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Serum concentrations of CA-125 in normal and Preeclamptic pregnancies

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ABSTRACT: *Aim The Present Study Aims To Investigate The Serum Concentrations Of Ca-125 In Normal And Preeclamptic Pregnancies And Investigate Clinical Utility Of This Biochemical Marker In Prediction, Diagnosis And Follow Up Of Preeclampsia.*

Methods :*The present study reviews a total 48 women with single pregnancy. These participants were categorized into control (n = 40), mild preeclampsia(n = 38) and severe preeclampsia (n = 10). The three study groups were statistically similar in aspects of maternal and gestational age and body mass index.*

KEY WORDS *: CA-125 ,Preeclampsia ,Pregnancy.*

I. INTRODUCTION

Hypertensive disorders related with pregnancy occur in nearly 7–10% of all pregnancies. Amongst them, preeclampsia is a major cause of high-risk pregnancies. Preeclampsia is characterized by hypertension and arteriolar vasoconstriction, which decrease the uteroplacental perfusion and ultimately result in placental hypoxia which if longlasts can impair fetal growth[1]. CA-125 is a glycoprotein antigen which is generally expressed in ovarian cancer and non-malignant pelvic diseases like endometriosis, fibroids, pregnancy, and pelvic inflammatory disease [2]. Fetal chorion, amniotic fluid and maternal decidua are potential sources of high serum CA-125 levels during the first gestational trimester and the postpartum period.The role of serum CA-125 levels within the perinatal period is still under study [3]. The clinical studies related to the use of CA-125 in hypertensive disorders of pregnancy are few and report conflicting results[4-7]. The present study aims to investigate the serum concentrations of CA-125 in normal and preeclamptic pregnancies and thereby to specify the clinical utility of this biochemical marker in prediction, diagnosis and follow up of preeclampsia.

Materials and methods

The study was conducted at the Department of Biochemistry and obstretrics and gynaecology,IPGMER,Kolkata.

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This study was undertaken in 30women with normal singleton pregnancies (control group) and48 women with preeclamptic singleton pregnancies (study group). The women who were diagnosed with preeclampsia after 32nd week of pregnancy at the study center were included in the study group. The women who attended the obstretrics & gynae OPD for routine prenatal visit after 32nd week of pregnancy were assigned. The 32nd week of pregnancy was arbitrarily chosen as an inclusion criterion. 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 [8]. Hypertension was described as an absolute blood pressure [140/90 mmHg after 20 weeks gestation which should be measured by at least two measurements. Proteinuria was defined as [0.3 g of urinary protein excretion. The exclusion criteria were diabetes mellitus, chronic hypertension, a known history of peripheral vascular disease and/or antihypertensive treatment and a body mass index (BMI) ≥ [30 kg/m2. Participants were categorized into three groups: control (n = 30), mild preeclampsia (n = 38) and severe preeclampsia (n = 10). Mild preeclampsia was defined as a blood pressure between 140/90 and 160/110 mmHg, and Proteinuria between 0.3 and2.0 g/day, while severe preeclampsia was defined as a blood pressure ≥160/110 mmHg and proteinuria 5.0 g/day. The three study groups were statistically similar in respect of maternal age, gestational age and BMI. Venous blood samples for complete blood count, creatinine, uric acid and CA-125

concentrations were drawn Venous blood samples for CA-125 were collected into anticoagulant-free glass tubes, centrifuged immediately at
6,420 g (4_C) and stored at -70_C. Not more than two
freeze–thaw cycles were applied for any sample. 24-h urine was collected from each participant so that the amount of protein excretion could be determined.
Serum levels of CA-125 were measured by ELISA method whereas complete blood count (CBC) parameters were determined by an automated blood counter. Serum creatinine and uric acid concentrations were measured by an automatic chemical analyzer, The normal range was ratified as 0–35 IU/ml for serum levels of CA-125. Age, parity, BMI, gestational age, systolic and diastolic blood pressures, treatment regimens, CBC parameters and serum concentrations of uric acid, creatinine and CA-125, the estimated fetal weight, the presence of intrauterine growth retardation (IUGR) and intrauterine death if any of all participants were recorded.

Results

The present study reviews a total of 48 women Serum CA-125 concentrations were found to have a positive correlation with systolic blood pressure ($r = 0.3360$, $p = 0.001$), diastolic blood pressure ($r = 0.352$, $p = 0.001$), platelet count ($r = 0.346$, $p = 0.001$), serum levels of uric acid ($r = 0.399$, $p = 0.001$) and urine concentrations of protein ($r = 0.328$, $p = 0.001$). CA-125 levels correlated negatively with estimated fetal weight ($r = -0.410$, $p = 0.001$) and birth weight ($r = -0.338$, $p = 0.001$). the cut-off point for serum CA-125 concentrations was accepted as 50 IU/ml, the sensitivity and specificity of CA 125 were, respectively, 91.0 and 80.2% for the detection of preeclamptic pregnancies. positive and negative predictive values for CA-125 were 88.7 and 91.1%, respectively, $p = 0.001$). Conclusion This study shows that CA-125 as a biochemical marker indicates the severity of the inflammatory process in preeclampsia. It seems to be a promising test for screening preeclampsia. The present study suggests 50 IU/ml as a cutoff point for CA-125 in screening preeclampsia Table 1 compares the clinical and demographic characteristics of the three study groups and Table 2 shows the perinatal outcome of the patients. Women diagnosed with severe preeclampsia had significantly low parity and platelet count whereas their systolic and diastolic blood pressure values ,serum concentrations of uric acid and CA-125 were significantly higher. Besides, the perinatal outcome was worse for the pregnancies of women with severe preeclampsia. $p = 0.001$). When the cut-off point for serum CA-125 concentrations was accepted as 50 IU/ml, the sensitivity, specificity, positive and negative predictive values of this unique biochemical marker were, respectively, 93.7, 88.0, 91.7 and 90.7%for the detection of preeclamptic pregnancies ($p = 0.001$) (Table 3).
Figure 1 shows the levels of CA-125 values within the control group and patients with mild and severe

TABLE 1

	normal pregnancy	Mild PET	Severe PET	P
Age	24.4±2.7	24.1±1.9	24.8±0.8	.432
Parity	1.6±0.3	0.8±0.2	0.5±0.1	0.001
Gestational age	36.2±3.4	35.4±1.7	35.2±2.3	0.355
BMI	23.7±2.9	23.9±1.8	24.1±1.4	0.658
BP	120/70±6.6/7.2	144/90±7.4/7.9	148/94±8.9/9.2	0.001
Platelet count	242±38.2	239±36.3	237±26.3	0.017
Serum uric acid(mmol/l)	0.31±0.04	0.33±0.03	0.36±0.06	0.001
Serum CA125(IU/ml)	47.3±3.34	53.7±8.52	58.5±4.02	0.001
Proteinuria(gms/dl)	0.1±0.2	1.2±0.7	4.9±10.7	0.001
Serum Creatinine(mmol/l)	0.61±6.2	0.63±5.0	0.66±7.1	0.670

* $p<0.05$ is accepted to be statistically significant

TABLE 2

Estimated foetal weight	2.75±450.8	2.72±520.1	2.62±510.0	0.001
IUGR	04	0.0	03	0.001
Intra uterine demise	0.0	0.0	1.0	0.001
Birth weight	3.56±390.4	3.42±282.3	2.71±510.2	0.001
Need for NICU	2	3	5	0.001

* $p<0.05$ is accepted to be statistically significant

TABLE 3

	Normal pregnancy	PET	Total

CA125<50IU/ml	27	06	33
CA125≥50IU/ml	03	42	45
Total	30	48	78

$p<0.05$ is accepted to be statistically significant

Discussion

Preeclampsia is a hypertensive disorder of pregnancy which may cause morbidity and even mortality for both the mother and the fetus. This disease may cause generalized damage to the maternal endothelium, kidneys and liver through the release of vasoconstrictive substances[9]. its exact pathogenesis remains uncertain. The current understanding of the syndrome is as a two-stage process. The first stage predisposes the placenta to hypoxia so that the cytokine release is enhanced. During the second stage, these cytokines cause endothelial cell injury, altered vascular reactivity, decreased intravascular volume and inflammation as well as glomerular endotheliosis. On the other hand, maternal susceptibility to the alterations is an important factor. The lack of immunological tolerance in pregnancy may provoke animmune response against the paternal antigens of the fetus and placenta. Therefore, placentation process is interrupted and cytotrophoblastic invasion is suppressed. So placenta becomes hypoxic and begins to secrete inflammatory mediators which act over the vascular endothelium[1,9,10,11].

CA-125 is a glycoprotein antigen which is located on cell surface. Fetal chorion, amniotic fluid and maternal decidua have been indicated as the potential sources of high serum CA-125 levels which are detected during the first trimester of pregnancy and postpartum period. This suggests disintegration of the maternal deciduas as a possible source of elevated CA125[2,3,12,13].

The same mechanism can suggest the aetiology for the pregnancies which were complicated with preeclampsia. It has been assumed that the failure in trophoblastic invasion and the induction of an inflammatory process within placenta may trigger the expression of CA-125. A few clinical studies have investigated whether this enhancement in CA-125 expression would become biochemically and clinically evident or not [4-7]. Schro¨cksnadel et al. compared the plasma CA-125 levels of 50 healthy Table 3 non-pregnant women, 50 pregnant patients with hypertensive disorders and 50 healthy women with singleton pregnancies at term. However, no statistically significant difference could be noted for CA- 125 [4-7]. a longitudinal which compared CA-125 values of healthy and preeclamptic subjects throughout a given time interval study documented that serum concentrations of CA-125 did not differ with respect to either pregnancy outcome or gestational age. However, there was a trend toward an elevation in CA-125 concentrations for pregnancies that are destined to develop preeclampsia[5]. Another study compared serum CA-125 concentrations of 120 women with pathological outcome of pregnancy (spontaneous abortion, fetal death, intrauterine growth retardation, chromosomal and structural abnormalities, and preeclampsia/ eclampsia) women with normal outcome of pregnancy. It was reported that maternal CA- 125 serum values were significantly higher in the first and the third trimesters of pregnancy when compared to those in the second trimester, but not significantly different from those values obtained in pathological pregnancies[14]. A recent study by Cebesoy et al. investigated 54 preeclamptic/ eclamptic women and 56 healthy pregnant women. The serum concentrations of CRP and CA-125 were found to be significantly higher in women with preeclampsia/ eclampsia when compared with healthy pregnant women. Also serum CRP and CA-125 levels of women with severe preeclampsia/eclampsia were significantly higher than those of the women with mild preeclampsia. Moreover, significant correlations were found between CRP, albumin, CA-125 and mean arterial pressure. Therefore, the authors concluded that CRP and CA- 125 are elevating markers in preeclampsia [7]. In accordance, the present study reports that CA-125 correlates directly with all of the biochemical markers which are commonly used to diagnose and follow women with preeclampsia. A significant but inverse relationship is also observed between the serum concentrations of CA-125 and perinatal outcome of preeclamptic women. The present study suggests that CA-125 is a biochemical marker which reflects the severity of the underlying inflammatory process in preeclampsia (with a cut-off point of 50 IU/ml). It may be assumed that the extension of decidual destruction and failure of trophoblastic invasion in preeclampsia may induce the secretion of CA-125 within placenta. we reviewed that the population in the present study is much smaller to come to a conclusion about a certain CA-125 value which would deliberately distinguish women who are to develop preeclampsia. The discrepancies between the present findings and the results of the previously published studies may be attributed to several factors including the size of the study sample, the differences within the demographic and clinical features of the reviewed patients and the utilization of different diagnostic criteria for hypertensive disorders of pregnancy. Another confounding factor may be the variance in the accuracy and reliability of CA-125 assays. Some studies mention an automated method for the determination of the soluble fms-like tyrosine kinase (sFlt- 1)/placental growth factor (PIGF) ratio in the assessment of preeclampsia and in the differential diagnosis of patients with atypical presentations of preeclampsia, are not suited for simple, low-cost, and rapid routine clinical screenings due to financial and

practical concerns. Since CA-125 is a much more available and relatively less expensive test, it seems to be a promising biochemical marker for screening preeclampsia [15,16]. Further research is needed to explain the exact pathogenesis of elevated serum concentrations of CA-125 in women with preeclampsia and to clarify the clinical utility of CA-125 in preeclampsia.

REFERENCES

[1]. Deruelle P, Girard JM, Coutty N, Subtil D (2010) Prevention of preeclampsia. Ann Fr Anesth Reanim 29(3):e31–e35

[2] Gadducci A, Cosio S, Carpi A, Nicolini A, Genazzini AR (2004) Serum tumor markers in management of ovarian, endometrial and cervical cancer. Biomed Pharmacother 58:24–38

[3] Predanic M (2000) Differentiating tubal abortion from viable ectopic pregnancy with serum CA-125 and beta-human chorionic gonadotropin determinations. Fertil Steril 73:522–525

[4] Schro¨cksnadel H, Daxenbichler G, Artner E, Steckel-Berger G, Dapunt O (1993) Tumor markers in hypertensive disorders of pregnancy. Gynecol Obstet Invest 35(4):204–208

[5] de Groot CJ, O'Brien TJ, Taylor RN (1996) Biochemical evidence of impaired trophoblastic invasion of decidual stroma in women destined to have preeclampsia. Am J Obstet Gynecol 175(1):24–29

[6] Bon GG, Kenemans P, Verstraeten AA, Go S, Philipi PA, van Kamp GJ, van Geijn HP, van Vugt JM (2001) Maternal serum CA-125 and CA 15–3 antigen levels in normal and pathological pregnancy. Fetal Diagn Ther 16(3):166–172

[7] Cebesoy FB, Balat O, Dikensoy E, Kalayci H, Ibar Y (2009) CA-125 and CRP are elevated in preeclampsia. Hypertens Pregnancy 28(2):201–211

[8] National High Blood Pressure Education Program Working Group (2000) Report on high blood pressure in pregnancy. National Institutes of Health Publication No. 00–3029. National Institutes of Health, Washington, DC

[9] Lindheimer MD, Taler SJ, Cunningham FG (2010) Hypertension in pregnancy. J Am Soc Hypertens 4(2):68–78

[10] Verlohren S, Galindo A, Schlembach D, Zeisler H, Herraiz I, Moertl MG, Pape J, Dudenhausen JW, Denk B, Stepan H (2010) An automated method for the determination of the sFlt-1/PIGF ratio in the assessment of preeclampsia. Am J Obstet Gynecol 202(2):161.e1–161.e11

[11] Hirashima C, Ohkuchi A, Arai F, Takahashi K, Suzuki H, Watanabe T, Kario K, Matsubara S, Suzuki M (2005) Establishing reference values for both total soluble Fms-like tyrosine kinase 1 and free placental growth factor in pregnant women. Hypertens Res 28(9):727

[12] Verlohren S, Galindo A, Schlembach D, Zeisler H, Herraiz I, Moertl MG, Pape J, Dudenhausen JW, Denk B, Stepan H (2010) An automated method for the determination of the sFlt-1/PIGF ratio in the assessment of preeclampsia. Am J Obstet Gynecol 202(2):161.e1–161.e11

[13] Malatyalioglu E, Ozer S, Kokcu A, Cetinkaya MB, Alper T (2006) CA-125 levels in ruptured and unruptured tubal ectopic pregnancies. J Obstet Gynaecol Res 32(4):422–427

[14] Schmidt T, Rein DT, Foth D (2001) Prognostic value of repeated serum CA 125 measurements in first trimester pregnancy. Eur J Obstet Gynecol Reprod Biol 97:168–173

[15] .Verlohren S, Galindo A, Schlembach D, Zeisler H, Herraiz I, Moertl MG, Pape J, Dudenhausen JW, Denk B, Stepan H (2010) An automated method for the determination of the sFlt-1/PIGF ratio in the assessment of preeclampsia. Am J Obstet Gynecol 202(2):161.e1–161.e11

[16] Hirashima C, Ohkuchi A, Arai F, Takahashi K, Suzuki H, Watanabe T, Kario K, Matsubara S, Suzuki M (2005) Establishing reference values for both total soluble Fms-like tyrosine kinase 1 and free placental growth factor in pregnant women. Hypertens Res 28(9):727–732