Association of Serum CA-125 with Preeclampsia in a Tertiary Care Hospital

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ABSTRACT

Background: Preeclampsia (PE) is a serious pregnancy-related hypertensive disorder causing significant maternal and perinatal complications; this study aimed to investigate the association of CA-125 as a potential biomarker for PE due to placental inflammation and impaired trophoblast invasion. **Methods & Materials:** The case-control study was carried in the Department of Obstetrics and Gynaecology, Institute of Child and Mother Health (ICMH), Matuail, Dhaka. The sampling method was purposive according to the availability of the patients. Data were collected from women aged 18-35 years where patients with PE (n=38) were considered as cases and the healthy pregnancy (n=38) were the controls. The serum CA-125 level of both cases and controls were measured in the laboratory of Biochemistry and Molecular Biology Department. The descriptive and inferential analysis was carried out using SPSSv26. p-value < 0.05 was considered as statistically significant. **Result:** The mean serum CA-125 level was significantly higher in PE (32.7 ± 6.97 U/ml) cases than in healthy women (14.6 ± 6.93 U/ml) (p=0.001). Patients with serum CA-125 level ≥ 35.0 U/ml had 6.07 times more chance to have PE compared to those with serum CA-125 level <35.0 U/ml (p=0.005; OR=6.07; 95% CI=1.56-23.55). There was a significant positive correlation of serum Ca-125 level with both systolic blood pressure (r=0.759, p<0.001) and diastolic blood pressure pressure (r=0.732, p<0.001) and also with proteinuria (rs=0.715, p<0.001). **Conclusion**: Serum CA-125 levels were significantly increased in preeclampsia with positively correlated with blood pressure.

Keywords: *Preeclampsia, CA-125, Hypertension in pregnancy, Proteinuria, Placental dysfunction, Maternal biomarkers.*

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INTRODUCTION

Preeclampsia (PE) is a common hypertensive disorder of pregnancy associated with significant maternal and neonatal morbidity and mortality worldwide. Currently, delivery remains the only definitive cure; therefore, identifying effective preventive and diagnostic strategies is essential [1]. PE is clinically defined as the new onset of hypertension (≥140 mmHg systolic or ≥90 mmHg diastolic on two occasions at least 4 hours apart) with proteinuria (≥300 mg in a 24-hour urine collection or ≥1+ dipstick) occurring after 20 weeks of gestation [2,3].

Severe preeclampsia is characterized by systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥110 mmHg accompanied by complications such as thrombocytopenia, renal insufficiency, pulmonary edema, or neurological disturbances [2]. Globally, preeclampsia complicates approximately 2–8% of pregnancies and remains a major contributor to maternal and perinatal mortality, particularly in low- and middle-income countries [4,5].

In Bangladesh, hypertensive disorders of pregnancy, including preeclampsia and eclampsia, account for about 16% of maternal deaths [6]. The condition is considered a multisystem disorder involving abnormal placentation, endothelial dysfunction, inflammation, oxidative stress, and imbalance between vasodilatory and vasoconstrictive factors [7]. Defective trophoblastic invasion of the maternal spiral arteries leads to placental ischemia and the release of inflammatory mediators and anti-angiogenic factors, which contribute to systemic vascular dysfunction and maternal organ damage [8]. Several maternal risk factors have been identified, including chronic hypertension, diabetes mellitus, renal disease, autoimmune disorders, multifetal pregnancy, obesity, nulliparity, advanced maternal age, and a history of preeclampsia or placental complications [9]. Because of the complex and multifactorial pathophysiology of PE, numerous biomarkers have been investigated to improve early prediction and diagnosis. These include markers related to renal function, placental hormones, endothelial dysfunction, and angiogenic factors such as sFlt-1 and PlGF [10]. Cancer antigen-125 (CA-125), also known as MUC16, is a high-molecular-weight glycoprotein commonly used as a tumor marker in ovarian cancer but is also expressed in several benign conditions, including pregnancy and inflammatory disorders [11]. During pregnancy, CA-125 may originate from the fetal chorion, amniotic fluid, and maternal decidua. Elevated levels have been associated with decidual damage and trophoblastic separation, processes that may occur in preeclampsia due to abnormal placentation and inflammatory responses [12]. However, the clinical significance of CA-125 in obstetrics remains uncertain, and existing studies have reported inconsistent findings regarding its association with preeclampsia [12].

Given the need for reliable biomarkers for early detection and monitoring of preeclampsia, the present study aimed to evaluate maternal serum CA-125 levels in normal and preeclamptic pregnancies and to explore the potential clinical utility of

this marker in the prediction and diagnosis of preeclampsia.

METHODS & MATERIALS

This case–control study was conducted in the Department of Obstetrics and Gynaecology at the Institute of Child and Mother Health (ICMH), Matuail, Dhaka, Bangladesh, over a 12-month period from July 2022 to June 2023. The study population comprised pregnant women attending the inpatient and outpatient departments. A total of 76 participants were enrolled using purposive sampling, including 38 cases (pregnant women with singleton pregnancy between 20–40 weeks of gestation diagnosed with preeclampsia) and 38 controls (normotensive healthy pregnant women with singleton pregnancy between 20–40 weeks of gestation). The calculated sample size was based on comparison of two means using previously reported serum CA-125 values. Women aged 18–35 years who provided informed written consent were included, while those with chronic hypertension, ovarian tumors, chronic renal disease, diabetes mellitus, or multiple pregnancies were excluded from this study. Preeclampsia was defined as blood pressure ≥140/90 mmHg measured on two occasions at least 4 hours apart after 20 weeks of gestation with proteinuria (≥1+ dipstick or ≥300 mg/24-hour urine). Data were collected using a semi-structured questionnaire including demographic information, antenatal history, clinical examination, and relevant investigations. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Five milliliters of venous blood were collected from the antecubital vein under aseptic conditions, centrifuged at 4000 rpm, and the serum stored at −20 °C until analysis. Serum CA-125 levels were measured using a chemiluminescent immunometric assay (CLIA) on the YHLO iFlash 3000 analyzer, with ≥35 U/mL considered elevated. Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) software, version 26.0. Descriptive statistics were expressed as frequency, percentage, mean, and standard deviation. Differences between groups were assessed using the unpaired t-test and Chi-square test, while Fisher's exact test was applied where appropriate. Odds ratios (OR) with 95% confidence intervals (CI) were calculated to determine the strength of associations. Pearson's correlation coefficient was used to assess the relationship between serum CA-125 levels and systolic and diastolic blood pressure, and Spearman's rank correlation was used for association with proteinuria. A p-value <0.05 was considered statistically significant. Ethical approval was obtained from the Institutional Review Board of the Institute of Child and Mother Health (ICMH), Matuail, Dhaka, Bangladesh.

RESULTS

Table I shows among the total 76 patients, 38 were included in the case group and 38 in the control group. Regarding age distribution, more than half of the patients in both groups were between 20–30 years. In the case group, 21 patients (55.3%) were aged 20–30 years, followed by 14 (36.8%) aged below 20 years and 3 (7.9%) aged above 30 years. In the control group, the majority 28 patients (73.7%) were aged 20–30 years, while 9 patients (27.3%) were below 20 years and only 1 patient (2.6%) was above 30 years. The mean age of the patients in the case group was 23.63 ± 4.54 years, whereas in the control group it was 23.89 ± 4.05 years (p = 0.268), and the difference in mean age was also not significant (p = 0.791). In the case group, 32 patients (84.2%) had SSC and below level education and 6 patients (15.8%) had education above SSC. Similarly, in the control group, 35 patients (92.1%) had SSC and below education, while 3 patients (7.9%) had education above SSC (p = 0.480). In the case group, 30 patients (78.9%) were housewives; while 4 patients (10.5%) were students and 4 patients (10.5%) were service holders. In the control group, the majority 36 patients (94.7%) were housewives and 2 (5.3%) were service holders, with no respondents being students. However, the difference in occupation between the two groups was not statistically significant (p = 0.070). Considering monthly family income, the mean family income of the case group was 27947.3 ± 2852.4 BDT, whereas the mean family income of the control group was 23289.4 ± 6501.1 BDT (p = 0.050).

Table I
Comparison of the respondents according to socio-demographic characteristics (*n*=76).

Socio-demographic variables	Case (n = 38)	Control (n = 38)	p value
Age (in years)			
< 20 years	14 (36.8)	9 (27.3)	0.268 b
20-30 years	21 (55.3)	28 (73.7)	
> 30 years	3 (7.9)	1 (2.6)	
Mean age	23.63 ± 4.54	23.89 ± 4.05	0.791c
Educational qualification			
SSC and below	32 (84.2)	35 (92.1)	0.480 b
Above SSC	6 (15.8)	3 (7.9)	
Occupation			
Housewife	30 (78.9)	36 (94.7)	0.070 b
Student	4 (10.5)	0 (0.0)	
Service holder	4 (10.5)	2 (5.3)	
Monthly family income			
Mean family income	27947.3 ± 2852.4	23289.4 ± 6501.1	0.050 c

Chi-square test was done to measure the level of significance; Fisher's exact test was done to measure the level of significance; Unpaired t-test was done to measure the level of significance. Figure within parentheses indicates percentage.

Table II presents the mean gestational age of the patients in the case group was 34.29 ± 4.76 weeks, whereas in the control group it was 35.42 ± 4.24 weeks. (p = 0.278). In the case group, 23 patients (60.5%) were multigravida and 15 patients (39.5%) were primigravida. Similarly, in the control group, 25 patients (65.8%) were multigravida, while 13 patients (34.2%) were primigravida (p = 0.812). The majority of patients in the case group had irregular ANC follow-up, accounting for 24 patients (63.2%), while 14 patients (36.8%) had regular ANC. In the control group, most patients had regular ANC, accounting for 18 patients (47.4%), whereas 20 patients (52.6%) had irregular ANC (p = 0.243). The majority of patients

in both groups had a history of OCP use. In the case group, 27 patients (71.1%) had a history of taking OCP, while 11 patients (28.9%) had no such history. Similarly, in the control group, 31 patients (81.6%) had a history of OCP use and 7 patients (18.4%) did not (p = 0.419). The majority of patients in the case group had a positive family history, accounting for 24 patients (63.2%), while 14 patients (36.8%) had no family history of hypertension. In contrast, in the control group, an equal proportion of patients reported and did not report a family history of hypertension, with 19 patients (50.0%) in each category (p = 0.355).

Table II
Comparison of the respondents according to their obstetrical characteristics and medical history by group (*n*=76).

Obstetrical characteristics	Case (n = 38)	Control (n = 38)	p value
Gestational age (in weeks)			
Mean ± SD	34.29 ± 4.76	35.42 ± 4.24	0.278 c
Gravida			
Primigravida	15 (39.5)	13 (34.2)	0.812a
Multigravida	23 (60.5)	25 (65.8)	
ANC			
Regular	14 (36.8)	18 (47.4)	0.243a
Irregular	24 (63.2)	20 (52.6)	
H/O taking OCP			
Yes	27 (71.1)	31 (81.6)	0.419a
No	11 (28.9)	7 (18.4)	
Family H/O hypertension			
Yes	24 (63.2)	19 (50.0)	0.355a
No	14 (36.8)	19 (50.0)	

Table III shows in the case group, the majority 30(78.9%) patients were overweight, followed by 4 (10.5%) had normal BMI and 4 (10.5%) were obese while in the control group, 32(84.2%) patients had normal BMI, followed by 6 (15.8%) were overweight, and none of the patients were obese. The mean BMI of the patients in the case group was 27.84 ± 1.94 kg/m², whereas the mean BMI in the control group was 23.27 ± 2.04 kg/m². (p < 0.001).

Table III
Comparison of the respondents according to BMI (*n*=76).

BMI (kg/m2)	Case (n = 38)	Control (n = 38)	p value
Normal (18.5 - 24.9)	4 (10.5)	32 (84.2)	<0.001 b
Overweight (25.0-29.9)	30 (78.9)	6 (15.8)	
Obesity (30 - 34.9)	4 (10.5)	0 (0.0)	
Mean ± SD\	27.84 ± 1.94	23.27 ± 2.04	<0.001

Fisher's exact test was done to measure the level of significance; Unpaired t-test was done to measure the level of significance; Figure within parentheses indicates percentage

Table IV shows the mean systolic blood pressure was much higher among patients in the case group compared to the control group. The mean systolic blood pressure in the case group was 156.32 ± 11.00 mmHg, whereas in the control group it was 107.37 ± 7.60 mmHg. Similarly, the mean diastolic blood pressure was also higher in the case group (103.95 ± 7.54 mmHg) compared to the control group (72.74 ± 8.71 mmHg). The differences in both systolic and diastolic blood pressure between the two groups were statistically highly significant (p < 0.001). The majority of patients in the case group, 18 (47.4%) patients had ++ proteinuria, followed by 17 (44.7%) had +++ proteinuria and 3 (7.9%) had + proteinuria. None of the patients in the case group had nil proteinuria. In contrast, all patients in the control group, 38 patients (100.0%), had no proteinuria (p < 0.001)

Table IV
Comparison of the respondents according to blood pressure and proteinuria (*n*=76).

Blood pressure and proteinuria	Case (n = 38)	Control (n = 38)	p value
Blood pressure			
Systolic blood pressure (Mean±SD)	156.32 ± 11.00	107.37 ± 7.60	<0.001c
Diastolic blood pressure (Mean±SD)	103.95 ± 7.54	72.74 ± 8.71	<0.001c
Proteinuria			
Nil	0 (0.0)	38 (100.0)	<0.001a
+	3 (7.9)	0 (0.0)	
++	18 (47.4)	0 (0.0)	
+++	17 (44.7)	0 (0.0)	

Chi-square test was done to measure the level of significance; Unpaired t-test was done to measure the level of significance; Figure within parentheses indicates percentage.

Table V presents the mean serum CA-125 level in the case group was 32.7 ± 6.97 U/ml, whereas in the control group it was 14.6 ± 6.93 U/ml. The difference in mean serum CA-125 level between the two groups was statistically highly significant (p< 0.001).

Table V
Comparison of mean (±SD) CA-125 level by group (*n*=76).

Serum CA-125 level (U/ml)	Case (n = 38)	Control (n = 38)	p value
Mean ± SD	32.7±6.97	14.6 ± 6.93	<0.001e

Unpaired t-test was done to measure the level of significance.

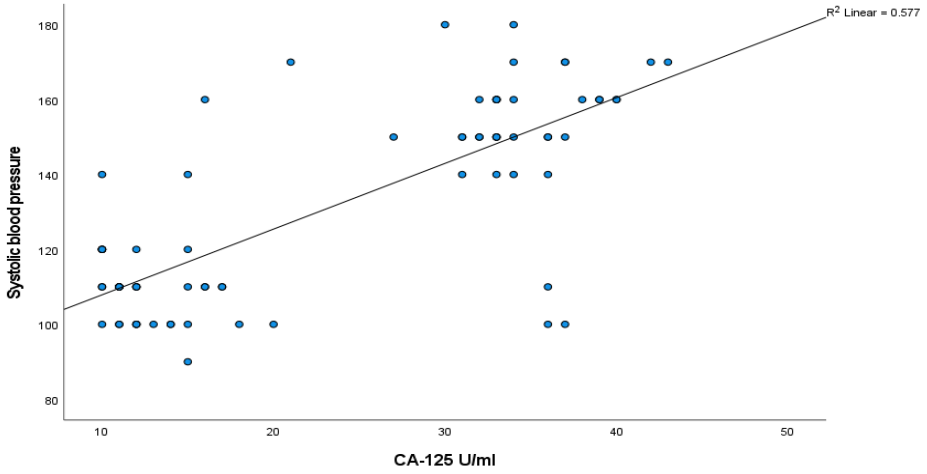

Figure 1 Scatterplot diagram showing the correlation between serum CA-125 level and systolic blood pressure (r=0.759, p<0.001)

Figure 1 shows patients with lower CA-125 levels tend to have lower systolic blood pressure, whereas patients with higher CA-125 levels tend to have higher systolic blood pressure(r=0.759, p<0.001).

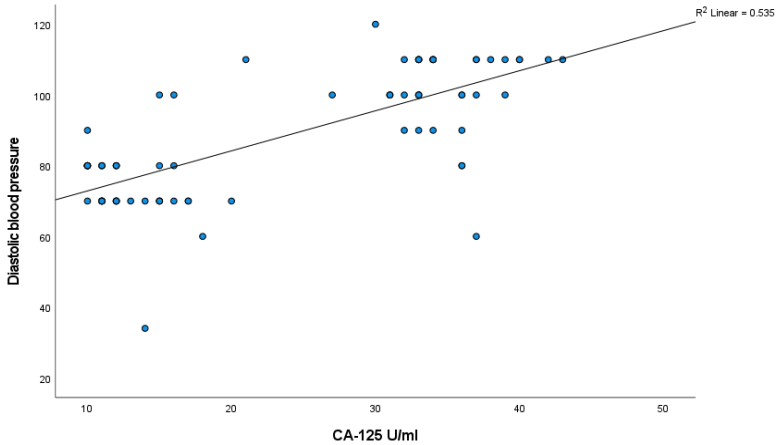

Figure 2 Scatterplot diagram showing the correlation between serum CA-125 level and diastolic blood pressure (r=0.732, p<0.001).

Figure 2 shows patients with lower CA-125 levels tend to have lower diastolic blood pressure, whereas patients with higher CA-125 levels tend to have higher diastolic blood pressure (r=0.732, p<0.001).

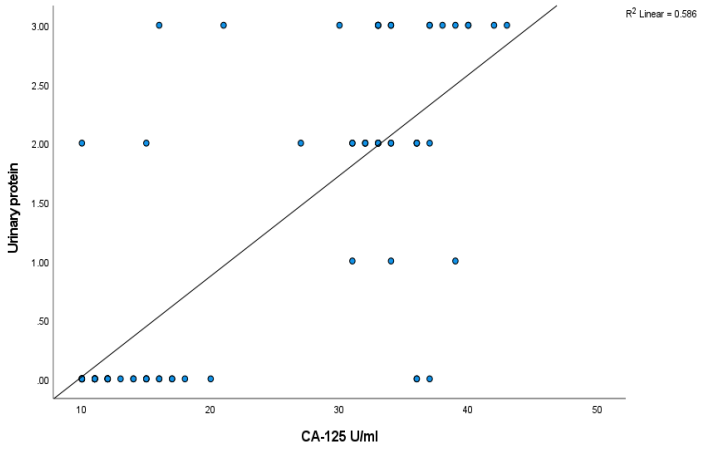

Figure 3 Scatterplot diagram showing the correlation of CA-125 with proteinuria (rs=0.715, p<0.001).

Figure 3 shows patients with lower CA-125 levels tend to have lower urinary protein levels, whereas patients with higher CA-125 levels tend to have higher urinary protein levels, indicating a positive correlation between CA-125 and proteinuria (rs = 0.715, p < 0.001).

Table VI shows patients with serum CA-125 levels ≥ 35.0 U/ml were significantly more likely to have preeclampsia compared to those with levels < 35.0 U/ml. Specifically, 34.2% of cases had CA-125 ≥ 35.0 U/ml compared to 7.9% of controls (p = 0.005). The odds of preeclampsia were over six times higher in patients with elevated CA-125 (OR = 6.07, 95% CI: 1.56–23.55).

Table VI
Odds ratios (OR) and 95% confidence intervals (CI) for preeclampsia according to serum CA-125 level in pregnancy (*n*=76).

Serum CA-125 level (U/ml)	Case (n = 38)	Control (n = 38)	p-value	Odds Ratio	(95% CI)
≥ 35.0 U/ml	13 (34.2)	3 (7.9)	0.005a	6.07	1.56-23.55
< 35.0 U/ml	25 (65.8)	35 (92.1)			

DISCUSSION

The study aimed to investigate the correlation between serum CA-125 levels and preeclampsia in pregnant women. This case-control study enrolled a total of 38 women with preeclampsia and 38 women with normal pregnancies during 20 to 40 weeks. The participants were recruited from the Department of Gynaecology and Obstetrics at ICMH, Matuail, Dhaka, Bangladesh [13].

The study found that the socio-demographic characteristics of the patients were similar in both the case (preeclamptic) and control (normal pregnancy) groups. Considering that advanced maternal age or teenage pregnancies were more prevalent in preeclamptic cases compared to normal pregnancies, we matched the ages between 18–35 years [14]. Additionally, no statistically significant differences were observed in obstetric characteristics between the two groups. However, a notable difference was identified in body weight, with a significant majority of preeclamptic patients being overweight, while the control group predominantly consisted of normal-weight individuals. This finding highlights the potential influence of body weight on the development of preeclampsia [15]. According to Poorolajal and Jenabi, overweight was linked to preeclampsia (OR = 1.73; 95% CI) and obesity (OR = 3.15; 95% CI).

Excess body mass index considerably increases pre-eclampsia risk. Obesity and overweight can predict preeclampsia, which is similar to this study [13]. In an analysis of 2,637 women, 9.0% developed preeclampsia. Notable risk factors included chronic hypertension, pregestational diabetes, multiple gestation, African American race, prior preeclampsia, nulliparity, assisted reproductive techniques, and being overweight or obese. Advanced maternal age was not a significant factor. There was a dose-response relationship between BMI and preeclampsia. Overweight or obesity was the most significant risk factor for both preeclampsia and severe preeclampsia, accounting for 64.9% and 64.4% of cases, respectively. These findings emphasize the importance of addressing weight-related factors in preeclampsia prevention efforts. This result is also similar to this study [14,15].

The study observed statistically significant differences in systolic and diastolic blood pressure as well as proteinuria between the preeclamptic and control groups. Preeclampsia patients exhibited higher blood pressure levels and proteinuria, which is consistent with the clinical criteria for diagnosing preeclampsia [16].

One of the key findings of this study was that preeclampsia patients had significantly higher serum CA-125 levels compared to the control group. Serum CA-125 level was positively correlated with systolic blood pressure (r=0.759, p<0.001), diastolic blood pressure (r=0.732, p<0.001), and proteinuria (rs=0.715, p<0.001) [17]. According to Osanyin et al., serum CA-125 levels were significantly higher in women with preeclampsia compared to those with normal pregnancy (53.17 IU/mL vs. 12.49 IU/mL, P < 0.05). CA-125 levels also correlated positively with blood pressure, serum uric acid levels, platelet levels, and urinary protein levels [18]. Similarly, Suliman et al. observed that CA-125 levels exhibited marked differences between groups, 21.94 ± 0.749 IU/ml in preeclampsia and 16.48 ± 0.584 IU/ml in controls (P < 0.001). These levels positively correlated with mean arterial blood pressure (r > 0.7; P < 0.001) and demonstrated strong diagnostic potential (AUC > 0.8; P < 0.001) [19]. Karrar et al. showed significantly higher CA-125 levels in preeclampsia cases (52.400 ± 2.550 U/ml) compared to the control group (27.800 ± 6.026 U/ml; p < 0.0001). CA-125 levels in preeclampsia correlated positively with blood pressure (r = 0.7275, p < 0.001) and proteinuria (r = 0.3740, p = 0.0174) [20].

The study also assessed the likelihood of developing preeclampsia based on CA-125

levels. It found that the risk of preeclampsia was 6.07 times higher in individuals with a CA-125 level of ≥ 35.0 U/ml compared to those with a CA-125 level < 35.0 U/ml. This observation underscores the potential utility of CA-125 as a parameter for preeclampsia [21]. Balint et al. assessed that CA-125 levels increased with hypertension, ranging from 8.97 U/mL in normotensive to 21.23 U/mL in preeclampsia. CA-125 correlated positively with blood pressure, proteinuria, and LDH, while negatively with platelet count, gestational age, and birth weight. CA-125 shows promise as a marker for preeclampsia management [22].

According to Oluwole et al., no significant differences in maternal age, parity, or gestational age at enrollment were observed between women with preeclampsia and normotensive controls. However, significant differences were observed in clinical and laboratory parameters, including blood pressure, proteinuria, platelet count, serum uric acid, serum creatinine, fetal birth weight, serum CA-125 levels, and perinatal death. The study used a detection limit of 47.4 mIU/L for CA-125 levels and found a sensitivity of 70.1% and specificity of 62.0% for detecting preeclampsia. Maternal serum CA-125 levels showed significant positive correlations with blood pressure, proteinuria, platelet count, and serum uric acid levels [23]. In conclusion, this thesis contributes valuable insights into the relationship between CA-125 levels and preeclampsia. Elevated CA-125 levels appear to signal an increased risk of preeclampsia.

CONCLUSION

The findings of this study suggest that serum CA-125 levels were significantly increased in preeclampsia with positively correlated with blood pressure. Therefore, this study concludes that raised serum CA-125 can be considered as important parameter for preeclampsia patients.

LIMITATIONS

This study had some limitations as well. The study was conducted in a single tertiary hospital. So, the result of the study may not be reflecting the exact status of the population. Study sample was limited and could not be increase due to financial constraints. Other factors that might have disrupted placental function and perfusion, vascular resistance, endothelial dysfunction, oxidative stress marker interact with PE were not investigated. Therefore, the study findings cannot be generalized to the entire population.

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