ROLE OF Ca-125 LEVEL AS A MARKER OF SEVERITY OF PRE-ECLAMPSIA

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ABSTRACT

Background:Pre-eclampsia is an idiopathic hypertensive disorder of pregnancy, it seems that failure of trophoblast invasion and induction of placental inflammation lead to the production of CA-125 , hence can be used for identification of pre-eclampsia.
Objectives: This study aims at measuring maternal serum CA-125 with the possibility of being used in early diagnosis of sever preeclampsia so it maybe used as a marker of the severity of the disease.
Methods: This case control study was conducted at Duhok Obstetric and Gynecology teaching hospital during the period between January 2023 and September 2023 . The study involved a 100 pregnant women, 50 normotensive patients (control group), and 50 pregnant women with pregnancy induced hypertention who were further subdivided to 3 subgruops , (n = 20) were PIH , (n = 20) were none sever pre-eclampsia , (n = 10)were severe pre eclampsia subgroup. All were tested for serum CA125 along with the clinical and biochemical parameters for evaluating pregnant women whose pregnancies were complicated by hypertension.
Results:. The mean level of CA-125 among the studied groups was statistically significant (p=0.000), the mean CA-125 in normotensive women was
(19.02±6.259) and in and in gestational hypertension (24.24±10.863), non-severe (33.96

±12.460) and in severe (62.89±16.011) .The mean of CA-125 was increasing with increasing of the severity of Pre-eclampsia.

Statistically significant positive correlation was found between CA-125 levels with MAP values (p = 0.000), a statistically significant negative correlation was found between CA-125 levels with platelet count and gestational age at time of termination and birth weight. CA-125 level at termination had the highest sensitivity and specificity for prediction of sever Pre-eclampsia with a cutoff of 41.72 U/mL.
Conclusions: The concentration of serum CA -125, is increased in preeclampsia and this was directly correlated with the severity of preeclampsia. **Keywords:** Pre-eclampsia , CA-125 , hypertensive disorder of pregnancy

INTRODUCTION

Hypertension complicates 6–12% of all pregnancies (1), and involves two relatively benign conditions (chronic and gestational hypertension) and the more severe conditions of preeclampsia or eclampsia. Maternal mortality remains significant, particularly in less-developed countries, accounting for 18% of all maternal deaths worldwide (2). Pre-eclampsia complicates 3–5% of all pregnancies, and is characterized by placental and maternal vascular dysfunction that may lead to adverse outcomes such as severe hypertension, stroke, seizure (eclampsia), renal and hepatic injury, haemorrhage, fetal growth restriction, or even death (3). CA-125, or MUC 16, is a large transmembrane glycoprotein part

of the mucin family , The subclass of membrane-associated mucins (MAMs). They are glycosylated in specific manners and exhibit functions dependent on the tissue in which they are located (4). elevated levels in maternal serum originate from decidual cells affected by chorionic invasion or placental separation .The extension of decidual destruction and separation of trophoblasts from deciduas are proposed as the underlying mechanism for elevation in serum (CA-125) in preeclampsia (5, 6). There are few clinical studies related to the use of CA-125 in hypertensive disorders of pregnancy with conflicting results (7). However, some studies reported positive correlations between serum CA-125 concentration and preeclampsia (8–11). Pre-eclampsia is traditionally defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg, associated with de novo proteinuria above a threshold of 300 mg/24 h or above a urinary protein/urine creatinine ratio ≥ 0.3 mg/mg. This subtype of HDP has been associated with an increased risk for adverse maternal and fetal outcomes compared with other subtypes (12). Gestational hypertension is defined as new hypertension (blood pressure ≥140/90) without significant proteinuria(13). The American College of Gynecologists and Obstetricians (ACOG) and the International Society for the Study of Hypertension in Pregnancy (ISSHP) define the mild preeclampsia as gestational hypertension of at least 140/90 mmHg on two separate occasions ≥4 hours apart accompanied by significant proteinuria of >30 mgs/mmol, arising de novo after the 20th week of gestation in a previously normotensive woman and resolving completely by the 6th postpartum week(14).

While the severe PE was defined as the presence of new onset of hypertension ≥160/110 mmHg occurs after 20 weeks' gestation (in a woman who had normal blood pressure before 20 weeks' gestation) or superimposed on pre-existing hypertension and one or more of the following:

1. proteinuria – spot urine protein:creatinine ratio ≥30 mg/mmol or ≥2+ on

dipstick testing confirmed by a protein creatinine ratio test

2. other maternal organ dysfunction:

– renal insufficiency (creatinine >90 μmol/L, urine output of <80mL/4hr)

– liver involvement – elevated transaminases (ALT & AST) – at least twice upper limit of normal (right upper quadrant or epigastric abdominal pain). Note normal ranges are:

ALT 0-30 u/L and AST 10-50 u/L

— neurological complications (eg, eclampsia, altered mental status, blindness, stroke or, more

commonly, hyperreflexia when accompanied by clonus, severe headaches and persistent visual scotomata)

— haematological complications (thrombocytopenia – platelet count below 100 x 109/L, haemolysis)

3. uteroplacental dysfunction (fetal growth restriction).(15, 16).

Cancer antigen 125 (CA-125) is a biomarker usually expressed at the atypical surface of the coelomic epithelium. It is high molecular weight mucin-like glycoprotein. This antigen appears in 80% of ovarian epithelial carcinomas and non-malignant pelvic conditions such as endometriosis, fibroids, pregnancy and pelvic inflammation, liver disease, kidney failure, and lung, colon, breast, and adenomyosis cancers (17,18). However there are many sources for CA125 during pregnancy such as fetal chorion, maternal decidua and amniotic are potential sources of high serum CA-125 levels in the first trimester of pregnancy due to damage in decidual cells duringchorionic villus invasion in this stage and duringthe separation of placenta at birth in the postpartum period, the dynamics of serum CA-125 levels in the perinatal period still need to be explained (33).

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 (19).Theories suggest a possible role in preeclampsia through the immunohistochemically proven presence of this marker in fetal tissues (pleura, peritoneum, and pericardium) and decidual tissue (20,21). Identifying a marker with a good predictive value for the severity of preeclampsia would allow for better selection of patients with severe pre-eclampsia and provide better management and timely interventions for the sake of the mother as well as the fetus. Moreover, it is a simple and affordable investigation, and it would allow better management of pre-eclampsia in limited resource settings. The current study was conducted to see whether this marker has role as a severity marker and whether it can be used to improve pre-eclampsia management allowing a better selection of high-risk patients, aiding in decision making related to hospitalization and/or timing of birth.

Patients and Methods

Study Design, Setting, and Data Collection Time:

This study was a case control study conducted at Duhok Obstetrics & Gynecology teaching Hospital in Duhok city, Kurdistan region , Iraq during the period between January 2023 and september 2023. After Ethical approval obtained from Scientific Council of Obstetrics& Gynecology / Iraqi Board For Medical Specializations and from the scientific committee of the Directorate of general of health／Duhok . Verbal consent was obtained from the patient before enrollment.

The study involved a 100 pregnant women, 50 were normotensive patients (control group), and 50 pregnant women with PIH(case group) , which was further subdivided to GH (20) and none sever PE (20) and sever PE (10)all tested for serum CA125.

Definition of cases :

Mild PE: Was defined as gestational hypertension of at least 140/90 mmHg on two separate occasions ≥4 hours apart accompanied by significant proteinuria of

normotensive woman and resolving completely by the 6th postpartum week according to the American College of Gynecologists and Obstetricians (ACOG) and the International Society for the Study of Hypertension in Pregnancy (ISSHP) (14).

Severe PE: was defined as the presence of new onset of hypertension ≥ 160/110 mmHg occurs after 20 weeks' gestation (in a woman who had normal blood pressure before 20 weeks' gestation) or superimposed on pre-existing hypertension and one or more of the following:

1. proteinuria – spot urine protein:creatinine ratio ≥30 mg/mmol or ≥2+ on dipstick testing confirmed by a protein creatinine ratio test
2. other maternal organ dysfunction:

– renal insufficiency (creatinine >90 μmol/L, urine output of <80mL/4hr)

– liver involvement – elevated transaminases (ALT & AST) – at least twice upper limit of normal (right upper quadrant or epigastric abdominal pain).

Note normal ranges are:

ALT 0-30 u/L and AST 10-50 u/L

— neurological complications (eg, eclampsia, altered mental status, blindness, stroke or, more

commonly, hyperreflexia when accompanied by clonus, severe headaches and persistent visual scotomata)

— haematological complications (thrombocytopenia – platelet count below 100 x 10^9/L, haemolysis)

3. uteroplacental dysfunction (fetal growth restriction) (15, 16).

Control group included : Any pregnant normotensive woman who was admitted to labor ward and accepted to participate in the research. **Inclusions Criteria included :** Pregnant women aged between 18-45 yrs. , Pregnant women admitted to labor ward and ended with vaginal or Cesarean delivery , Pregnant women with confirmed proteinuria and high blood pressure and other

biochemical and clinical markers consistent with HDP .**Exclusions Criteria included:** a history of chronic hypertension, renal or hepatic disease, diabetes mellitus, known gynecologic pathology (ovarian or uterine disease), multiple pregnancies, known fetal anomalies. pregnancies achieved by ART and Patients refusal of enrollment.

No patient preparation is needed prior to the collection of the sample , nearly 3cc of blood was drawn from the patients through Venipuncture and collected into a Yellow Cap Vacuum Gel And Clot Activator Blood Collection Tube The American Association for Clinical Chemistry (AACC) recommends analyzing serum shortly after centrifugation of the obtained blood specimen. The serum specimen can then be stored at either 4°C (1-5 days) or -20°C (2 weeks to 3 months) in the short term or -70°C in the long term to ensure stability (22). In this study the blood was taken directly for the test but if it was not possible the sample was stored for 1-5 days and then transported to the laboratory and the samples were measured using the ECLIA method (electro chemiluminescent immunoassay).

The reference range of CA 125 is 0-35 units/mL (0-35 kU/L).
The cutoff of 35 kU/L for CA 125 was determined from the distribution of values in healthy individuals to include 99% of the normal population (23).

Statistical analysis :The data collected during the study were summarized in sheets of Microsoft Excel 2010. The statistical analysis performed by using IBM-SPSS 26. The means and standard deviations for the studied parameters were calculated. One-Way ANOVA was done to calculate the difference among more than three groups and the post Hoc test was done afterward for the significant ANOVA test. The t-test for independent two means was used. ROC test was done to determine the area under the curve, sensitivity, specificity, positive and negative predictive values for CA-125. P-value ≤ 0.05 considered as significant.

RESULTS:

This study included 100 women admitted to DMH. The comparison of the studied parameters among the studied group (PMH, PDH ,ANC , NICU admission , mode of delivery)was demonstrated in table (1) and showed that only 15.0% and 40.0% of the women with gestational hypertension and severe PE respectively reported previous history of PE while 60.0% of the mild PE reported such history; the difference was statistically significant (p=0.014). Regarding NICU admission 50% in severe PE group were admitted as opposed to 10% and 15% in GH and mild group respectively, the difference was statistically significant (p=0.03).

		GH (n = 20)	**mild PE (n=20)**	**Severe PE (n=10)**	**p-value***
		No. (%)	No. (%)	No. (%)	
History of PE	Yes				
	No				
Dexamethasone	Yes				
	No				
Aspirin	Yes				

	No	*16(80.0)*	*13(65.0)*	*8(80.0)*	
ANC	*Yes*	*14(70.0)*	*13(65.0)*	*7(70.0)*	*1.000*
	No	*6(30.0)*	*7(35.0)*	*3(30.0)*	
Admission to NICU	*Yes*	*2(10.0)*	*3(15.0)*	*5(50.0)*	***0.033***
	No	*18(90.0)*	*17(85.0)*	*5(50.0)*	
Mode of delivery	*Vaginal*	*8(40.0)*	*10(50.0)*	*4(40.0)*	*0.845*
	AVD	*2(10.0)*	*2(10.0)*	*0(0.0)*	
	CS	*9(50.0)*	*8(40.0)*	*6(60.0)*	
Anti HT	*Yes*	*19(95.0)*	*19(95.0)*	*10(100.0)*	*1.000*
	No	*1(5.0)*	*1(5.0)*	*0(0.0)*	
	Yes	*0(0.0)*	*2(10.0)*	*0(0.0)*	

LMWH	*No*	*20(100.0)*	*18(90.0)*	*10(100.0)*	*0.347*

**Freeman-Halton Exact test*

The comparison of the study characteristics including age, parity, gestational at birth, and birth weight among the studied groups was demonstrated in table 3.1 which showed the means of maternal age and parity were lower in the normotensive group (27.64±5.885) and (1.66±1.349) respectively, while the mean gestational age was higher in the normotensive group (38.14±1.690) in comparison to the cases groups but with no statistically significant differences. The study also showed a statistically significant difference concerning the birth weight (p=0.000) and showed that the mean birth weight for neonates of the normotensive women (3282.8±539.784 g) by using post hoc test was significantly higher than those among the gestational hypertension (2942.5±370.374 g), mild PE (2936.0±347.129 g), and severe PE (2565.0±248.383 g) with no significant differences among the cases groups themselves.

	Normotensive (n = 50)	***GH (n = 20)***	***mild PE (n = 20)***	***Severe PE (n = 10)***	***p-value****
	Mean ±SD	*Mean ±SD*	*Mean ±SD*	*Mean ±SD*	
Age	*27.64±5.885*	*30.30±7.854*	*29.10±6.632*	*28.10±7.578*	*0.476*
Parity	*1.66±1.349*	*2.00±1.589*	*1.80±1.765*	*1.70±2.162*	*0.875*
GA at birth (weeks)	*38.14±1.690*	*37.60±1.957*	*37.95±1.877*	*36.80±1.751*	*0.165*
Birth weight (grams)	*3282.8±539.784 A*	*2942.5±370.374 B*	*2936.0±347.129 B*	*2565.0±248.383 B*	***0.000***

**One-Way ANOVA with post hoc test; same letters mean no significance while different letters mean significant difference*

Comparison of the measurements and investigations among the studied groups was demonstrated in table 3.2. This table elicited that the mean MAP (95.82±13.137)

was statistically lower tin the normotensive group in comparing to the remaining cases groups (p=0.000).

The mean platelet count among the women with severe PE (154.80±93.542) was statistically lower than those of the cases groups and normotensive group (p=0.000).

Regarding S. uric acid, SGOT, and SGPT, the women in the normotensive group had the lowest level with the highest levels in the severe PE; the differences were statistically significant.

The mean level of CA-125 among the studied groups was statistically significant (p=0.000), the post hoc test showed that the real differences were between normotensive women (19.02±6.259) and women with PE whether non-severe (33.96±12.460) or severe (62.89±16.011) but not with women with gestational hypertension (24.24±10.863).

Albumin in urine among the severe PE was significantly higher than that in mild PE while no significant difference was found between these two groups concerning protein-creatinine ratio.

BMI, Hb, blood urea, s. creatinine showed no significant statistical differences.

Table 3.3: Comparison of the measurements and investigations among the studied groups.

	Normotensive (n = 50)	**GH (n = 20)**	**mild PE (n = 20)**	**Severe PE (n = 10)**	**p-value**
	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD	
MAP	95.82 ±13.137 A	113.58 ±5.678 B	117.47 ±7.286 C	131.95 ±8.749 D	**0.000***
BMI	25.80±4.150	24.25±4.216	25.75±4.399	25.30±4.522	0.566*
HB	10.71±1.396	11.08±1.346	11.04±1.422	11.14±1.309	0.635*
Platelet count	292.5 ±87.216 A	321.1 ±108.436 A	272.0 ±76.211 A	154.80±93.542 B	**0.000***
S uric acid	3.91 ±0.964 A	4.67 ±1.050 B	5.29 ±1.173 BC	6.19 ±1.153 CD	**0.000***
Blood urea	18.28±6.104	18.51±4.060	19.69±4.137	22.97±7.722	0.105*
S creatinine	0.523±0.306	0.536±0.235	0.618±0.236	0.545±0.264	0.630*
Albumin in urine	------	------	1.95±0.223	2.60±0.516	**0.000****
SGPT	16.62 ±6.104 A	26.50 ±11.00 A	22.75 ±7.832 A	91.50 ±99.052 B	**0.000***
SGOT	14.02 ±5.804 A	26.45 ±10.128 A	21.26 ±8.271 A	71.0 ±64.296 B	**0.000***
Protein creatinine ratio	------	------	0.820±0.447	0.820±0.358	1.000**
S ca125	19.02 ±6.259 A	24.24 ±10.863 A	33.96 ±12.460 B	62.89 ±16.011 C	**0.000***

*One-Way ANOVA with post hoc test; same letters mean no significance while different letters mean significant difference

**t-test for independent two means.

Statistical significance of CA-125 levels between study subgroups was evaluated by using Tukey post hoc test which showed that the association between each two group was statistically significant (p=0.000) except between normotensive group and gestational hypertension group (p=0.198) as demonstrated in table 3.4.

Table 3.4: Statistical significance of CA-125 UI/mL levels between

Studied groups	***Significance***	***GH***	***mild PE***	***Severe PE***	***Normotensive***
GH	*p-value*	—	*0.013*	*0.000*	*0.198*
Non-Severe PE	*p-value*		—	*0.000*	*0.000*
Severe PE	*p-value*			—	*0.000*
Normotensive	*p-value*				—

*The correlations of the CA-125 mean levels with clinical–biological parameters was demonstrated in table 3.5 by using **Pearsons's Correlation Coefficient (r)** which revealed significant direct correlations with MAP(0.606), S.uric acid (0.394), SGOT(0.503) , SGPT(0.458) and albumin in urine (0.608) and indirect correlations with platelet count (-0.327) , gestational age (-0.258) , and birth*

weight(-0.329) , while no significant correlations were found with S. creatinine and protein-creatinine ratio.

Table 3.5: CA-125 levels' correlations with clinical–biological parameters.

Parameter	***Pearsons's Correlation Coefficient (r)***	***p-Value***
MAP	*0.606*	***0.000***
Platelets count	*-0.327*	***0.001***
S Uric Acid	*0.394*	***0.000***
SGPT (mg/dL)	*0.458*	***0.000***
SGOT(mg/dL)	*0.503*	***0.000***
Creatinine (mg/dL)	*0.031*	*0.758*
Protein–Creatinine Ratio	*0.163*	*0.388*
Gestational age at birth	*-0.258*	***0.010***
Birth weight	*-0.329*	***0.001***
Albumin in Urine	*0.608*	***0.000***

The ROC test to estimate the critical area under the curve for the CA-125 was demonstrated in table 3.5 and figure 3.1. This table revealed significant association for this indicator with the severity of the PE with area under the curve was (0.984).

Table 3.6: ROC test and area Under the Curve for the validity of serum Ca 125 test.

Area	Std. Error[a]	p-value[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.940	0.043	**0.000**	0.856	1.000

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

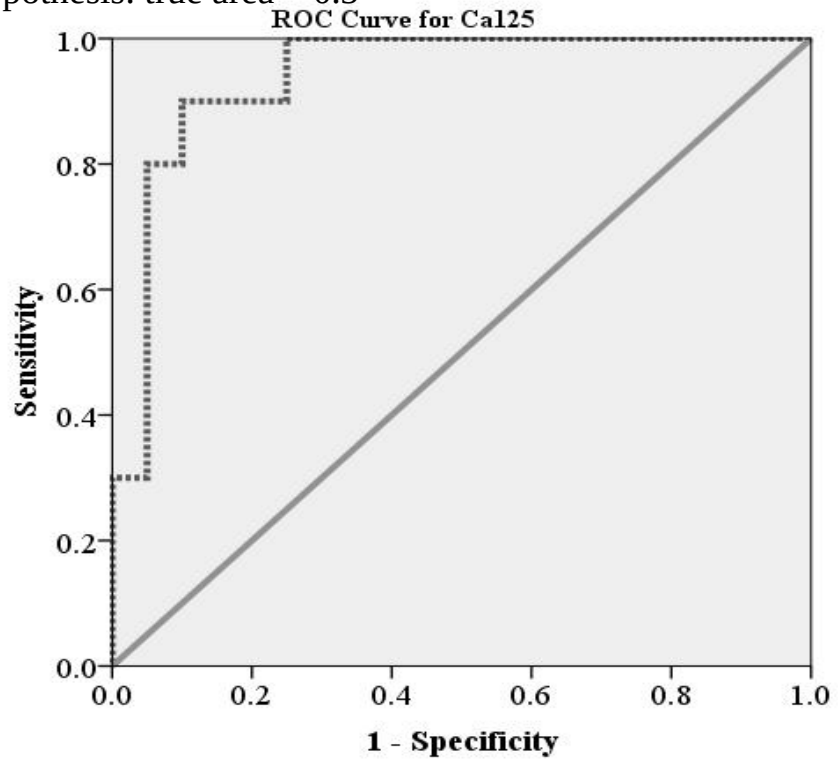

Figure 2 : ROC test and area Under the Curve for the validity of serum Ca 125 test.

The ROC test to estimate the critical area under the curve for the CA-125 and S.uric acid was demonstrated in table 3.5 and figure 3.1. This table revealed significant association for the Ca 125 with the severity of the PE with area under the curve was (0.940) while the area of the S.uric acid was lower (0.685) and not significant.

Table 3.7: ROC test and area Under the Curve for the validity of serum Ca 125 and S.uric acid tests.

Test	*Area*	*Std. Error*[a]	*p-value*[b]	*Asymptotic 95% Confidence Interval*	
				Lower Bound	*Upper Bound*
Ca 125	*0.940*	*0.043*	***0.000***	*0.856*	*1.000*
S. uric acid	*0.685*	*0.102*	*0.104*	*0.486*	*0.884*

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

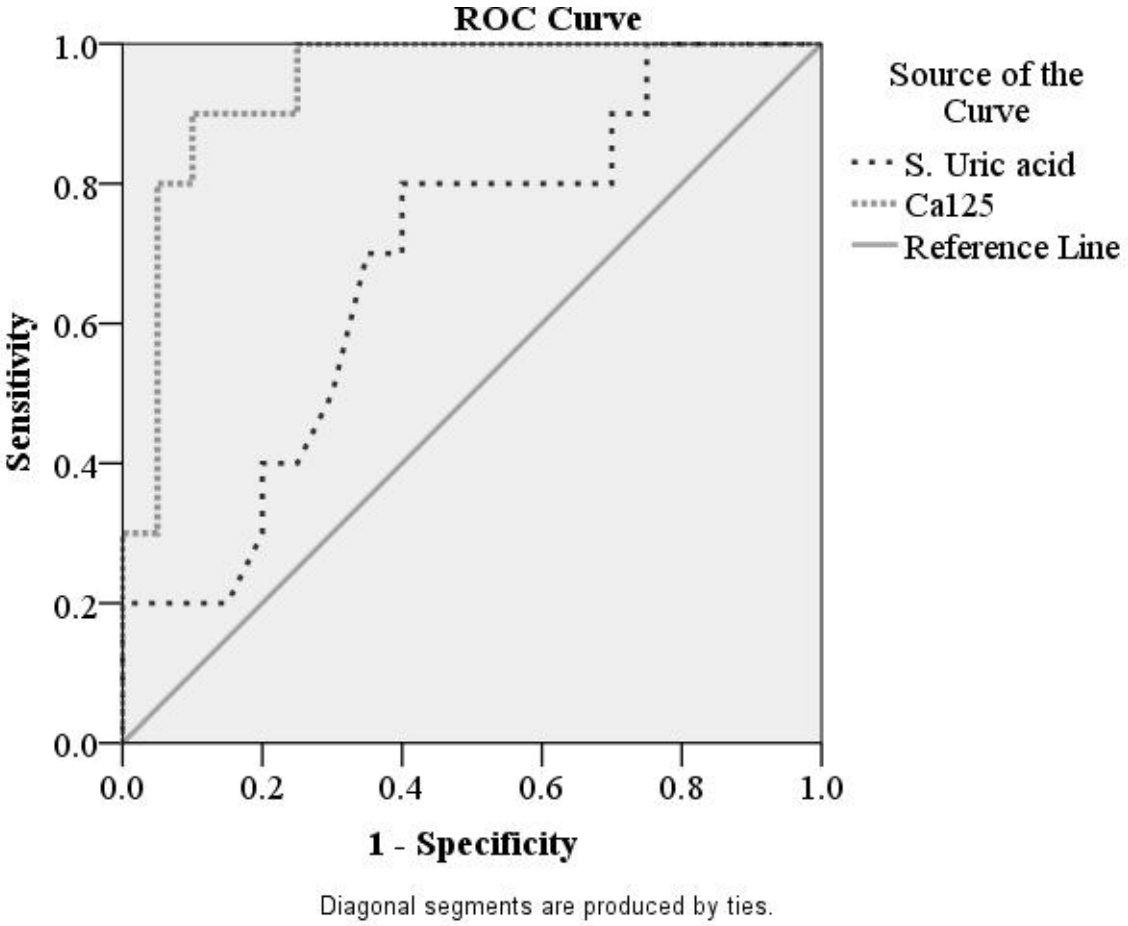

Figure 3: ROC test and area Under the Curve for the validity of serum Ca 125 and S.uric acid tests.

The cut-off points with sensitivity, specificity, PPV, and NPV were demonstrated in table 3.6 and showed that the optimal cut-off point was 41.72

mUI/mL ***Table 3.8: cut-off points for serum Ca 125 test***

Positive if Greater Than or Equal To[a]	Sensitivity%	Specificity%	PPV%	NPV%
14.66	100.0	0.0	50.0	------
18.18	100.0	5.0	51.3	100.0
20.79	100.0	10.0	52.6	100.0
21.12	100.0	15.0	54.1	100.0
21.67	100.0	20.0	55.6	100.0
24.51	100.0	25.0	57.1	100.0
27.94	100.0	30.0	58.8	100.0
29.23	100.0	35.0	60.6	100.0
30.52	100.0	40.0	62.5	100.0
31.57	100.0	45.0	64.5	100.0
33.41	100.0	50.0	66.7	100.0
35.53	100.0	55.0	69.0	100.0
36.44	100.0	60.0	71.4	100.0
37.80	100.0	65.0	74.1	100.0
38.76	100.0	70.0	76.9	100.0
39.17	100.0	75.0	80.0	100.0
39.65	90.0	75.0	78.3	88.2
39.94	90.0	80.0	81.8	88.9
41.72	90.0	90.0	90.0	90.0
45.58	80.0	90.0	88.9	81.8
51.880	80.0	95.0	94.1	82.6
53.97	70.0	95.0	93.3	76.0
56.95	60.0	95.0	92.3	70.4
60.17	50.0	95.0	90.9	65.5

63.12	40.0	95.0	88.9	61.3
68.18	30.0	95.0	85.7	57.6

71.78	*30.0*	*100.0*	*100.0*	*58.8*
78.41	*20.0*	*100.0*	*100.0*	*55.6*
87.75	*10.0*	*100.0*	*100.0*	*52.6*
92.20	*0.0*	*100.0*	*100.0*	------

The cut-off points with sensitivity, specificity, PPV, and NPV were demonstrated in table 3.7 and showed that the optimal cut-off point was 5.25 mUI/mL . ***Discussion :***

Hypertensive disorder during pregnancy have a substantial threat to both maternal and fetal health conditions (24). Preeclampsia is one of the most well-known medical conditions that belong to this disease spectrum, which also accounts for one of the most common documented gestational complications, with a prevalence of approximately 2 to 15% of all pregnancies (25,26). The exact cause of PE is unknown however; the basic pathology is endothelial dysfunction and intense vasospasm (27).The current study found no statistically significant differences among the normotensive group and the three gestational hypertensive , mild and sever preeclampsia regarding materanal age , parity and gestational age at birth, However the means of maternal age and parity were lower in the normotensive group, while the mean gestational age was higher in the normotensive group , these results coincide with the results of Thuria Ahmed et al (28) prospective case control study at Suez canal university hospitals in Egypt regarding maternal age between normotensive and mild PE and sever PE but it contradicts it in showing statically difference among the above mentioned groups regarding gestational age at birth these finding was confirmed by Danisman and Rousso 2011 (29) which also revealed statistically difference among the groups regarding gestational age which can be attributed to preterm delivery of the fetuses in preeclampsia with increasing severity of the disease.

. The study also showed a statistically significant difference concerning the birth weight (p=0.000) and showed that the mean birth weight for neonates of the normotensive women was significantly higher than those among the gestational

hypertension , mild PE , and severe PE , with no significant differences among the cases groups themselves. In our study the mean serum concentration of CA-125 was (19.02±6.259),(24.24±10.863),(33.96±12.460) , (62.89 ±16.011) in normotensive , geatational hypertensive , mild and sever PE respectively which indicates that serum CA125 level increase with increasing severity of preclampsia this was in agreement withThuria Ahmed et al (2019) in which the mean serum concentration of CA-125 was (32.59±1.6) , (39.70 ±1.19)., (52.92±2.88) in control mild and sever PE , also the same conclusion was reached by Karamanand Ark (2013) (30) . and the results of Geya Gottipati et al (31) 2019 a cross-sectional study was conducted at a Tertiary Care Hospital, Mangaluru, India. In which the mean serum concentration of CA-125 was (14.7±8.4) , (56.6±88.2)., in GH and sever preeclampsia group respectively.

This increase may be related to impaired placentation which causes intermittent disruption of placental perfusion , oxidative stress and systemic inflammatory response which worsens with the severity of preeclampsia. This is inturn favors the hypothesis that increasing severity of the disease leads to increased release of CA-125 . There was a slight deference in the Mean value of CA-125 in the preeclampsia group in the present study was 62.89 IU/mL which was near the results of Bhattacharya and Saha (58.5 IU/mL) (32), whereas value was slightly higher when compared to Karaman et al. (38.8 IU/mL) (33)and Hassan et al. (38.04 IU/mL) (34). This difference can be the result of wide difference in the standard deviation obtained in our study as much higher values of CA-125 were observed in a few patients with severe

form of PE resulting in higher mean values compared to other two above-mentioned studies. Furthermore, in the present study, the results showed that the mean

CA-125 had a significant difference in women of the control group compared with mild preeclampsia (p= 000), which was similar to the results of other studies (35,36,37). Only in the study conducted by Karaman et al., no significant difference was reported between the two groups of control and mild preeclampsia (33) and this could be due to genetic differences in the studied populations in recent studies compared to the presentstudy, or the lack of control of confounders and also the method of conducting the study.

The study also concluded that ; The mean level of CA-125 among the studied groups was statistically significant (p=0.000) and the real differences were between normotensive women and women with PE whether non-severe or severe but not with women with gestational hypertension. This is in concordant with that revealed by WasanW.Ibrahem et al (37)

A prospective case-control study which was carried out in the department of gynecology and obstetric at Baghdad teaching hospital in 2015 which showed statistically significant differences between control and mild preeclamptic group (p value < 0.0001) and between mild and severe preeclamptic group (p value < 0.0001). Which is also mentioned by Ozatet al, 2010 study done in Turkey, in which they found that the CA125 is biochemical marker that reflects the severity of the underlying inflammation processes in PE in third trimester (38). Also same results obtained by Dr. Miami Abdul Hassan Ali et al (39) A case control study was carried out in the department of gynecology and obstetrics at Al-Yarmouk teaching hospital (Baghdad\Iraq) in which it showed that CA-125level was significantly higher in preeclampsia and eclampsia than control group as the P value was (0.0001).

The results of the different mentioned studies earlier contradicts the results of Bon et.al 2001(40) who assessed CA125 and CA15-3 and compared their levels in women with a normal pregnancy outcome and pathological pregnancies including PE, they found that maternal serum levels of CA125 & CA15-3 were significantly higher in the first and the third trimester of pregnancy, but no significant difference found in normal pregnancy from that obtained in pathological one including PE patients but this finding might probably be due to different timing of measurement during pregnancy in their study (first & third trimesters) while the other studies where taken after 24 weeks gestational age that's to say patients in late second and third trimester.

In the current study A cut-off value was calculated using the receiver operating characteristics (ROC)Curve which was (0.685). The best cut off value for severe pre-eclampsia, with a sensitivity of 90.0% and specificity of 90.0%, was a CA-125 of 41.72 U/mL. This level was associated with a negative predictive value (NPV) of 90.0%.

The our study compared ca125 with s. uric acid which revealed significant association for the Ca 125 with the severity of the PE with area under the curve was (0.940) with confidence interval upper limit equal to 1.000 which indicates best accuracy and more have more value for prediction of the disease while the area of the S.uric acid was lower (0.685) and not significant with confidence interval upper limit equal to 0.884. the best value of serum uric acid for the diagnosis of severe preeclampsia was 5.2500 with a lower sensitivity of 80% and a specificity of 60% than that of serum ca125 concentration.

Conclusion :

The concentration of serum Cancer antigen -125, is increas in preeclampsia and there is a wide difference between gestational HTN , mild and severe form PE being more increased in sever form of the disease.

There was a correlation between increase serum
CA125 with adverse fetal perinatal outcome in severe cases of pre-eclmpsia but further studied are needed to confirm this correlation.

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