

## The Association of Serum Cancer Antigen 125 and C - reactive protein Level with The Severity of Preeclampsia.

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### Abstract

**Background:** It has been assumed that the failure in trophoblastic invasion and the induction of an inflammatory process within placenta in patients with preeclampsia may trigger the expression of Cancer antigen 125. C-reactive protein is a marker of tissue damage and inflammation; increased C-reactive protein may reflect endothelial cell dysfunction in preeclampsia and may be a potential marker of preeclampsia.

**Objectives:** To evaluate the association of serum Cancer antigen 125 and C-reactive protein level with the severity of preeclampsia. .

**Patients & methods:** A case control study was carried out in the department of gynecology and obstetrics at Al-Yarmouk teaching hospital (Baghdad\Iraq) for one year from April 2010 to March 2011. Hundred singleton pregnant women were divided into fifty patients with preeclampsia and fifty healthy pregnant women as control group. Blood samples were taken for measurement of serum cancer antigen-125 and C-reactive protein for both groups.

**Results :**The mean level of cancer antigen-125 in mild, severe preeclampsia and eclampsia groups was  $32.57\pm 8.08$ (IU/ml),  $38.04\pm 9.44$ (IU/ml) and  $47.60\pm 12.09$ (IU/ml) respectively which was significantly higher in comparison to the control group (sampled at the same time) which was  $13.70\pm 8.44$ (IU/ml) the P value was (0.0001). The mean level of c-reactive protein in mild, severe preeclampsia & eclampsia was  $15.80\pm 6.69$ (mg/L),  $30.64\pm 15.66$ (mg/L) and  $42.60\pm 13.70$ (mg/L) which was significantly higher in comparison to the control group which was  $7.92\pm 4.05$ (mg/L) the P value was( 0.0001).

**Conclusion:** Serum cancer antigen 125 and C - reactive protein were significantly higher in preeclampsia groups in comparison to the control group and the increment was directly correlated with the severity of preeclampsia.

**Keywords:** Cancer antigen 125, C-reactive protein, preeclampsia.

### Introduction

Preeclampsia is a disease of pregnancy associated with endothelial cell damage, systemic inflammatory process and hypercoagulation<sup>(1)</sup>. Elevated CA 125 levels in maternal serum originate from the decidual cells affected by chorionic invasion or placental separation<sup>(2)</sup>. The extension of decidual destruction and separation of trophoblasts from deciduas are proposed as the underlying mechanism for the elevation in the serum cancer antigen (CA-125) in preeclampsia<sup>(3)</sup>. In pregnancy systemic maternal inflammatory response to pregnancy is responsible for the endothelial dysfunction which

gives the clinical and pathological picture of preeclampsia<sup>(4)</sup>. Mediators of an inflammatory response is altered in women with preeclampsia, including increased C-reactive protein (CRP) which is a sensitive marker of tissue damage and inflammation<sup>(5)</sup> and is part of the acute phase immune response<sup>(6)</sup>. The association between first trimester C-reactive protein levels and subsequent preeclampsia supports the hypothesis that systemic inflammation is involved in the pathogenesis of preeclampsia & risk factors such as elevated CRP levels can also promote endothelial dysfunction by quenching the production of nitric oxide and diminishing its bioactivity<sup>(7)</sup>.

## Objectives

To measure the association of serum CA-125 and CRP level with the severity of preeclampsia.

## Patients & methods

A case control study was carried out in the department of **gynecology** and obstetrics at Al-Yarmouk teaching hospital (Baghdad\ Iraq) for one year from April 2010 to March 2011. Hundred singleton pregnant women were divided into two groups: Fifty women with preeclampsia and fifty control healthy pregnant women.

**The inclusion criteria:** Singleton pregnancy, gestational age 28-40 weeks relying on the date of the last menstrual period or early ultrasonography.

**Exclusion Criteria:** Diabetes, chronic hypertension, renal disease, cardiovascular disease, symptomatic infectious diseases, premature rupture of membranes or clinical chorioamnionitis, chronic inflammatory problems and ovarian diseases

**The Study groups:** included 50 pregnant women presented with pre-eclampsia selected randomly as:

First group: 15 patients with mild pre-eclampsia.

Second group: 25 patients with Severe pre-eclampsia.

Third group: 10 patients with eclampsia.

**The Control group:** included 50 singleton pregnant normotensive women who were attended to the antenatal care unit and selected according to inclusion criteria.

Method: Complete history and examination was done for all the patients

and investigations in form of: complete blood count, renal function, liver function, urine analysis, coagulation screen and ultrasound to assess the fetal condition. CA-125 was measured by enzyme - linked immunosorbent assay (ELISA) method using Bio check CA-125 Enzyme immunoassay kit, CRP level measurement was done by direct latex test

Blood pressure was measured by mercury sphygmomanometer in left lateral position, hypertension considered when systolic pressure more than 140mmHg or diastolic pressure more than 90mmHg, MAP (mean arterial pressure) was calculated using the following formula:  $MAP = (\text{systolic blood pressure} + 2 \times \text{diastolic blood pressure}) / 3$

**Statistical analysis:** Analysis of data was carried out using the available statistical package of SPSS-18 (Statistical Packages for Social Sciences- version 18 "PASW").

The significance of difference of independent means (quantitative data from different PE groups and from control group) was tested using analysis of variance (ANOVA) for more than two groups. Pearson correlation was calculated for the correlation between two quantitative variables with its t-test for testing the significance of correlation. Statistical significance was considered whenever the P value was less than 0.05.

## Results

In the current study, the two groups of patients (mild and severe preeclampsia) were of comparable maternal age and gestational age as shown in table 1.

**Table1** Distribution of maternal age and gestational age in both study & control groups :

	Control No.(50)	Mild PE No (15)	Severe PE No (25)	Eclampsia N0(10)	P value
Mother age (years) Mean±SD	29.40±6.04	28.07±4.42	26.96±5.36	28.80±6.34	0.368
Gestational age (weeks) Mean±SD	33.84±3.03	34.73±2.43	34.04±2.82	31.9±2.42	0.107

Significant difference among independent means using ANOVA test at 0.05 level of significance

The mean level of CRP in mild, severe PE & eclampsia was  $15.80 \pm 6.69$ ,  $30.64 \pm 15.66$  and  $42.60 \pm 13.70$  which was significantly higher in comparison to the control group which was  $7.92 \pm 4.05$  the P value was (0.0001).

The mean level of CA-125 in mild, severe PE and eclampsia group was  $32.57 \pm 8.08$ ,  $38.04 \pm 9.44$  and  $47.60 \pm 12.09$  respectively which was significantly

higher in comparison to the control group was  $13.70 \pm 8.44$  the P value was (0.0001).

The MAP in mild, severe PE and eclampsia was  $111.87 \pm 3.56$ ,  $144.04 \pm 13.34$ ,  $164.80 \pm 7.51$  respectively which was significantly higher in comparison to the control group was  $84.34 \pm 9.00$  the P value was (0.0001) as shown in table (2).

**Table 2:** CRP, CA-125 and MAP in both the study & the control groups

	Control no.50	Mild PE no.15.	Severe PE no. 25	Eclampsia no.10	
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	p value
CRP (mg/L)	$7.92 \pm 4.05$	$15.80 \pm 6.69$	$30.64 \pm 15.66$	$42.60 \pm 13.70$	0.0001*
CA-125 (IU/ml)	$13.70 \pm 8.44$	$32.57 \pm 8.08$	$38.04 \pm 9.44$	$47.60 \pm 12.09$	0.0001*
MAP (mmHg)	$84.34 \pm 9.00$	$111.87 \pm 3.56$	$144.04 \pm 13.34$	$164.80 \pm 7.51$	0.0001*

CA-125 level was significantly & directly correlated with CRP in mild, severe PE & eclampsia as the r value was (0.895\*\*,0.900\*\*and 0.959\*\*) respectively while in the control group the coefficient correlation was not significant & inverse correlated (the r value was -0.038) as shown in table (3).

According to the Pearson correlation test, MAP was found to have a significant direct correlation with CRP in mild, severe PE and eclampsia (the r value was 0.841\*\*, 0.884\*\* & 0.773\*\*) respectively while in the control group, it was not significant & inverse correlated (the r value was -0.266) as shown in figure no.(1). CA-125 level was significantly & directly correlated with MAP in mild, severe PE & eclampsia (the r value was 0.753\*, 0.738\*\*and 0.853\*\*) respectively, while for the control group the coefficient correlation was not significant & inverse correlated (the r value was -0.001) as shown in table (4) and figure no ( 2).

## Discussion

The current study showed that the level of CRP is higher in the PE groups in comparison to the control group and the correlation was direct and significant with severity of PE (the P value was 0.0001). Similarly Y. Ustun et al 2005<sup>(8)</sup> measured the level of plasma fibrinogen and CRP in 58 women with PE compared to 54 normotensive women, they found that the level of CRP was significantly higher in women with mild and severe preeclampsia than in normotensive women. And this result was reported by Cebesoy et al 2009<sup>(9)</sup>, who found that the CRP level was significantly higher in the study group compared to the control group. In contrast with Milan stefanović et al 2009<sup>(10)</sup> who studied the relationship between insulin resistance and C-reactive protein as a marker of inflammation in 17 pre-eclamptic women and compared to 20 normotensive women, they found no difference between pre-eclamptic and normotensive women with regard to the CRP concentration.

Table 3. Shows coefficient correlation(r) of CRP with CA-125 and MAP in comparison between PE and control groups.

	CRP (mg/L)			
	Control	Mild PE	Severe PE	Eclampsia
CA-125 (IU/ml)	-0.038	0.895**	0.900**	0.959**
MAP (mmHg)	0.266-	0.841**	0.884**	0.773**

\*. Correlation is significant at the 0.05 level (2-tailed).

\*\* . Correlation is significant at the 0.01 level (2-tailed).

The  $r < 0.5$  weak correlation,  $> 0.5$  mild strength,  $> 0.7$  strong correlation

The  $r +$  is direct correlation,  $-$  is inverse correlation. The Pearson correlation coefficient (r)

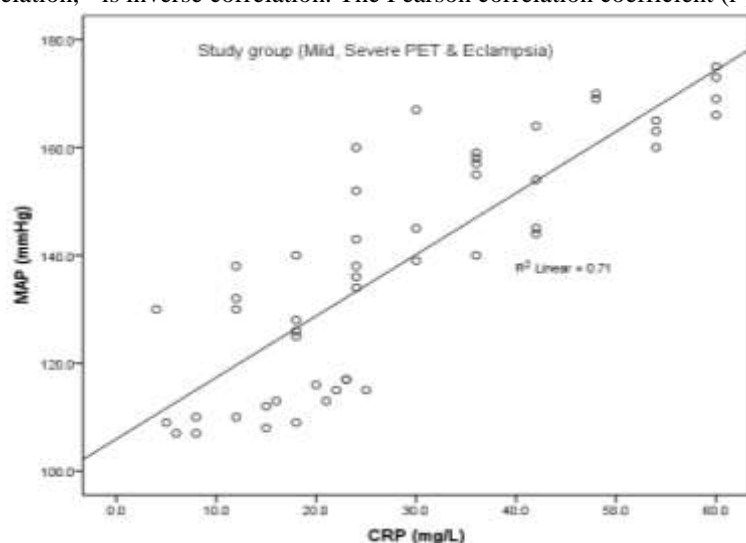


Figure 1: The correlation between CRP & MAP in the study groups & the control group

Table 4. The coefficient correlation(r) of CA-125 with MAP in comparison between PE & control groups

	CA-125 (IU/ml)			
	Control	Mild PE	Severe PE	Eclampsia
MAP (mmHg)	-0.001	0.753*	0.738**	0.853**

\*. Correlation is significant at the 0.05 level (2-tailed).

\*\* . Correlation is significant at the 0.01 level (2-tailed).

The  $r < 0.5$  weak correlation,  $> 0.5$  mild strength,  $> 0.7$  strong correlation

The  $r +$  is direct correlation,  $-$  is inverse correlation

The current study showed that CA-125 level was significantly higher in preeclampsia and eclampsia than control group as the P value was (0.0001). Cebesoy et al 2009 (9) reported the same result stated that the CA125 increases with severity of PE. These results also seen by Ozat et al 2010 (3), they found that the CA-125 is a biochemical marker which reflects the severity of the underlying inflammatory process in preeclampsia. While Bon et.al 2001(11) 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. This finding probably due to different timing of measurement during pregnancy in their study (first & third trimesters) while the current study done on patients in third trimester.

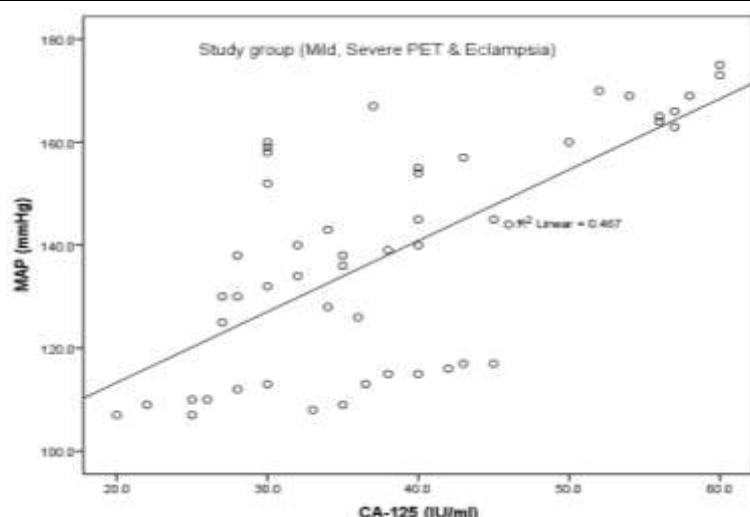


Figure 2: The correlation between CA-125& MAP in the study &control groups.

## Conclusion

Serum cancer antigen 125 and C - reactive protein were significantly higher in preeclampsia groups in comparison to the control group and the increment was directly correlated with the severity of preeclampsia.

## Recommendation

Further research is required to clarify the clinical utility of CA-125 and CRP as predictors' preeclampsia.

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