($p>0.05$) between two groups. Similarly, Grum *et al.* [41] study observed that primigravida to be risk factor for developing preeclampsia 2.68 times higher in primigravida comparing to the multigravida women having 95% CI: 1.38, 5.22. Paul *et al.* [32] observed 65.0% patients had primi gravida in group I and 70.0% in group II. The difference was statistically not significant ($p>0.05$) between two groups. Sun *et al.* [42], Yelikar *et al.* [43] and Wadhvani *et al.* [44], which are consistent with the current study. In this current study, it was observed that the mean height was 153.43±5.50 cm in group I and 153.97±5.61 cm in group II. The difference was statistically not significant ($p>0.05$) between two groups. Bakacak *et al.* [34] study found the mean height was 161.06.47 cm in preeclampsia and 160.4±5.04 cm in healthy pregnant. The difference was statistically not significant ($p>0.05$) between two groups, which is a little higher with the

present study. In this present study, it was observed that the mean weight was 61.13 6.05 kg in group I and 56.77±7.32 kg in group II. The mean weight was significantly ($p<0.05$) higher in patients with preeclampsia. Bakacak *et al.* [34] study the mean weight was 75.9±10.89 kg in preeclampsia and 78.61±9.17 kg in healthy pregnant. The difference was statistically not significant ($p>0.05$) between two groups, which is higher with the present study. Lopez-Jaramillo *et al.* [45] mentioned that obese people has increased production of leptin and decreased production of adiponectin which are associated with the systemic low-degree inflammation and insulin resistance, observed in preeclampsia, type 2 diabetes mellitus and cardiovascular diseases, which explaining the increased risk of developing these diseases present in people with obesity, particularly abdominal obesity. In this current study, it was observed that the mean BMI was 26.09 6.05 kg/m² in group I and 24.1242.81 kg/m² in group II. The mean BMI was significantly ($p<0.05$) higher in patients with preeclampsia. Similarly, Osman *et al.* [35] observed that the mean BMI was 29.06±1.78 kg/m² in case and 25.92±0.89 kg/m² in control. The mean BMI was significantly ($p<0.05$) higher in patients with preeclampsia. On the other hand Bakacak *et al.* [34] found the mean BMI was 29.3±4.75 kg/m² in Preeclampsia and 30.6±3.72 kg/m² in healthy pregnant. The difference was statistically not significant ($p>0.05$) between two groups. Similarly in another study, Siddiqui *et al.* [37] showed that mean BMI was 32.116.28 kg/m² in preeclampsia and 31.1±5.20 kg/m² in normal. The difference was statistically not significant ($p>0.05$) between two groups. The above findings differ with the current study. Preeclampsia usually occurs after the 34th week of gestation, but it can develop after the infant is delivered. It is usually presents after 20 weeks' gestation [45]. Similarly, in this current study, it was observed that 53.3% patients belonged to duration of pregnancy >34-36 in group I and all patients belonged to duration of pregnancy >36 in group II, which is comparable with Aghade and Bavikar *et al.* [33] and Dabbaghmanesh *et al.* [46] studies.

In this present study, it was observed that the mean systolic blood pressure was 152.33±6.53 mmHg. Aghade and Bavikar *et al.* [33] mentioned in their study that the systolic and diastolic blood pressures were significantly increased in preeclamptic patients compared with normal pregnant women. In another study Paul *et al.* [32] found the mean systolic blood pressure was 145.75±18.44 (mmHg) in preeclamptic patients. Similar observations also observed by Osman *et al.* [35], Bakacak *et al.* [34] and Dabbaghmanesh *et al.* [46]. In this current study, it was observed that the mean diastolic blood pressure was 97.83±4.85 mmHg. Similarly Bakacak *et al.* [35] found the mean diastolic blood pressure was 105.7±6.62 mmHg in preeclampsia patients. Similar observations regarding the diastolic blood pressure also observed by Paul *et al.* [32], Nidumuru and Reddy [47] and Serrano *et al.* [48], Aghade and Bavikar [33] and Dabbaghmanesh *et al.* [46]. Abnormal placentation in preeclampsia leads to decreased activation, increased catabolism, and impaired placental uptake of vitamin D and is unable to produce sufficient levels of 1,25-(OH)₂ vitamin D [33]. In this present study, it was observed that 53.3% patients belonged to vitamin D level <10 ng/ml in group I and 16.7% in group II. Serum vitamin D level <10 ng/ml is a risk factor for developing preeclampsia and the risk is 5.71 times higher in vitamin D level <10 ng/ml comparing to Serum vitamin D level >10 ng/ml women having 95% CI: 1.51, 22.84. The mean serum vitamin D level was 9.77±1.98 ng/ml in group I and 12.78±3.01 ng/ml in group II. The mean serum vitamin D level was significantly ($p<0.05$) lower in patients with preeclampsia. Bakacak *et al.* [34] obtained in their study that

vitamin D levels were lower in preeclamptic patients compared to healthy normotensive pregnant women ($p < 0.001$). Vitamin D supplementation is considered to decrease the risk of preeclampsia in the patient population at risk for vitamin D deficiency. The authors reported that vitamin D level was found to be 19.3 ± 4.31 ng/ml and 23.7 ± 5.93 , in preeclamptic women and in healthy pregnant women respectively. Vitamin D deficiency is around 66-100% in women with a dark skin color [49, 50]. Vitamin D has been thought to play a potent endocrine suppressor role in renin biosynthesis for the regulation of the renin-angiotensin system (RAS). In addition, in other studies on the role of vitamin D in the development of preeclampsia, vitamin D has been emphasized to play an immunomodulatory and anti-inflammatory role in many systems [51]. Vitamin D also has been suggested to play a role in major signal and gene regulations in the development of placental trophoblasts in the placental growth phase (Novakovic *et al.* 2009 and Diaz *et al.* 2009) [52, 53].

Dabbaghmanesh *et al.* [46] study results also observed the mean maternal serum D levels 12.7 ± 5.4 ng/ml and 15 ± 5.1 ng/ml in preeclampsia and healthy group respectively, which is comparable with the current study. At present, there is insufficient evidence to justify setting dietary vitamin D recommendations based on the avoidance of gestational hypertensive disorders alone. Two meta-analyses of observational studies that have shown a significant association between vitamin D deficiency and preeclampsia risk [54, 55]. In this current study, it was observed that 90.0% patients had ++ urine protein and 10.0% had +++ urine protein. Preeclampsia is a condition characterized by an onset of hypertension and proteinuria after 20 weeks of gestation in a previously normotensive pregnant woman [56, 57]. According to the new ACOG (American College of Obstetricians and Gynecologists), diagnostic criteria for pre-eclampsia the presence of proteinuria has been eliminated. In absence of proteinuria new-onset hypertension with thrombocytopenia, elevated liver enzymes, renal insufficiency, pulmonary edema and cerebral or visual symptoms are defined as pre-eclampsia [1]. In this current study, it was observed that 90.0% patients had ++ urine protein and 10.0% had +++ urine protein. Paul *et al.* [32] study found that 65.0% patients had urine protein ++, 17.5% in + and 17.5% had +++, which is comparable with the present study. In this present study, it was observed that negative significant Pearson's ($r = -0.384$; $p = 0.002$) between serum vitamin D level with systolic blood pressure and there was also a negative significant Pearson's ($r = -0.366$; $p = 0.004$) between serum vitamin D level with diastolic blood pressure.

Conclusion

This study was undertaken to evaluate the association of maternal serum vitamin D level with preeclampsia. Most of the patient's age belonged to 20 -30 years, came from urban area, poor educational level, housewife and belonged to low income status. This study demonstrates that vitamin D plays a role in the development of preeclampsia. This study revealed a relationship between vitamin D and preeclampsia, where vitamin D levels significantly lesser in patients with preeclampsia. Significant negative correlation was found between vitamin D with systolic blood pressure and diastolic blood pressure.

Limitations

1. The study population was selected from one selected hospital in Dhaka city, so that the results of the study may not be reflect the exact picture of the country.

2. The present study was conducted at a very short period of time.

Recommendations

To undertake further study with a larger sample size to find out the validity of the findings of the present study. Vitamin D supplementation can be a part of pre-pregnancy counseling increasing intake of vitamin D during pregnancy, period particularly in those with detected severely abnormal lower serum levels, may protect against preeclampsia.

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Author's Contribution

Not available

Conflict of Interest

Not available

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