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Original Research Article

Serum CA 125 level in normotensive and pre-eclamptic pregnancies in a tertiary care hospital

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ABSTRACT

Background: Preeclampsia is one main reason for high-risk pregnancy. Among the disorders in hypertension, preeclampsia develops in antenatal period and it is defined by high blood pressure of more than 140/90 mmHg and arteriolar vasoconstriction, both of which lower uteroplacental perfusion and ultimately lead to placental hypoxia. The objectives of this study was (a) to estimate CA125 level in normotensive and pre eclamptic pregnancies; and (b) to predict severity of pre-eclampsia with CA125 levels with cut off value of CA125 level as 23.7 IU/ml.
Methods: This two year cross sectional study was conducted on all antenatal mothers bestween 20 -40 weeks gestational age getting admitted RLJH and research centre Tamaka (January 2021-December 2022), for the period of 2 years who fulfilled inclusion and exclusion criteria. Detailed clinical history along with antenatal examination was done. For each study subject the blood pressure was recorded. Complete blood picture was done and CA125 levels were done of the study subjects.
Results: Mean CA125 among normal subjects was 24.24±13.71 IU/ml and Mean CA125 among pre-eclampsia subjects was 30.61±15.69 IU/ml. There was a statistical significance found between two groups with respect to CA125.
Conclusions: In pre-eclampsia, CA125 was increased more compared to normotensive group. This indicates the importance in estimation of CA125 level in preeclampsia. The same has been determined with significant p value.

Keywords: Pre-eclampsia, Pregnancy, CA125, Hypertension

INTRODUCTION

Pre-eclampsia and it's spectrum of disorders affect 7.7% of primigravida women and are the leading cause of maternal and foetal morbidity and mortality in the world.[1] Among the hypertensive disorders, pre-eclampsia develops during pregnancy and is defined by high blood pressure and arteriolar vasoconstriction, both of which lower uteroplacental perfusion and ultimately lead to placental hypoxia. Fetal growth may be hampered by persistent placental hypoxia.[2] Hypertensive diseases are estimated to be the cause of 16% of maternal deaths.[3] In high income countries pre-eclampsia is associated with decreased mortality.[4] Pre-eclampsia is associated with race and ethnicity and it is most prevalent in In India, research found that the frequency of hypertensive disorders during pregnancy was 7.8%, with pre-eclampsia occurring in 5.4% of the population.[5]

Pre-eclampsia's most well-supported etiology has been linked to defective placentation, which causes placental ischemia, aberrant spiral artery remodelling, hypoxia, and oxidative stress.[6]

Risk factors for pre-eclampsia and other hypertensive disorders during pregnancy include nulliparity, pre-eclampsia in a prior pregnancy, chronic hypertension, pregestational diabetes, gestational diabetes, and so many others.[7]

Pre-eclampsia can be diagnosed by (a) blood pressure measurements of (i) systolic blood pressure of 140 mmHg or more; or (ii) diastolic blood pressure of 90 mm Hg in atleast two occasions of four hours interval after the period of viability in female with a previous normal level of blood pressure; (b) proteinuria if the protein/creatinine ratio is more than or equal to 0.3 mg/dl, or if the proteinuria is 300 mg or more per 24-hour urine collection. Dipstick reading of urine is 2± or more.[8]

The fetal chorion, amniotic fluid, and maternal decidua are likely sources of the high levels of blood CA -125 during pregnancy. CA125 is a useful marker for other gynecological illnesses and has been used for flowing up in ovarian cancers.[9]

CA125 serum levels may function as prognostic indicators.[10] The original test is a radioimmunoassay that uses the OC 125 monoclonal antibody to identify the antigenic determinant factors on the CA125 glycoprotein.[11]

Objectives

The objectives of the study was (a) to estimate CA125 level in normotensive and pre eclamptic pregnancies; and (b) to predict severity of Pre eclampsia with CA125 levels with cut off value of CA125 level as 23.7 IU/ml.

METHODS

Source of data

Pregnant women between 20-40 weeks gestational age admitted at RLJH and Research Center, Tamaka complying with inclusion criteria and exclusion criteria.

Study design

Cross-sectional study was the study design.

Study period

The study period was 2 years (January 2021-December 2022).

Sample size

Total sample size was n=100 which was grouped as normotensive n=50 and pre-eclamptic pregnancy n=50.

Sample size is calculated based on CA125 levels as an indicator for pre-eclampsia with reference to the study conducted by Geya et al, Supriya et al published in Journal of South Asia Federation of Obstetrics and Gynaecology: a prospective analysis performed in a tertiary care hospital, Mangaluru.[12]

Considering alpha error of 1% with power of 90%, the estimated sample.

Size was derived at n=50 in normotensive group and pre-eclampsia group at n=50.

The sample size was calculated using nMaster 2.0 software.

The sample size calculation included allocation of subjects as per BP recording as high or normal.

Inclusion criteria

Study subjects were proposed at the start of study to be between 20 to 35 years with gestational age between 20 weeks-40 weeks. However, the lowest was we could document was 18 years and the upper age limit was 37 years, pre-eclampsia, singleton pregnancy were included.

Exclusion criteria

Pregnant women with risk factors such as chronic hypertension, renal disease, multiple pregnancy were excluded.

A written informed consent was taken from the study subjects after confirming about inclusion criteria and exclusion criteria. Patient information sheet to the study subjects of their understandable language was given.

Fifty normotensive and fifty pre-eclamptic subjects were recruited for the study. Detailed clinical history of the study subjects along with antenatal examination was done. For each study subject the blood pressure was recorded. Study subjects with first recorded increased BP reading were repeated one more reading of blood pressure after an interval of four hours and that BP reading was documented. Urine was examined for proteinuria. Complete blood picture was done to all study subjects white blood cell count, platelet count and CA125 levels were done of the study subjects. The entire procedure for the CA125 has been done using electrochemiluminescence instrument.

Statistical analysis

Data were entered in Microsoft excel data sheet and were analyzed using SPSS-22 increased version software. Frequencies and proportions were used to represent categorical data. To test the significance of qualitative data, the Chi-square test or Fischer's exact test (for 2×2 tables only) was used. The mean±standard deviation was used to represent continuous data. The independent t-test was used as a statistical test to determine the mean difference between two quantitative variables. For the determination of specificity, sensitivity, positive predictive value and negative predictive value, the receiver operating characteristic (ROC) curve and optimal cut-off values were chosen. The test was interpreted based on a prediction of overall result and an area under ROC curve of value 0.5. An area under ROC curve greater than 0.8 indicated reasonably good prediction.

Graphical representation of data

Data graphs were created using MS excel and MS word was used.

P value of less than 0.05 was considered statistically significant.

Statistical software

To analyse data, MS excel and SPSS version 22 (IBM SPSS Statistics, Somers, NY, USA) were used.

RESULTS

In age frequency distribution, with lower limit of age as 18 years and with upper limit as 37 years, the study subjects were distributed under fixed interval. P value 0.067, there was no statistical significance between the two groups in terms of age. Twenty-four (48%) pre-eclamptic subjects were belonging to early age group of 18-22 years. This indicates that in this study population, lower the age group higher the risk of pre-eclampsia whereas literature says advancing maternal age is one of the risk factors for pre-eclampsia. Thirty pre-eclamptic subjects were primigravida constituting the maximum of the study population about 60%. P value of 0.131 indicates that there was no statistically significance found between two groups with respect to parity.

In pre-eclampsia, the maximum number of subjects (31 cases) belonged to term gestation of 37-40 weeks of about 62%. P value of 0.023 indicates that there was statistical significance found between two groups with respect to gestational age.

P value of 0.088, indicates that there was no significant difference seen statistically between two groups with respect to mode of delivery. Mean CA125 among normal subjects was 24.24±13.71 IU/ml and Mean CA125 among pre-eclampsia subjects was 30.61±15.69 IU/ml. There was a statistical significance found between two groups with respect to CA125. In pre-eclampsia, CA125 was increased by around 126.27% more compared to normotensive group. This indicates the importance in estimation of CA125 level in pre-eclampsia. The same has been determined with significant p value. P value of less than 0.001, indicates there was a statistical significance found between severities of pre-eclampsia with respect to CA125. Among the subgroup classification in present study, we documented CA125 levels highest among antepartum/postpartum eclampsia compared to pre-eclampsia where it has elevated around 2.73 times, which indicates CA125 to be a better predictor in antepartum/postpartum eclampsia. With respect to receiver operating curve for CA125, it has been observed in our study that CA125 is a specific marker with a specificity value of 90% and sensitivity of 58%. However, the sensitivity depends on various factors and observer bias; specificity helps clinicians to make a critical decision in pre-eclampsia and use CA125 as a good predictor.

Among the 31 subjects whose CA125 is >32.1 IU/ml, most of them (twenty six study subjects) belonged to pre-eclamptic group. Association of CA125 level in pre-eclampsia is highly specific (90%) with a positive predictive value of 83.9% but less sensitive (52%) and has a negative predictive value of 65.2%.

Table 1: Age-case frequency distribution.

Age (years)	Normal		Pre-eclampsia		P value
	N	%	N	%	
18-22	13	26.0	24	48.0	0.022
23-27	23	46.0	13	26.0	0.037
28-32	12	24.0	9	18.0	0.461
33-37	2	4.0	4	8.0	0.399

Table 2: Parity case frequency distribution.

Gravida	Normal	Pre-eclampsia	Total	P value
Primi	20	30	50	0.131
	40.0%	60.0%	50.0%	
2	17	12	29	
	34.0%	24.0%	29.0%	
3	6	6	12	
	12.0%	12.0%	12.0%	
4	7	2	9	
	14.0%	4.0%	9.0%	

Table 3: Gestational age-case frequency distribution.

Frequency (weeks)	Normal		Pre-eclampsia		P value
	N	%	N	%	
29-32	4	8.0	4	8.0	1.00
33-36	4	8.0	15	30.0	0.005
37-40	40	80.0	31	62.0	0.047
41-44	2	4.0	0	0	0.468

Table 4: Mode of delivery- case frequency distribution.

Mode of delivery	Normal	Pre-eclampsia	Total	P value
Lower segment caesarean section	38	29	67	0.088
	76.0%	58.0%	67.0%	
Vaginal delivery	12	21	33	
	24.0%	42.0%	33.0%	
Total	50	50	100	
	100.0%	100.0%	100.0%	

Table 5: Distribution of subjects with preeclampsia according to fetal outcome.

Subjects	N	%
Baby mother's side	28	56.0
IUD	5	10.0
NICU	17	44.0

Table 6: Comparison of mean CA125 between two groups.

Variables	Mean	SD	P value
Normal	24.24	13.71	0.033
Pre-eclampsia	30.61	15.69	

Table 7: Subgroup classification of preeclampsia and CA125 value.

Sub-groups	Mean	SD	P value
Pre-eclampsia	24.10	9.59	<0.001
Severe pre-eclampsia	32.77	12.97	
Imminent eclampsia	58.28	9.53	
Antepartum/post-partum eclampsia	65.80	0.71	

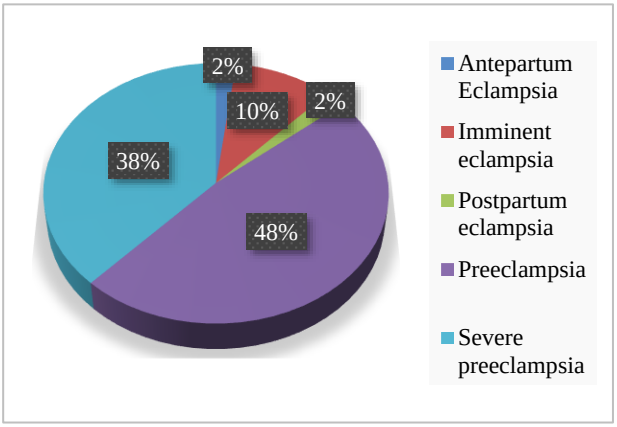

Figure 1: Distribution of pre-eclamptic subjects according to severity of preeclampsia.

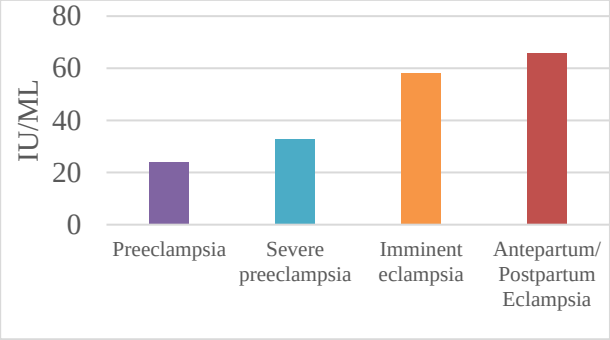

Figure 2: Comparison of mean CA125 according to severity of preeclampsia.

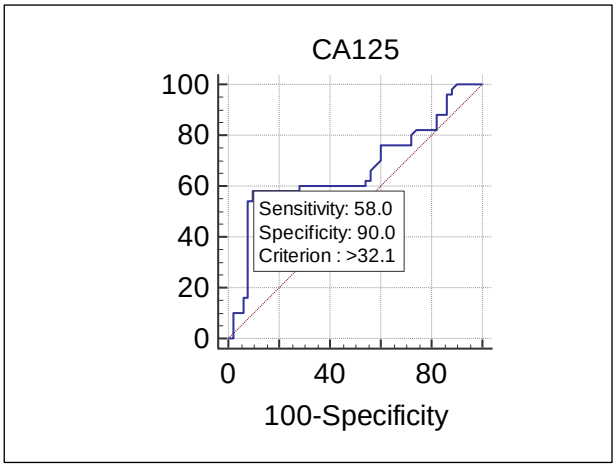

Figure 3: ROC curve for CA125 in predicting Pre-eclampsia.

DISCUSSION

Our study findings were consistent with findings of the study done by Gottipati et al.[12] We documented antepartum eclampsia [1 (2.0%) pre-eclampsia] followed by imminent eclampsia [5 (10.0%) pre-eclampsia], postpartum eclampsia [1 (2.0%) pre-eclampsia], pre-eclampsia [24 (48.0%) pre-eclampsia] and severe pre-eclampsia [19 (38.0%) pre-eclampsia]. Comparison of mean CA125 according to severity of pre-eclampsia: pre-eclampsia (mean 24.10 and SD=9.59), severe pre-eclampsia (mean=32.77 and SD=12.97), imminent eclampsia (mean=58.20 and SD=9.53) and antepartum/ postpartum eclampsia (mean 65.80 and SD=0.7071). P value less than 0.001, indicating a statistical significance among severities of pre-eclampsia and CA125. In our study, CA125 in determining pre-eclampsia at cut off 32.1: sensitivity [value (52.0%) and 95% CI (37.4-66.3%)], specificity [value (90.0%) and 95%CI (78.2-96.7%)], positive predictive value [value (83.9%) and 95% CI (68.3-92.5%)] and negative predictive value [value (65.2%) and 95% CI (58.7-71.4%)] which were consistent with previous studies. Sensitivity value of 70.1% and specificity value of 62.0% were reported from a 2018 study by Gbemisola et al using ROC curve to analyze connection between maternal CA125 and increased blood pressure readings.[13] Study by Mukherjee et al in 2020, Sensitivity and specificity 92.1% and 97.1%, with cut-off 35 IU/ml serum CA125. 95.5% of predictions were correct, whereas 94.4% of predictions were incorrect.[14] From the study by Sane et al in 2021, it was shown that the level of CA125 in non-severe pre-eclampsia and normal pregnancy did not vary significantly. The difference between severe and non-severe pre-eclampsia was negligible.[15] During pre-eclampsia-related pregnancies, inability of trophoblast penetration and onset of inflammation in the placenta result in production of biomarkers, with CA125 predominating. As a result, CA125 is biomarker of magnitude of inflammation in pre-eclampsia and fit to be used as supplement test as well as surrogate test to

detect pre-eclampsia with atypical features or to detect its severity early.[16]

Limitation

Small sample size, and generalising results requires evidence from comparable large studies.

CONCLUSION

In the current study, we found a statistical significance in gestational age between two groups. The mean CA125 among pregnancies with normal study subjects was observed to be significantly low when compared with preeclamptic in this study. Furthermore, a connection was identified between serum concentration of CA125 and severity of pre-eclampsia. CA125 has been identified as a potential biomarker that can be used for pre-eclampsia diagnosis and follow-up, and it matches up markedly with the severity of pre-eclampsia. As a result, we recommend that more robust longitudinal studies with maternal CA125 patterns in pregnancy be conducted to assess its applicability as a predictive marker for pre-eclampsia and to establish an acceptable cut-off value, particularly among Indian women who have a proclivity to present with severe disease and a poor pregnancy outcome.

Recommendations

The use of CA125 for timely identification of pre-eclampsia is recommended in this study so that effective management methods can be initiated as soon as possible for good maternal and neonatal outcomes.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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