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Serum CA-125: A Potential Biomarker for Pre Eclampsia and Its Severity

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Abstract

Background: Pre-eclampsia is a pregnancy-specific multisystem disorder characterised by new onset of hypertension after the 20th week of gestation and atleast one of the following complications, including proteinurea, significant end organ dysfunction or uteroplacental dysfunction. It poses significant risks to maternal and fetal health, necessitating early detection and management. Given pre-eclampsia's inflammatory nature and CA-125's role in the choriodecidual unit, it may serve as a marker for detecting pre-eclampsia and its severity.

Aim: This study aimed to compare serum levels of Cancer Antigen 125 (CA-125) in preeclamptic patients and normotensive pregnant women to evaluate its potential as a biomarker for pre-eclampsia and its severity.

Methods: A comparative study was conducted at SMS Medical College, Jaipur, from January 2023, including 50 preeclamptic and 50 normotensive women between 32-34 weeks of gestation. Participants were selected based on defined inclusion and exclusion criteria. Detailed clinical assessments and routine blood investigations were performed, followed by the collection of fasting venous blood samples for CA-125 analysis via ELISA. Statistical analyses included unpaired t-tests, chi-square tests, and correlation evaluations, with a significance threshold set at $p < 0.05$.

Results: The preeclampsia group (mean age: 30.88 ± 3.86 years) exhibited significantly higher mean CA-125 levels (43.73 ± 9.05 U/mL) compared to the normotensive group (12.02 ± 4.27 U/mL; $p < 0.0001$). Elevated CA-125 levels correlated positively with systolic blood pressure ($r = 0.91$) and negatively with platelet count ($r = -0.304$). ROC analysis indicated an optimal cut-off for CA-125 at 30.5 U/mL, achieving a sensitivity of 96% and specificity of 98%.

Conclusion: This study establishes CA-125 as a promising biomarker for pre-eclampsia, particularly in identifying disease severity. Implementing CA-125 screening in clinical practice may facilitate early detection and improve maternal and fetal outcomes.

Keywords: Pre-eclampsia, CA-125, biomarkers, hypertension, pregnancy.

Introduction

Pre-eclampsia is a pregnancy-specific multisystem disorder characterised by new onset of hypertension after the 20th week of gestation and atleast one of the following complications, including proteinurea, significant end organ dysfunction or uteroplacental

dysfunction.[1] Hypertension is defined as a diastolic blood pressure (DBP) above 110 mmHg on a single occasion or a DBP of 90 mmHg or more on two occasions, at least four hours apart. Proteinuria is identified when a 24-hour urine collection exceeds 300 mg of prot**:** Pre-eclampsia is a pregnancy-specific multisystem disorder characterised by new onset of hypertension after the 20th week of gestation and atleast one of the following complications, including proteinurea, significant end organ dysfunction or uteroplacental dysfunction. ein, or when two clean-catch urine samples show 2+ protein.[2]

The pathophysiology is linked to incomplete trophoblast invasion, causing placental hypoxia and an inflammatory response that results in fetal growth restriction.

Given the lack of specific treatments, research has focused on early diagnosis and prevention through various screening methods such as biomarkers, maternal characteristics, and Doppler ultrasound.[3] One such biomarker, Cancer antigen-125 (CA-125), is a glycoprotein produced by the coelomic and Müllerian epithelia.[4] Although CA-125 is widely used as a tumor marker in gynecology, its role in pregnancy remains unclear. It is known to rise during the first trimester and puerperium, and return to normal levels in the second and third trimesters. This increase may be related to damage to the maternal decidua, amniotic fluid, or epithelial basement membrane.[5]

Given pre-eclampsia's inflammatory nature and CA-125's role in the choriodecidual unit, it may serve as a marker for detecting pre-eclampsia and its severity. Other markers like PlGF and VEGF are being studied, but CA-125 is simpler and more accessible.[6]

This study aims to compare serum CA-125 levels in normotensive and pre-eclamptic pregnancies to evaluate its potential as a marker for pre-eclampsia severity, aiding in better management and outcomes.

Material & Method

This comparative study was conducted in the Department of Obstetrics and Gynecology at SMS Medical College, Jaipur, from January 2023 onwards. The sample size was calculated based on a 95% confidence level and α error of 0.05, with 50 subjects in each group (preeclampsia and normotensive pregnancies).

Selection Criteria

Inclusion Criteria

- Pregnant women with a singleton live pregnancy between 32-34 weeks, with preeclampsia (Cases) or normotensive (Controls).
- Participants who provided informed and written consent.

Exclusion Criteria

- Patients with chronic hypertension, ovarian disease, endometriosis, tuberculosis, diabetes mellitus, renal disease, or other metabolic disorders.

Methodology

Antenatal cases between 32-34 weeks of gestation were included, and informed written consent was obtained. Detailed history, including obstetric, menstrual, medical, and surgical history, was recorded. General physical and obstetric examinations were performed. Routine blood investigations, such as CBC, ABO, RH typing, blood sugar (DIPSY), RFT, LFT, VDRL, HBsAg, HIV, Anti-HCV, thyroid profile, urine analysis, and culture, were conducted. Participants were divided into two groups: Group A (preeclampsia) and Group B (normotensive). A 3 ml fasting venous blood sample was collected aseptically, centrifuged, and stored at -20°C for CA-125 analysis using ELISA.

Statistical Analysis

Continuous variables were summarized as mean ± SD, and categorical variables as percentages. Unpaired t-tests and other parametric tests were applied for continuous

data, while chi-square tests were used for categorical data. The effect was measured using odds ratios, and a p-value of < 0.05 was considered statistically significant. SPSS Software was used for ROC analysis and Pearson's correlation.

Result and Observation

Demographic Profile

In Group A (mean age: 30.88 ± 3.86 years) and in Group B (mean age: 29.28 ± 5.91 years). Group A: 66% Hindu, 34% Muslim; 44% rural, 56% urban; 26% nulliparous, 74% multiparous. Group B: 64% Hindu, 36% Muslim; 52% rural, 48% urban; 22% nulliparous, 78% multiparous. Mean gestational age: Group A 32.92 ± 0.75 weeks, Group B 32.82 ± 0.78 weeks.

Table 1: Distribution of study population according to CA-125

CA-125	Group A		Group B	
	No. of Patients	Percentage	No. of Patients	Percentage
≤30	1	2	40	80
31-40	8	16	8	16
41-50	15	30	2	4
51-60	14	28	0	0
>60	12	24	0	0
Total	50	100	50	100
Mean±SD	43.73±9.05		12.02±4.27	
P-Value	<0.0001			

The table compares CA-125 levels between Group A and Group B. Group A has significantly higher CA-125 levels, with a mean of 43.73 ± 9.05 U/mL, compared to Group B's mean of 12.02 ± 4.27 U/mL.

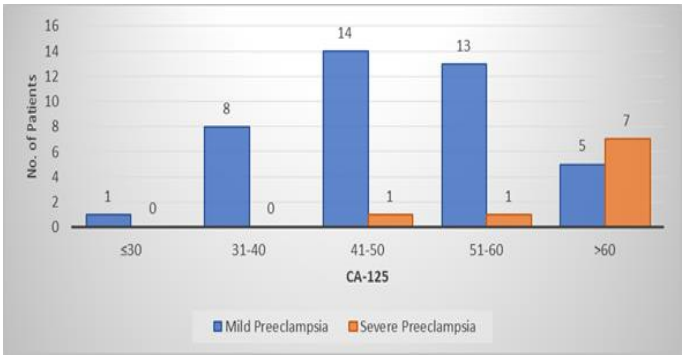

Figure 1: Correlation of severity of Pre-eclampsia with CA-125.

The Figure shows the distribution of CA-125 levels in patients with mild and severe preeclampsia. In mild preeclampsia, the highest proportions are in the 41-50 range (34.15%) and 51-60 range (31.71%), with smaller percentages in the ≤30 (2.44%), 31-40 (19.5%), and >60 (12.20%) ranges. In severe preeclampsia, 87.5% of patients had CA-125 levels >60, and 12.5% were in the 41-50 range, with no patients in the ≤30, 31-40, or 51-60 ranges. This indicates significantly higher CA-125 levels in severe preeclampsia.

In Group A, the mean systolic and diastolic blood pressures are 145.98 ± 18.61 mmHg and 93.76 ± 10.6 mmHg, significantly higher than Group B's 124.56 ± 9.92 mmHg and 84.2 ± 12.69 mmHg (p < 0.0001). Group A has a higher mean MAP (111.16 ± 10.06 mmHg) compared to Group B (97.65 ± 10.04 mmHg) (p < 0.0001). Urine albumin is present in 68% of Group A vs. 22% in Group B. Pallor (22% vs. 14%) and icterus (10% vs. 2%) are more common in Group A, but not significant. Edema is significantly higher in Group A (34% vs. 4%, p < 0.0001). Hemoglobin is borderline

lower in Group A (10.35 ± 2.05 g/dL vs. 11.07 ± 1.71 g/dL, p = 0.05). Platelet count is significantly lower in Group A (1.68 ± 1.01 vs. 2.17 ± 1.01 × 10^9/L, p = 0.01), while Total Leukocyte Count shows no significant difference.

Table 2: Pearson correlation of CA-125 with different parameters

Parameter	SBP	DBP	Platelet Count	SGOT	SGPT	S.Creatinine	Uric acid	USG- Gestational age
r-value	0.91	0.28	-0.304	-0.11	-0.117	0.28	0.31	-0.24
p-value	<0.00001	0.04	0.03	0.44	0.41	0.048	0.02	0.09

The r-value for SBP is 0.91 (p < 0.00001), indicating a very strong, statistically significant positive correlation. DBP has an r-value of 0.28 (p = 0.04), showing a weak positive correlation. Platelet count shows a moderate negative correlation (r = -0.304, p = 0.03). SGOT (r = -0.11, p = 0.44) and SGPT (r = -0.117, p = 0.41) show very weak, non-significant negative correlations. Serum creatinine has a weak positive correlation (r = 0.28, p = 0.048), while uric acid also has a weak positive correlation (r = 0.31, p = 0.02). The r-value of -0.24 (p = 0.09) indicates a weak negative, non-significant correlation.

Table 3: ROC Analysis to predict severity of pre-eclampsia using CA-125

ROC Analysis	CA-125
AUC	0.99
P-value	<0.0001
Cut-off	30.5
Sensitivity	96
Specificity	98
Accuracy	95

The ROC analysis for CA-125 shows excellent diagnostic accuracy, with an AUC of 0.99, indicating a strong ability to distinguish between conditions. The p-value is highly significant (<0.0001), confirming the statistical reliability. The optimal cut-off value for CA-125 is 30.5, yielding a sensitivity of 96% (correctly identifying 96% of affected patients) and a specificity of 98% (correctly identifying 98% of non-affected patients).

Discussion

Preeclampsia, a serious pregnancy-related hypertensive disorder, affects both maternal and fetal health by damaging the endothelium, kidneys, and liver through vasoconstrictive substances. Though its exact cause remains unclear, inadequate immunological tolerance may lead to immune reactions against fetal antigens, disrupting placentation and cytotrophoblast invasion, causing placental hypoxia and endothelial inflammation. CA-125, a glycoprotein antigen, is present in the fetal chorion, amniotic fluid, and maternal decidua. Elevated CA-125 levels in pregnancy are linked to decidual destruction and trophoblast detachment, potentially reflecting placental inflammation in preeclampsia.[7] Ongoing research investigates whether this elevation correlates with clinical symptoms. This study evaluates CA-125's role in preeclampsia.

We observed significantly higher CA-125 levels in Group A compared to Group B, with Group A having a mean of 43.73 ± 9.05 U/mL and Group B at 12.02 ± 4.27

U/mL ($p < 0.0001$). CA-125 levels ranged from 22 to 62.2 U/mL in Group A and 5.8 to 25 U/mL in Group B. In mild preeclampsia, most patients had levels in the 41-50 (35.71%) and 51-60 (30.95%) ranges, while severe preeclampsia showed 87.5% of patients with levels above 60. The mean CA-125 levels were 48.41 ± 9.68 in mild and 66.6 ± 4.30 in severe preeclampsia ($p < 0.0001$). Similar findings were reported by Sivaprasad S et al[8] and Sayyadi B M et al[9], who found significantly higher CA-125 levels in preeclampsia compared to normotensive groups ($p < 0.01$ and $p = 0.033$).

The r-value for SBP is 0.91 ($p < 0.00001$), indicating a very strong positive and statistically significant correlation. For DBP, the r-value is 0.28 ($p = 0.04$), showing a weak but statistically significant correlation. Study by Mukherjee B et al[10] similarly reported significant positive correlations of CA-125 levels with SBP ($r = 0.78$, $p < 0.001$) and DBP ($r = 0.79$, $p < 0.001$). Bhatia P et al[11] found Pearson's correlation coefficients of 0.275 ($p = 0.002$) for SBP and 0.203 ($p = 0.026$) for DBP.

Our data shows very weak negative correlations for SGOT ($r = -0.11$, $p = 0.44$) and SGPT ($r = -0.117$, $p = 0.41$), neither of which is statistically significant. In contrast, Bhatia P et al[11] reported moderate positive correlations between CA-125 and SGOT ($r = 0.473$, $p < 0.001$) as well as SGPT ($r = 0.422$, $p < 0.001$), indicating significant associations between CA-125 levels and these liver enzymes in their study.

Correlation analysis showed a weak positive correlation between CA-125 and serum creatinine ($r = 0.28$, $p = 0.048$), indicating statistical significance. A similar weak positive correlation was found with uric acid ($r = 0.31$, $p = 0.02$), also significant. Similarly, Nasir S K et al[12] reported higher serum creatinine levels in severe pre-eclampsia compared to mild pre-eclampsia and controls ($p = 0.0001$). In contrast, Balint O et al[13] found no significant difference in creatinine levels across groups ($p = 0.145$).

The ROC analysis for CA-125 demonstrates excellent diagnostic performance, with an AUC of 0.99, indicating a strong ability to distinguish between conditions. The analysis yielded a highly significant p-value of <0.0001, with an optimal cut-off value of 30.5, resulting in a sensitivity of 96% and specificity of 98%. In comparison, Gaya G et al.[14] established a CA-125 cutoff value of 23.7 IU/mL, achieving a sensitivity of 83.6% and specificity of 98.2%. Sivaprasad S et al.[8]found CA-125 levels in preeclampsia to be highly specific (90%) with a positive predictive value of 83.9%, although sensitivity was lower at 52% with a negative predictive value of 65.2%.

Conclusion

In conclusion, this study found significantly elevated serum CA-125 levels in the pre-eclampsia group compared to controls, with higher levels correlating with more severe forms of the condition. These findings support CA-125 as a valuable predictive biomarker for pre-eclampsia, indicating its potential as a screening test with a proposed cutoff of 30.5 U/mL. Utilizing CA-125 in routine screening may enhance early detection and management of pre-eclampsia, improving outcomes for both mothers and infants.

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