ORIGINAL ARTICLE

Maternal Serum Cancer Antigen 125: A Marker of Severity of Preeclampsia

Gottipati Geya[1], Kantharaju Supriya[2]

Abstract

Aim: The aim of this study is to study the levels of cancer antigen 125 (CA-125) in normal, preeclampsia, and gestational hypertension study groups and correlate with other parameters which mark the severity of the disease.

Materials and methods: A cross-sectional study was conducted at a Tertiary Care Hospital, Mangaluru, India. A total of 165 subjects were divided into three study groups: preeclampsia, gestational hypertension, and normal pregnancy, and each group consisted of 55 subjects. CA-125 levels were measured in these study groups.

Results: The mean value of CA-125 in the preeclampsia group was 56.7 IU/mL which was significantly higher compared with other two study groups. CA-125 was found to have a positive correlation with systolic blood pressure (BP) (*r* value = 0.4, *p* value = 0.001), diastolic BP (*r* value = 0.3, *p* value = 0.001), and uric acid (*r* value = 0.2, *p* value = 0.001) and also an association was observed between increasing CA-125 and proteinuria (*p* value = 0.001) oligohydramnios (*p* value = 0.001) fetal growth restriction (*p* value = 0.03) and onset of the disease (*p* value = 0.001). However, a negative correlation with platelets (*r* value = −0.14, *p* value = 0.06) and birth weight (*r* value = −0.113, *p* value = 0.15) was observed.

Conclusion: CA-125 is a marker indicating increasing severity of the disease. It is a biochemical marker which can be used in the screening of preeclampsia. Further studies are needed for the evaluation of raising serial CA-125 levels as a marker of progression of the disease.

Clinical significance: Hypertensive disorders of pregnancy are one of the most common causes of death due to pregnancy. CA-125 was proposed to be elevated in patients with hypertension due to chronic inflammation. Hence, CA-125 levels if used as a screening tool can estimate the severity of the disease and help clinicians in identifying women who are at risk for further complications and act accordingly.

Keywords: CA-125 levels, Gestational hypertension, Preeclampsia.

Journal of South Asian Federation of Obstetrics and Gynaecology (2019): 10.5005/jp-journals-10006-1669

Introduction

Hypertensive disorders of pregnancy are one of the most common causes of death due to pregnancy.[1] Incidence of preeclampsia alone is identified in 3.9% of all pregnancies.[2] CA-125 or MUCIN 16 is a membrane protein and possesses a single transmembrane domain and it is the most frequently used biomarker in ovarian cancer detection.[3] Decidual cells affected by chorionic invasion or placental separation are a source of CA-125. The underlying mechanism proposed for the increased CA-125 levels in preeclampsia is the extension of decidual destruction and separation of trophoblasts from the decidua.[4] This theory has been supported by various studies and they have proposed that increasing levels of CA-125 is an indicator of increasing the severity of the disease. All the studies so far compared levels of CA-125 in mild and severe preeclampsia with that of normal pregnancy. In the present study, we compared levels of CA-125 in gestational hypertension and preeclampsia with that of normal pregnancy. Relation of CA-125 levels with various other outcomes and parameters of preeclampsia were analyzed and a mean value of CA-125 in gestational hypertension and preeclampsia group has been derived.

Materials and Methods

This study was a cross-sectional study performed during a study period of 2 years from September 2014–July 2016 in a Tertiary Care Center after obtaining Institutional Ethics Committee approval. A total of 165 subjects divided into three study groups between 20 weeks and 42 weeks period of gestation with singleton pregnancies fulfilling inclusion criteria were included. Written informed verbal consent was obtained from all the subjects. Three study groups included the normal pregnancy group, the gestational hypertension group, and the preeclampsia group consisting of 55 subjects each. Preeclampsia was diagnosed and classified according to the criteria specified by the technical bulletin of the American College of Obstetricians and Gynecologists and the National High Blood Pressure Education Program Working Group Report on High Blood Pressure in Pregnancy. Multiple gestation and patients with chronic hypertension, ovarian diseases, tuberculosis, overt diabetes mellitus, and renal disease were excluded. BP recording was done in the right arm sitting position. Venous blood samples for complete blood count, renal function test, uric acid, liver function test, and CA-125 levels were drawn from all participants. Routine urine analysis was done in all participants and the 24 hour urine protein was done. Samples collected were centrifuged within 2 hours of collection and the serum was stored at −20°C. Samples collected were processed within 3 months of collection. An enzyme-linked immunosorbent assay (ELISA) was used to estimate the CA-125 levels.

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How to cite this article: Geya G, Supriya K. Maternal Serum Cancer Antigen 125: A Marker of Severity of Preeclampsia. J South Asian Feder Obst Gynae 2019;11(2):100–102.

Source of support: Nil

Conflict of interest: None

Statistical Analysis

Data were analyzed using the Chi-square and Fisher's exact tests and Pearson correlation coefficient. The *p* value <0.05 was considered significant, $r < 0.5$ is the weak correlation, >0.5 the mild strength, and >0.7 the strong correlation. The $r +$ is the direct correlation and − is the inverse correlation. A statistical package SPSS (Chicago, Illinois) version 17.0 was used for data analysis.

Results

All three study groups were comparable in demographic characters like age, parity, and period of gestation. Preeclampsia had a mean systolic BP of 153.6 mm Hg and diastolic BP of 101.9 mm Hg which was statistically highly significant (*p* value = 0.000). The mean systolic BP in gestational hypertension was 141.8 mm Hg and diastolic BP was 91.6 mm Hg. The mean birth weight among study subjects in preeclampsia is 2.1 kg which is lower compared with the other two study groups (*p* value = 0.000). The mean gestational age at the onset of the disease is 31 weeks for the preeclampsia group and 35 weeks for the gestational hypertension group indicating the earlier onset of disease in the preeclampsia group (*p* value = 0.000).

Table 1 shows that the mean value of CA-125 in the preeclampsia group was 56.6 IU/mL which was highly significant compared with the other two study groups ($p = 0.000$).

Table 2 shows that CA-125 had a significant association with the onset of the disease ($p = 0.000$) indicating that earlier the onset of disease, higher the value and had a significant association with other markers of severity of disease like uric acid ($p = 0.000$), proteinuria ($p = 0.000$), fetal growth restriction ($p = 0.000$), and oligohydramnios ($p = 0.000$).

As shown in Table 3, CA-125 had a positive correlation with systolic BP ($r = 0.4$) and diastolic BP ($r = 0.3$) and uric acid ($r = 0.2$), creatinine ($r = 0.2$), and BMI ($r = 0.1$) and a negative correlation with birth weight ($r = -0.113$) and platelets ($r = -0.145$).

The cutoff value of CA-125 in the present study is 23.7 IU/mL with a sensitivity and a specificity of 83.6% and 98.2%, respectively, obtained from the receiver operating characteristic (ROC) curve as shown in Figure 1.

Table 1: Distribution of CA-125 in IU/mL

CA-125	*Mean*	*SD*	*Range*	*p value*
CA-125 gestational hypertension	15.7	8.4	13.4–17.9	
Preeclampsia	56.6	88.2	32.7–80.4	0.000 (HS)
Normal pregnancy	7.9	4.1	6.8–9.02	

HS, highly significant

Table 2: Association of CA-125 with other parameters

	Onset	*Uric acid*	*Proteinuria*	*FGR*	*Oligohydramnios*
p value	0.001	0.001	0.001	0.030	0.001

FGR, fetal growth restriction

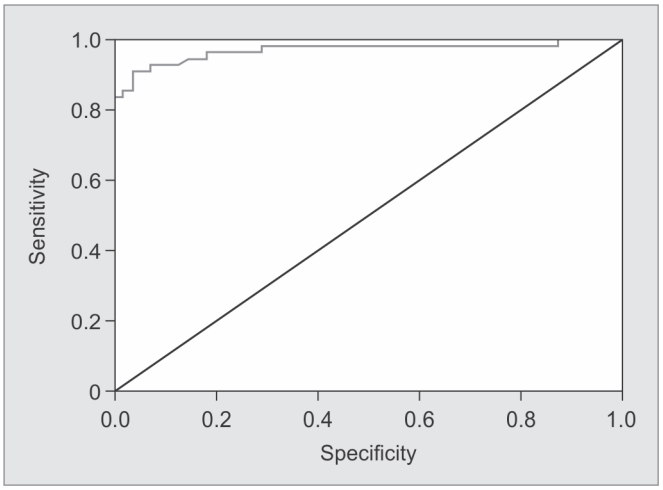

Fig. 1: ROC curve obtained for CA-125 values

Discussion

Preeclampsia is disease specific to pregnancy affecting almost every organ.[5] Reduced trophoblastic migration into the maternal decidua in preeclampsia causes chronic inflammation leading to an increased expression of CA-125.[6]

Table 4 depicts a comparison of mean values and cutoff values of CA-125 with other studies. The mean value of CA-125 in the preeclampsia group in the present study was 56.6 IU/mL which was similar to Bhattacharya and Saha[7] (58.5 IU/mL), whereas the value was slightly higher when compared with Karman et al.[8] (38.8 IU/mL) and Hassan et al.[9] (38.04 IU/mL). This difference in the mean can be explained by a wide difference in the standard deviation obtained in the present study as much higher values of CA-125 were observed in a few patients with a severe form of disease resulting in higher mean values compared to other two above-mentioned studies.

CA-125 values of the gestational hypertension group of the present study were comparable to the mild preeclampsia group of Karman et al.[8] (18.8 IU/mL). Bhattacharya and Saha[7] (53.7 IU/mL) and Hassan et al.[9] (32.5 IU/mL) observed the much higher value of CA-125 in the mild preeclampsia group compared with the gestational hypertension group. This difference in results can be explained by increased inflammatory response in the preeclampsia group when compared with the gestational hypertension group leading to increased release of CA-125 which is proposed as an inflammatory marker. In the present study, a difference between mean values of CA-125 in the gestational hypertension group and the preeclampsia group is noted. This is in favor of the hypothesis that increasing severity of the disease leads to an increased release of CA-125.

The cutoff value of CA-125 in the present study is 23.7 IU/mL with a sensitivity and a specificity of 83.6% and 98.2%, respectively, which is lower compared with other studies. Ozat et al.[10] obtained a cutoff value of 50 IU/mL with a sensitivity of 93.7% and a specificity of 88%. But the specificity of the cutoff value of the present study is higher. Cebesoy et al.[6] derived a cutoff value of 35 IU/mL but did not measure sensitivity and specificity. This difference in cutoff values

Table 3: Correlation of CA-125 with other parameters

	Systolic blood pressure (SBP)	*Diastolic blood pressure (DBP)*	*Platelet*	*Uric acid*	*Birth weight*	*BMI*	*Creatinine*
r value	0.4	0.3	−0.145	0.2	−0.113	0.1	0.2
p value	0.000	0.000	0.06	0.000	0.15	0.18	0.003

Table 4: Comparison of mean and cutoff values of CA-125 with other studies

	Mean value (IU/mL)		*Cutoff value (IU/mL)*
Study	*Mild preeclampsia/ gestational hypertension**	*Severe preeclampsia*	*Preeclampsia*
Bhattacharya and Saha[7]	53.7	58.5	
Karaman et al.[8]	18.8	38.8	
Hassan et al.[9]	32.5	38.04	
Ozat et al.[10]	—	—	50
Cebesoy et al.[6]	—	—	35
Present study*	15.7	56.6	23.7

*Gestational hypertension in the present study

can probably be due to the inclusion of severe preeclampsia as a separate group in other studies.

CA-125 was found to have a positive correlation with systolic BP, diastolic BP and mean arterial pressure (MAP), uric acid and creatinine, and total urinary concentration and a negative correlation with platelets and birth weight in the present study.

Ozat et al.[10] and Bhattacharya and Saha[7] found a positive correlation between CA-125 and other variables similar to the present study. But platelets had a positive correlation with CA-125, whereas in the present study, platelets had a negative correlation. This difference in results can be explained due to a variation in the sample size.

The mean birth weight in the preeclampsia group in the present study is 2.1 kg indicating that a lower birthweight in the preeclampsia group is probably due to fetal growth restriction which is one of the manifestations of the disease or preterm deliveries due to labor induction for the termination of pregnancy.

Similar outcomes were found by Karmann et al.,[8] wherein the mean birthweight was lower in the mild and severe preeclampsia groups. The mean values of age, BMI, and serum creatinine and platelets are comparable with the present study.

In a study done by Bhattacharya and Saha[7] estimated fetal weight in all three study groups are similar which differs from the present study probably due to the difference in inclusion criteria, as the study population included pregnant women beyond 32 weeks period of gestation only unlike the present study which included women beyond 20 weeks of gestation leading to higher birth weight even in the preeclampsia group. Mean values of age, BMI, and serum creatinine and platelets are comparable to the present study.

Mean CA-125 values were higher in the preeclampsia group in all studies including the present study, thus, supporting the hypothesis that increasing severity of the disease leads to increased inflammatory response causing increased CA-125 release.

Conclusion

The present study aimed at measuring CA-125 levels in the preeclampsia and gestational hypertension and in the normal pregnancy. It was found to be significantly elevated in the preeclampsia group. The CA-125 value had a positive correlation with other clinical parameters like systolic and diastolic BP, uric acid, and other outcomes of preeclampsia like fetal growth restriction and oligohydramnios. Thus, indicating that it is a marker of increasing severity of the disease. CA-125 is a biochemical marker which can be used in the screening of preeclampsia. Further studies are needed for the evaluation of raising serial CA-125 levels as a marker of progression of the disease.

Clinical Significance

Hypertensive disorders of pregnancy are one of the most common causes of death due to pregnancy. CA-125 was proposed to be elevated in patients with hypertension due to chronic inflammation. Hence, CA-125 levels if used as a screening tool can estimate the severity of the disease and help clinicians in identifying women who are at risk for further complications and act accordingly.

Acknowledgments

The authors would like to extend their thanks to the Department of Biochemistry, Kasturba Medical College, Mangaluru, for carrying out ELISA tests and to the Head of the Department, Obstetrics and Gynaecology for giving them this opportunity to carry out their study. It is a self-aided study.

References

1. Arulkumaran N, Lightstone L. Severe pre-eclampsia and hypertensive crises. Best Pract Res Clin Obstet Gynaecol 2013;27(6):877–884. DOI: 10.1016/j.bpobgyn.2013.07.003.
2. Martin JNJ, Owens MY, et al. Standardized Mississippi Protocol treatment of 190 patients with HELLP syndrome: slowing disease progression and preventing new major maternal morbidity. Hypertens Pregnancy 2012;31(1):79–90. DOI: 10.3109/10641955.2010.525277.
3. Suh KS, Park SW, et al. Ovarian cancer biomarkers for molecular biosensors and translational medicine. Expert Rev Mol Diagn 2010;10(8):1069–1083. DOI: 10.1586/erm.10.87.
4. Malatyalioglu E, Ozer S, et al. CA-125 levels in ruptured and unruptured tubal ectopic pregnancies. J Obstet Gynaecol Res 2006;32(4):422–427. DOI: 10.1111/j.1447-0756.2006.00424.x.
5. Lindheimer MD, Taler SJ, et al. Hypertension in pregnancy. J Am Soc Hypertens 2010;4(2):68–78. DOI: 10.1016/j.jash.2010.03.002.
6. Cebesoy FB, Balat O, et al. CA-125 and CRP are elevated in preeclampsia. Hypertens Pregnancy 2009;28(2):201–211. DOI: 10.1080/10641950802601187.
7. Bhattacharya DA, Saha R. Serum concentrations of CA-125 in normal and Preeclamptic pregnancies. IOSR J Pharm 2014;8:14–17.
8. Karaman E, Karaman Y, et al. Maternal serum CA-125 level is elevated in severe preeclampsia. Pregnancy Hypertens 2014;4(1):29–33. DOI: 10.1016/j.preghy.2013.08.003.
9. Hassan MA, Hameed BH, et al. The Association of Serum Cancer Antigen 125 and C-reactive protein Level with the Severity of Preeclampsia. Karbala J Med 2012;5(1):1322–1327.
10. Ozat M, Kanat-Pektas M, et al. Serum concentrations of CA-125 in normal and preeclamptic pregnancies. Arch Gynecol Obstet 2011;284(3):607–612. DOI: 10.1007/s00404-010-1736-2.