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ORIGINAL ARTICLE

Serum Catestatin Level in Preeclampsia

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Abstract

Background/Aim: Preeclampsia, a significant cause of maternal morbidity and mortality, is linked to increased cardiovascular risks. Catestatin regulates cardiovascular function which indicates its usefulness in understanding pathophysiology of preeclampsia and its severity. Aim of this study was to evaluate association of catestatin in preeclamptic women and control non preeclamptic women and assess its association with presence and severity of preeclampsia.

Methods: A case-control study at Al-Zahraa Teaching Hospital, Iraq, performed from January to December 2023 involved 90 pregnant women: 30 with severe preeclampsia, 30 with mild preeclampsia and 30 healthy controls. Inclusion criteria were preeclamptic pregnant women at 27-40 weeks of gestation and age ranging from 20-40 years and similar non-eclamptic controls. Exclusions were smokers, chronic drug users and those with chronic illnesses. Data collection included general and clinical information, BMI, vital signs, examinations and laboratory tests including serum catestatin.

Results: Catestatin levels varied significantly among severe preeclampsia, mild preeclampsia and control groups. Average catestatin level in severe preeclampsia group was markedly lower at 29.01 ng/mL, compared to 43.67 ng/mL in mild preeclampsia and 59.96 ng/mL in controls. The diagnostic performance of catestatin for severe preeclampsia was notable, with a cutoff point of ≤ 37.165 ng/mL, sensitivity of 80 % and specificity of 83.3 %, highlighting its potential as a critical biomarker in preeclampsia evaluation.

Conclusion: Catestatin level was significantly lower in sever preeclampsia compared to mild and control group, which may indicate its association with preeclampsia. Lower catestatin in sever preeclampsia suggest its inverse relation with preeclampsia severity.

Key words: Catecholamines; Chromogranins; Chromogranin A; Preeclampsia.

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Introduction

Catestatin (CST) is a peptide derived from chromogranin A, known for its role in inhibiting catecholamine release and modulating cardiovascular function. It acts as a feedback inhibitor, regulating the release of epinephrine and norepinephrine. CST exerts cardioprotective effects by reducing myocardial oxygen demand and promoting coronary dilation.[1] It also stimulates angiogenesis and exhibits anti-inflammatory properties. Dysregulation of CST levels has been associated with hypertension, heart failure and preeclampsia (PE). Overall, CST is a multifunctional peptide involved in maintaining cardiovascular homeostasis and presents potential as a therapeutic target for cardiovascular disorders.[2]

CST has been implicated in various aspects of pregnancy, particularly in relation to the pathophysiology of PE. Studies have shown alterations in maternal serum CST levels in women with PE compared to those with normal blood pressure during pregnancy. Some studies have reported significantly lower CST levels in women with PE, while others have found higher levels. The exact relationship between CST and PE is still being investigated and more research is needed to elucidate the mechanisms involved.[3]

CST has been implicated in regulating angiogenesis/arteriogenesis and vasculogenesis, processes critical for proper placental development and function.[3] CST plays a role in modulating autonomic cardiovascular control and has been shown to have vasodilatory effects and inhibit catecholamine release. It may help counteract the increased sympathetic activity and endothelial dysfunction seen in PE.[4]

The reduced CST levels in early onset preeclampsia (EOPE) may contribute to the altered foetal cardiac function observed in these cases.[5] Given the cardioprotective and vasodilatory effects of CST, it has been suggested as a potential therapeutic target in the management of PE.

The future implications of CST in PE include its potential as a diagnostic biomarker and risk predictor for PE. CST may also serve as a therapeutic target to mitigate PE-related processes such as endothelial dysfunction and increased sympathetic activity.[5]

Aim of this study was to evaluate the association of ST in preeclamptic women and control non preeclamptic women and assess its association with presence and severity of PE.

Methods

This was a prospective case control study conducted in the Department of Obstetrics and Gynaecology at Al-Zahraa Teaching Hospital, Iraq, during a period from January 2023 till December 2023. The study included 90 pregnant women (30 women who suffered from severe PE, 30 women who suffered from mild PE and another 30 healthy pregnant women with similar maternal and gestational ages as control group) in the third trimester that had been admitted at Consultant Obstetric and Gynaecological Clinic at Al-Zahraa Teaching Hospital triage room and labour room.

Inclusion criteria were pregnant woman with PE with mild or severe form; from 27-40 weeks of gestation and 20-40 years of age. Control group was of similar age and gestation. Smoker pregnant women or chronic drug users and women who had chronic medical illness (diabetes mellitus, chronic hypertension, connective tissue disease) were not included in the study.

All cases were informed about the nature of the study and verbal consent was obtained from them, as well as demographic and full history from the patient as maternal age, educational level, occupation, residency, parity.

Study patients underwent general examination, vital signs (systolic blood pressure (SBP) and diastolic blood pressure (DBP)), abdominal and obstetric examination. Body mass index (BMI) was calculated by weight (kg) divided by the square of height (m). Weight and height were measured by the same scale for all the subjects,[6] laboratory investigation and sonographic examination were performed:

- The BP of the patient measured by mercury sphygmomanometer at right sitting position.

- When the measured BP was ≥ 140/90 mm Hg but < 160/110 mm Hg, the BP was reassessed after about four hours, if still the same reading or more, then urine sample was sent for albumin. If the result was + 1 then the patient was diagnosed to have mild PE[7] and included in the study, after that blood sample was drown for investigations (which included blood test sent for liver function test, haemoglobin level, platelet count, renal function test, serum CST).

- When the measured BP was < 140/90 mm Hg the woman is considered as a control group along with normal investigation and negative protein in urine.

Five mL of venous blood was collected from the participants before receiving any medication. Five mL of whole blood was collected into tubes with anticoagulant (EDTA or citrate) to measure liver function test, haemoglobin level, platelet count, renal function test, serum CST). After incubated at room temperature for 10-20 minutes, tubes were centrifugated for 20 min at 2,000-3,000 rpm. The supernatant was carefully col-

lected as plasma sample. If precipitates appeared during reservation, the sample was centrifugated again. After collection of plasma, either freezing into -4 °C was done (to be thawed before measurement), or measurement was performed directly using (Human Catestatin (CST) ELISA KIT Catalogue Number: EKHU-2331) and loaded into analyser.

Statistical analysis

All data were introduced into Microsoft Excel 16 and statistical analysis were conducted using IBM-SPSS. Data were presented in the form of counts, percentage, mean, standard deviation (SD), minimum (Min) and maximum (Max) and presented in the form of tables or graphs. Testing of the level of significance of the categorical data was conducted using Chi square or Fisher exact test while continuous variables were tested using Student t-test or Mann Whitney U-test when appropriate. Receiver operator characteristics curve (ROC) was used to estimate the best cutoff points (after running of Yoden J index test) at which estimation of the area under the curve (AUC), sensitivity (SN), specificity (SP) positive predictive value (PPV), negative predictive value (NPV), accuracy of the test (Acc) and relative risk of each variable.

Results

The study included 90 women and divided into 3 groups: severe PE group (30 cases), mild PE group (30 cases) and control group (30 cases).

Table 1 showed that the mean age was not significantly different among the three groups, with severe PE having a mean age of 30.4 ± 8.02, mild PE at 29.4 ± 6.44 and the control group at 26.47 ± 4.06 (P1: Severe vs Mild = 0.856, P2: Severe vs Control = 0.054, P3: Mild vs Control = 0.098). Parity did not significantly differ among the groups, with values of 2.5 ± 1.78 for severe, 2.13 ± 1.91 for mild and 1.8 ± 1.35 for the control group (P1 = 0.722, P2 = 0.208, P3 = 0.716). The gestational age was similar across all groups with no significant difference (severe: 35.53 ± 3.39, mild: 34.83 ± 5.72, control: 34.93 ± 4.47; P1 = 0.833, P2 = 0.828, P3 = 0.997). The BMI was significantly higher in the severe PE group (33.16 ± 7.74) compared to the control group (25.77 ± 5.38), with a p-value < 0.0001. Mild PE (31.1 ± 6.03) also showed a significantly higher BMI than the control group (P3 = 0.002). However, the difference between severe and mild PE was not statistically significant (P1 = 0.493).

Table 1: Demographics of participants

Variables	Severe PE	Mild PE	Control	P-value		
	Mean ± SD	Mean ± SD	Mean ± SD	P1	P2	P3
Age (years)	30.40 ± 8.02	29.4 ± 6.44	26.47 ± 4.06	0.856	0.054	0.098
Parity	2.50 ± 1.78	2.13 ± 1.91	1.80 ± 1.35	0.722	0.208	0.716
Gestational age (weeks)	35.53 ± 3.39	34.83 ± 5.72	34.93 ± 4.47	0.833	0.828	0.997
BMI (kg/m^2)	33.16 ± 7.74	31.10 ± 6.03	25.77 ± 5.38	0.493	< 0.0001	0.002

PE: preeclampsia; Control: healthy women in third trimester; P1: Severe vs Mild; P2: Severe vs Control; P3: Mild vs Control; BMI: body mass index;

Table 2: Comparison of blood pressure between the three groups

Variables	Severe PE	Mild PE	Control	P-value		
	Mean ± SD	Mean ± SD	Mean ± SD	P1	P2	P3
SBP (mm Hg)	176.38 ± 14.01	150.20 ± 8.72	129.57 ± 5.20	< 0.001	< 0.001	< 0.001
DBP (mm Hg)	115.52 ± 7.22	96.50 ± 6.99	83.21 ±4.20	< 0.001	< 0.001	< 0.001
Proteinuria (g/day)	0.90± 0.66	0.73 ± 0.90	0.00 ± 0.00	< 0.001	< 0.001	< 0.001

PE: preeclampsia; Control: healthy women in third trimester; P1: Severe vs Mild; P2: Severe vs Control; P3: Mild vs Control; SBP: systolic blood pressure; DBP: diastolic blood pressure;

Table 2 shows SBP values. The mean SBP was significantly higher in the severe preeclampsia group (176.38 ± 14.01 mm Hg) compared to the mild preeclampsia (150.2 ± 8.72 mm Hg) and control groups (129.57 ± 5.20 mm Hg), with a p < 0.0001 for both comparisons (P1 and P2). The difference between mild preeclampsia and control was also significant (P3 < 0.0001).

Similarly, the mean DBP was significantly higher in the severe preeclampsia group (115.52 ± 7.22 mm Hg) compared to the mild preeclampsia (96.5 ± 6.99 mm Hg) and control groups (83.21 ± 4.20 mm Hg), with a p < 0.0001 for both comparisons (P1 and P2). The difference between mild preeclampsia and control was also significant (P3 < 0.0001).

The p < 0.0001 suggested that there is a statistically significant difference in the distribution of proteinuria levels between the groups with the control group showing no proteinuria and an increasing prevalence and severity of proteinuria in the mild and severe PE groups there was also complicated cases (HEELP 6 cases, eclampsia 2 cases and abruption 3 cases). This aligns with the clinical understanding that proteinuria is a hallmark of PE and its severity can vary with the condition's severity.

Table 3 shows platelet counts. Platelet counts ($x10^3/\mu L$) showed a significant decrease in the severe PE group (102.21 ± 1.03) compared to both the mild PE (150.3 ± 83.98) and control groups (405.93 ± 10.7), with all p values indicating statistical significance (P1 = 0.007, P2 = 0.002, P3 = 0.030). Urea levels (mg/dL) followed a similar pattern, being highest in the severe PE group (29.13 ± 8.28) and lowest in the control group (15.43 ± 4.34), with significant differences noted across all group comparisons (P1 = 0.02, P2 = 0.007, P3 = 0.006).

Creatinine levels (mg/dL) were also observed to be highest in the severe PE group (2.9 ±4.83) and lowest in the control group (0.81 ±1.31), with statistically significant differences across all comparisons. Liver enzymes, glutamic-oxaloacetic transaminase or aspartate aminotransferase (SGOT) and serum glutamic-pyruvic transaminase or alanine transaminase (SGPT), showed significantly higher levels in the severe PE group compared to both the mild PE and control groups, with P values indicating strong statistical significance in all comparisons.

Table 4 shows that the average CST level was significantly lower in the severe PE group (29.01 ng/mL) compared to the mild PE (43.67 ng/mL) and the control group (59.96 ng/mL). This gradient suggests that serum CST levels may be inversely related to the severity of PE.

There was greater variability in the control group (SD = 37.48 ng/mL) compared to the mild (SD = 13.22 ng/mL) and severe (SD = 11.14 ng/mL) preeclampsia groups. The high SD in the control group may reflect a wider range of normal CST levels in the general population. The minimum recorded level of CST was much lower in the severe group (5.17 ng/mL) compared to the mild (22.57 ng/mL) and control groups (18.06 ng/mL), suggesting that very low levels of CST were asso-

Table 3: Distribution of haematological and biochemical findings in the three groups

Variables	Severe PE	Mild PE	Control	P-value		
	Mean ± SD	Mean ± SD	Mean ± SD	P1	P3	P3
Platelet count ($x10^3/\mu L$)	102.21 ± 1.03	150.30 ± 83.98	405.93 ± 10.70	0.007	0.002	0.030
Urea (mg/dL)	29.13 ± 8.28	22.26 ± 4.03	15.43 ± 4.34	0.020	0.007	0.006
Creatinine (mg/dL)	2.90 ± 4.83	1.58 ± 0.30	0.81 ± 1.31	0.020	0.030	0.010
SGOT (U/L)	104.58 ± 16.65	62.64 ± 32.61	25.07 ± 8.81	0.001	0.007	0.001
SGPT (U/L)	128.07 ± 33.21	76.09 ± 22.12	27.06 ± 8.97	0.001	0.002	0.001

PE: preeclampsia; Control: healthy women in third trimester; P1: Severe vs Mild; P2: Severe vs Control; P3: Mild vs Control; SGOT: glutamic-oxaloacetic transaminase or aspartate aminotransferase; SGPT: serum glutamic-pyruvic transaminase or alanine transaminase;

Table 4: Distribution of catestatin (CST) level (ng/mL) between the three groups

Catestatin	Severe PE	Mild PE	Control
Mean	29.01	29.01	29.01
Standard deviation	11.14	11.14	11.14
Minimum	5.17	5.17	5.17
Maximum	54.87	54.87	54.87
Percentile 25	23.44	23.44	23.44
Median	27.12	27.12	27.12
Percentile 75	36.36	36.36	36.36
	P1: < 0.0001; P2: < 0.0001; P3: 0.077		

PE: preeclampsia; Control: healthy women in third trimester; P1: Severe vs Mild; P2: Severe vs Control; P3: Mild vs Control;

ciated with more severe cases of PE. The maximum value was considerably higher in the control group (195.06 ng/mL) than in the mild (82.71 ng/mL) or severe groups (54.87 ng/mL), which might indicate the presence of outliers or a wide range of normal levels in the control group.

The comparison of CST levels between the severe and control groups (P1 < 0.0001) and between the mild and control groups (P2 < 0.0001) showed highly significant differences, indicating that CST levels were markedly different in PE patients compared to healthy controls. The comparison between severe and mild PE groups (P3 = 0.077) was not statistically significant, suggesting that while CST levels were associated with PE, they may not differentiate well between the severities of the condition.

The data indicated that lower serum CST levels were significantly associated with the presence of PE and there was a trend towards lower levels as the severity of the condition increased. However, the overlap in CST levels between the severe and mild PE groups suggests that additional factors may be necessary to discriminate between different severities of PE.

There was a moderate negative correlation between CST levels and SBP (Pearson correlation r = -0.443) as shown in Figure 1. This means that as CST levels increased, SBP tended to decrease and *vice versa*. The significance level (p-value) was < 0.0001.

The negative correlation between CST levels and DBP was slightly stronger (r = -0.499) compared to SBP as shown in Figure 2.

This also indicates an inverse relationship where

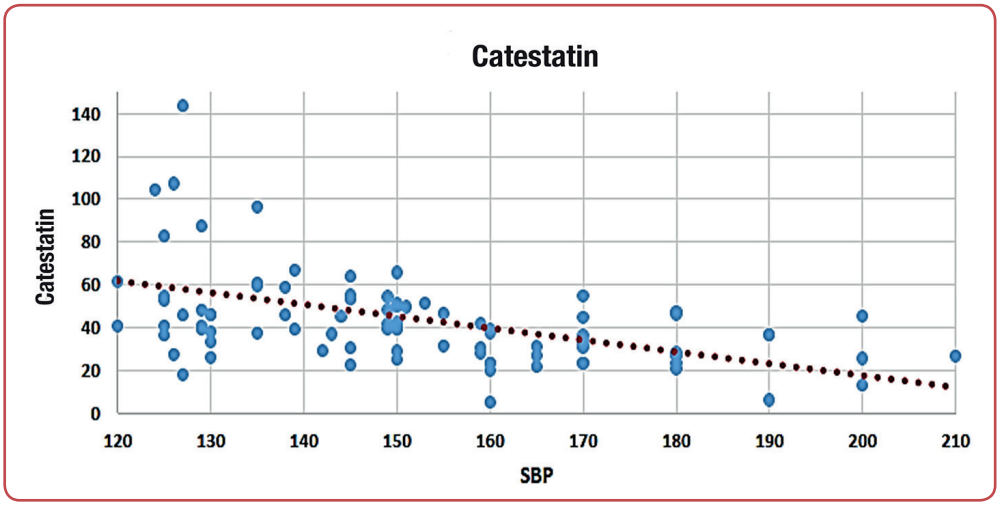

Figure 1: Correlation analysis between catestatin (CST) level (ng/mL) and systolic blood pressure (SBP) (mm Hg)

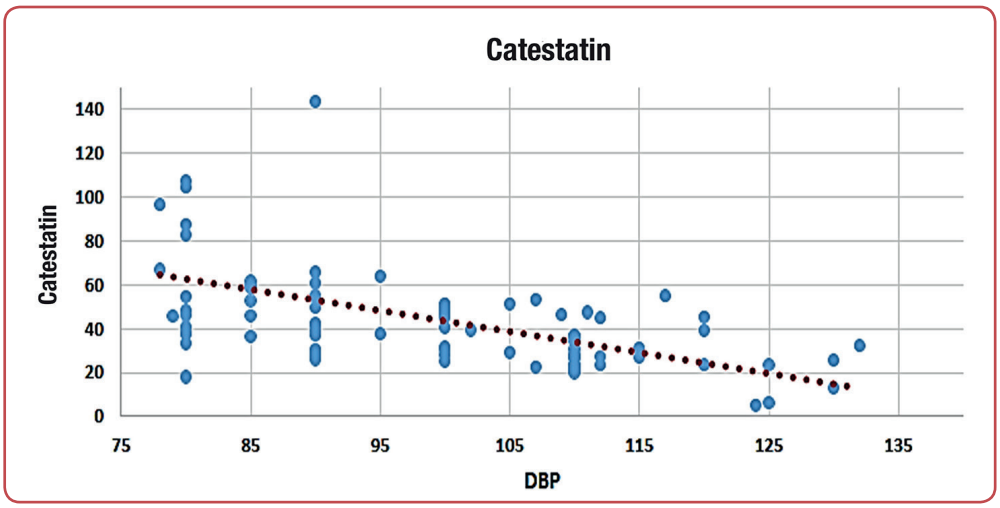

Figure 2: Correlation analysis between catestatin (CST) level (ng/mL) and diastolic blood pressure (DBP) (mm Hg)

higher CST levels were associated with lower DBP. The significance of this correlation was also < 0.0001. Overall, there was a significant inverse relationship between serum CST levels and both SBP and DBP. This could imply that CST has a physiological role in blood pressure regulation and its levels are relevant in the context of PE, where hypertension is a key symptom.

The analysis of ROC curve presented the diagnostic capability of CST for identifying severe and mild PE. In the context of severe PE, CST levels showed a strong diagnostic performance, as indicated by an area under the curve (AUC) of 0.869 as shown in Figure 3. This high AUC value suggests that CST was a reliable marker for severe PE, with the optimal cutoff point identified at a CST level of ≤ 37.165. With this cutoff, the sensitivity of the test was 80 %. The specificity was also high, at 83.3 %, indicating that it correctly recognised the majority of non-severe cases. In terms of predictive values, the positive predictive value (PPV) was 82.8 % and the negative predictive value (NPV) was 80.6 %. The overall accuracy of CST in diagnosing severe PE stand at 81.7 %.

In contrast, the diagnostic utility of CST for mild PE was moderate. The AUC for mild PE was 0.616, which indicated less discriminative power compared to its use in severe PE as shown in Figure 4. The same cutoff point of ≤ 37.165 was applied; however, the sensitivity dropped significantly to 33.3 %, which means it only correctly identifies a third of the true mild PE cases. Despite this, the specificity remained consistent with that of severe PE, at 83.3 %. The PPV for mild PE was 66.7 % and the NPV decreases to 55.6 %. The accuracy of CST in diagnosing mild PE was relatively low at 58.3.

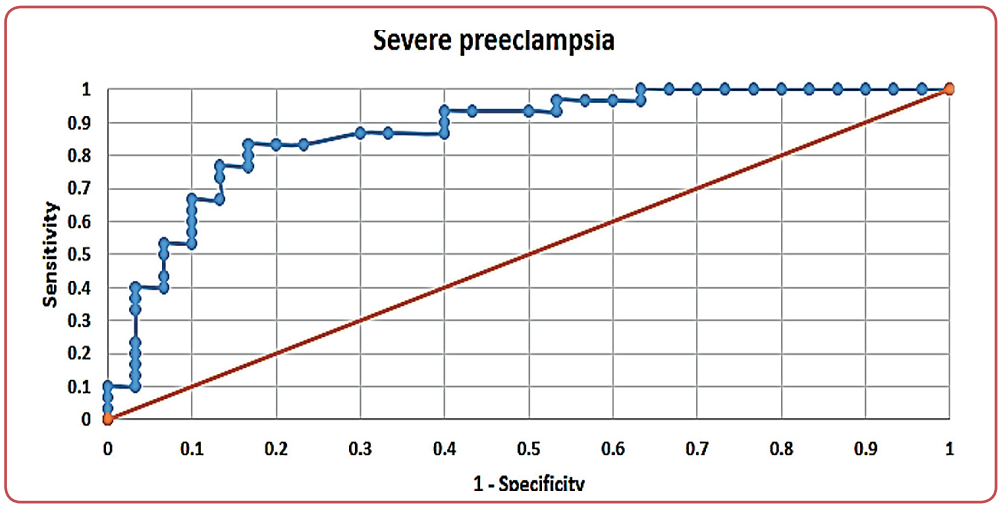

Figure 3: Receiver operator curve (ROC) analysis for catestatin (CST) in diagnosing severe preeclampsia

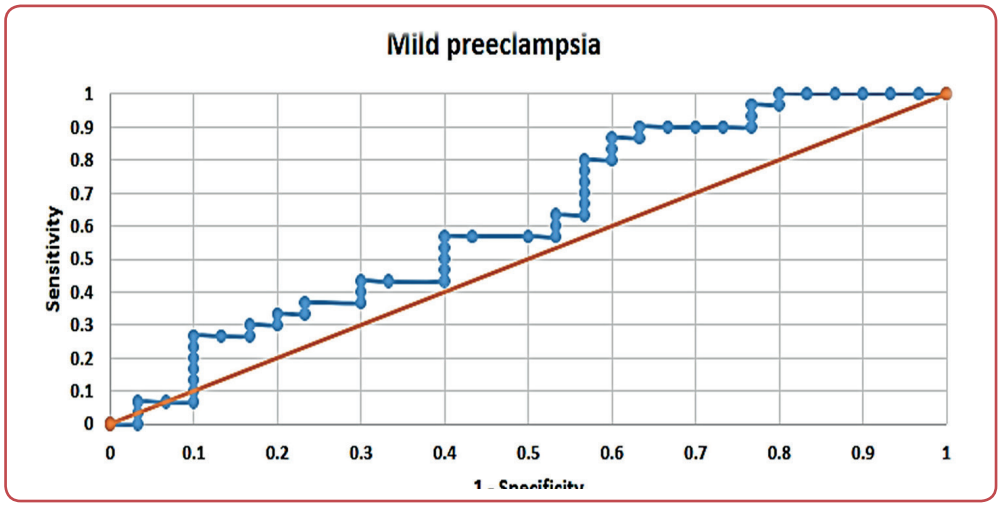

Figure 4: Receiver operator curve (ROC) analysis for catestatin (CST) in diagnosing mild preeclampsia

The data suggests that CST was a more effective biomarker for detecting severe PE than mild PE, with higher sensitivity, accuracy and both PPV and NPV for the more severe condition. This difference in diagnostic performance may necessitate the consideration of different CST level thresholds for severe and mild PE to improve the test's efficacy.

Discussion

CST has been implicated in various aspects of pregnancy, particularly in relation to the pathophysiology of PE.[8] The current study included three groups of mild and severe PE with healthy control, intending to investigate the risk factors and associated factors with PE. Mean age of the participants was not different, although cases of PE tend to occur in older pregnant women as stated by Sheen et al,[9] Khalil et al,[10] Wadhwani et al[11] and Miller et al.[12]

The mean BMI was significantly higher in PE patients than control. According to the studies by Robillard et al[13] and Jiang et al[14] there is linear relationship between BMI and increased risk of development of PE. All three groups were selected at around the same gestational age, no statistically significant difference was discovered. The blood pressure was significantly higher in the case of preeclampsia (by definition), than control.

The current study found that low platelet count was associated with increased severity of PE, as it is part of HELLP syndrome, which is marker of severe PE, similar to the result found by Lisonkova et al[15] and Yang et al.[16] Blood urea and serum creatinine were both elevated in cases of PE, which gives idea about the damaging effect of high blood pressure on the kidneys with superimposed proteinuria which further affect filtration gradients. Similar result found by Charles et al[17] (n = 144) who compared 72 cases of PE and 72 normotensive women in regards renal function and electrolytes and found worsening renal function associated with increased severity of PE.

The liver enzymes were significantly higher in cases of PE than control. This elevation highlights the effect of PE on the endothelial lining of hepatic circulation, making the liver more prone to injury and development of HELLP syndrome. This result was similar to what found by Munazza et al[18] (n = 100) who compared 50 women with PE with another 50 women without PE and found that eclampsia cases associated with higher liver enzymes than control.

There was significant decline in CST levels in sever PE compared to mild and control group. This pattern suggests a potential inverse relationship between CST levels and the severity of PE. The reduced CST levels in severe cases could be indicative of more pronounced physiological changes associated with PE and its severity. The variability in CST levels, as indicated by the standard deviation, is notably greater in the control group compared to the PE groups. This could reflect a natural range of CST levels in a healthy population, while the PE groups exhibit more uniform alterations due to the disease. The observation of extreme minimum and maximum values in the control group of the study warrants a more detailed analysis.

The study also revealed a moderate negative correlation between CST levels and both SBP and DBP, highlighting a potential physiological role of CST in regulating blood pressure. This is particularly relevant in the context of PE, where hypertension is a hallmark symptom.

The diagnostic capability of CST, as illustrated by the ROC curve analysis, is notable. In severe PE, CST levels demonstrate a strong diagnostic performance, suggesting its reliability as a biomarker for this condition. However, its utility in diagnosing mild PE appears moderate, indicating a potential need for different diagnostic thresholds or additional biomarkers for mild cases.

On the other hand, the research by Özalp et al,[3] Palmrich,[8] Bralewska[19] indicated a notable connection between CST levels and the severity of early-onset PE, particularly concerning foetal cardiovascular dysfunction. Early-onset PE, which develops before 34 weeks of gestation, is often more severe compared to its late-onset counterpart and poses greater risks to both the mother and the foetus. One of these risks includes complications related to the foetal cardiovascular system.

The previous studies showed a discrepant finding as the study by Tüten et al[5] found increased mean serum CST levels in women with PE compared to controls, contrasting with the findings of this study where decreased levels were observed, especially in severe cases, furthermore

found a positive relationship between CST level and blood pressure. Tüten et al explained the different findings by their study by a genetic variant of CST that could be investigated by different CST kit.[5] Studies evaluating CST levels in preeclamptic pregnancies should also include genetic variants in their evaluations.

The physiological role of CST in regulating catecholamine release and vascular tone might provide a basis for understanding its inverse relationship with PE severity. The complex pathophysiology of PE involves a multifaceted interplay of factors, where CST levels could be influenced variably, contributing to the differences observed across studies.

Conclusion

Lower CST levels were found in severe PE compared to mild cases and controls indicating an inverse relationship with disease severity. A value of ≤ 37.165 ng/mL for CST was indicated as a cutoff point for distinguishing between severe and mild PE. Overall, the study showed the potential of CST as a biomarker, particularly in identifying severe PE with higher accuracy.

Ethics

The study was approved by the Ethics Committee of the Scientific Council of Obstetrics and Gynaecology, Iraqi Board for Medical Specialisations, decision No: EAC-4528, dated 15 November 2022.

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None.

Conflicts of interest

The authors declare that there is no conflict of interest.

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Data access

The data that support the findings of this study are available from the corresponding author upon reasonable individual request.

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References

1. Bourebaba Y, Mularczyk M, Marycz K, Bourebaba L. Catestatin peptide of chromogranin A as a potential new target for several risk factors management in the course of metabolic syndrome. Biomed Pharmacother. 2021 Feb;134:111113. doi: 10.1016/j.biopha.2020.111113.

2. Zalewska E, Kmieć P, Sworczak K. Role of catestatin in the cardiovascular system and metabolic disorders. Front Cardiovasc Med. 2022 May 19;9:909480. doi: 10.3389/fcvm.2022.909480.
3. Özalp M, Yaman H, Demir Ö, Garip SA, Aran T, Osmanağaoğlu MA. The role of maternal serum catestatin in the evaluation of preeclampsia and fetal cardiac functions. Turk J Obstet Gynecol. 2021 Dec 24;18(4):272-8. doi: 10.4274/tjod.galenos.2021.34946.
4. Mahata SK, Kiranmayi M, Mahapatra NR. Catestatin: a master regulator of cardiovascular functions. Curr Med Chem. 2018;25(11):1352-74. doi: 10.2174/0929867324666170425100416.
5. Tüten N, Güralp O, Gök K, Hamzaoglu K, Oner YO, Makul M, et al. Serum catestatin level is increased in women with preeclampsia. J Obstet Gynaecol. 2022 Jan;42(1):55-60. doi: 10.1080/01443615.2021.1873922.
6. Centers for Disease C, Prevention [Internet]. Assessing your weight. Division of Nutrition, Physical Activity, and Obesity. 2015. [Accessed: 31-Dec-2023]. Aailable at: https://www.cdc.gov/cdi/indicator-definitions/npao.html.
7. Hypertension in pregnancy: diagnosis and management. London: National Institute for Health and Care Excellence (NICE); 2019 Jun 25. (NICE Guideline, No. 133.) [Accessed: 31-Dec-2023]. Aailable at: https://www.ncbi.nlm.nih.gov/books/NBK546004/.
8. Palmrich P, Schirwani-Hartl N, Haberl C, Haslinger P, Heinzl F, Zeisler H, et al. Catestatin-A potential new therapeutic target for women with preeclampsia? An analysis of maternal serum catestatin levels in preeclamptic pregnancies. J Clin Med. 2023 Sep 12;12(18):5931. doi: 10.3390/jcm12185931.
9. Sheen J-J, Huang Y, Andrikopoulou M, Wright JD, Goffman D, D'Alton ME, et al. Maternal age and preeclampsia outcomes during delivery hospitalizations. Am J Perinatol. 2020 Jan;37(1):44-52. doi: 10.1055/s-0039-1694794.
10. Khalil A, Syngelaki A, Maiz N, Zinevich Y, Nicolaides KH. Maternal age and adverse pregnancy outcome: a cohort study. Ultrasound Obstet Gynecol. 2013 Dec;42(6):634-43. doi: 10.1002/uog.12494.
11. Wadhwani P, Saha PK, Kalra JK, Gainder S, Sundaram V. A study to compare maternal and perinatal outcome in early vs. late onset preeclampsia. Obstet Gynecol Sci. 2020 May;63(3):270-7. doi: 10.5468/ogs.2020.63.3.270.
12. Miller EC, Wilczek A, Bello NA, Tom S, Wapner R, Suh Y. Pregnancy, preeclampsia and maternal aging: From epidemiology to functional genomics. Ageing Res Rev. 2022 Jan;73:101535. doi: 10.1016/j.arr.2021.101535.
13. Robillard P-Y, Dekker G, Scioscia M, Bonsante F, Iacobelli S, Boukerrou M, et al. Increased BMI has a linear association with late-onset preeclampsia: A population-based study. PLoS One. 2019 Oct 17;14(10):e0223888. doi: 10.1371/journal.pone.0223888.
14. Jiang L, Lin J, Yan J, Lin X, Han Q, Zhang H. Prepregnancy body mass indexes are associated with perinatal outcomes in females with preeclampsia. Exp Ther Med. 2020 Jul;20(1):500-4. doi: 10.3892/etm.2020.8677.
15. Lisonkova S, Bone JN, Muraca GM, Razaz N, Wang LQ, Sabr Y, et al. Incidence and risk factors for severe preeclampsia, hemolysis, elevated liver enzymes, and low platelet count syndrome, and eclampsia at preterm and term gestation: a population-based study. Am J Obstet Gynecol. 2021 Nov;225(5):538.e1-538.e19. doi: 10.1016/j.ajog.2021.04.261.
16. Yang SW, Cho SH, Kwon HS, Sohn IS, Hwang HS. Significance of the platelet distribution width as a severity marker for the development of preeclampsia. Eur J Obstet Gynecol Reprod Biol. 2014 Apr;175:107-11. doi: 10.1016/j.ejogrb.2013.12.036.
17. Charles N, Amarachukwu N, Ekpo E, Cajethan E. Changes in renal function among women with preeclampsia in a tertiary health institution in Nigeria. Int J Womens Health Rep Sci. 2020;8(3):272-5. doi: 10.15296/ijwhr.2020.44.
18. Munazza B, Raza N, Naureen A, Khan SA, Fatima F, Ayub M, et al. Liver function tests in preeclampsia. J Ayub Med Coll Abbottabad. 2011 Oct-Dec;23(4):3-5. PMID: 23472397.
19. Bralewska M, Biesiada L, Grzesiak M, Rybak-Krzyszkowska M, Huras H, Gach A, et al. Chromogranin A demonstrates higher expression in preeclamptic placentas than in normal pregnancy. BMC Pregnancy Childbirth. 2021 Oct 7;21(1):680. doi: 10.1186/s12884-021-04139-z.