Serum procalcitonin and plasma D-Dimer evaluation in pregnancy Conjugate with pre-eclampsia mild & severe pre-eclampsia versus normal pregnancy

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Abstract

Pre- eclampsia is a common and heterogeneous syndrome of human pregnancy. Normal pregnancies are associated with inflammatory and hemostatic changes. The maternal syndrome of pre- eclampsia results from a systemic inflammatory response that involves the entire inflammatory network of the circulation, including the endothelium. Procalcitonin is an inflammatory marker which is raised in pre eclampsia .Normal pregnancy causes the maternal plasma D-Dimer level to increase progressively from conception until delivery .It is accepted that the hemostatic system is disturbed in pre eclamptic patients , but the effect or relationship with d dimer level and PET remains to elucidate .

Aim of this study was to evaluate serum procalcitonin (PCT) , and plasma D-Dimer levels in mild and severe pre-eclampsia.

Prospective case control study carried out in department of obstetrics and gynecology /Baghdad Teaching Hospital /Medical City /Baghdad /Iraq .

Serum procalcitonin (PCT), and D-Dimer levels were determination in 40 cases with pre-eclampsia as the study group and 40 healthy pregnant women in the third trimester as the control group. Pre-eclamptic group consisted of mild (n = 20) and severe pre-eclamptic subgroup (n = 20).

Laboratory results were compared between the groups and diagnostic usefulness of these parameters were evaluated.

Serum procalcitonin (PCT) PCT, and D-Dimer levels were significantly higher in study group than the control group (P <0.001). PCT, and D-Dimer were significantly higher in the patients with severe pre-eclampsia than mild VIII pre-eclampsia(p=0.012)There were significant positive correlations between these markers and mean arterial pressure (MAP). Logistic regression analysis using the control and pre-eclampsia group showed that higher PCT (OR,6.12; 95%-CI, 3.30-13.50), and D-Dimer levels (OR,4.41; 95%-CI,2.8-9.18)were found to be risk factors significantly associated with pre-eclampsia.

This study results confirm that evidence of a possible exaggerated systemic inflammatory response in pre eclampsia especially
in severe pre- eclampsia

تقييم مستوى البروكاليستونين في المصل وفي الدي – دايمر في البلازما في الحمل المقترن بمقدمات الارتعاج مقارنتها الحمل الطبيعي

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الخلاصة
ان مقدمة الارتعاج هي احدى المتلازمات الشائعة والمتغايرة من الحمل البشري . يترافق الحمل الطبيعي مع التغيرات الالتهابية المرقئة . تنتج متلازمة مقدمة الارتعاج الامومية عن الاستجابة الالتهابية المجموعة التي تضم الشبكة الالتهابية لجهاز الدوران باكملها وبضمنها بطانة الاوعية . يعتبر البروكالستونين احد الهلامات الواسمة الالتهابية التي يرتفع مستواها في حالة مقدمة الارتعاج . يعمل الحمل الطبيعي على زيادة مستوى دي دايمر في بلازما الام بشكل متصاعد منذ بدء الحمل وحتى الولادة . ان من المتفق عليه القول بان الجهاز المرقئ يضطرب لدى المرضى المصابيين بمقدمة الارتعاج ، ولكن يبقى تاثيره او علاقته بمستوى دي دايمر وبين (PET) مسالة تقضي التوضيح.
تهدف هذه الدراسة الى تقييم مستويات البروكالستونين ودي دايمر في حالات مقدمة الارتعاج البسيطة والشديدة .اجريت دراسة الحالة والشاهد والاستباقية في قسم التوليد والنسائية / مستشفى بغداد التعليمي /مدينة الطب /بغداد / العراق .
تم تحليل البروكالستونين في المصل ودي دايمر البلازما لدى 40 حالة مصابة بمقدمة الارتعاج واعتبرت كمجموعة الدراسة و40 حالة من السناء الحوامل السليمات في الثلث الاخير من الحمل واعتبرت كمجموعة ضابطة . تألفت مجموعة النساء المصابات بمقدمة الارتعاج من مجموعتين ثانويتين الاولى بسيطه وعددها 20 امرأة والثانية شديدة وعددها 20 امراة . تمت مقارنة النتائج المختبرية بين المجموعات وكذلك تقييم الفائدة التشخيصية لهذه الاختبارات .
كان مستوى كل من البروكالستونين ودي دايمر اعلى من مجموعة الدراسة بشكل ملحوظ من المجموعة الضابطة ($P< 0.001$) .كان مستوى البروكالستونين ودي دايمر اعلى في مجموعة المرضى شديدي الاصابة بشكل ملحوظ من مجموعة المرضى بسيطي الاصابة ($p< 0.012$) . وكانت هناك علاقات ايجابية مهمه بين هذه العلامات وبين متوسط الضغط الشرياني . اظهر تحليل الانحدار اللوجستي عند استخدام المجموعة الضابطة ومجموعة المصابات بمقدمة الارتعاج ان اعلى مستوى من البروكاليستونين وهي (OR,6.12; 95%-CI, 3.30-13.50) هي مستويات عوامل الاختطار المرتبطة الى حد كبير بمقدمة الارتعاج .
تؤكد نتائج هذة الدراسة على هناك دليل لوجود استجابة التهابية مجموعية مبالغ بها في حالات مقدمة الارتعاج وخاصة الشديدة منها .
مفتاح البحث : الارتعاج , البروكاليستونين, متوسط الضغط الشرياني

Introducation

Pre-eclampsia is a common and heterogeneous syndrome of human pregnancy . These changes constitute the maternal immune response. [1] Pre-eclampsia can develop in the presence of a normal placenta in woman who is susceptible to systemic inflammation , such as diabetes or chronic cardiovascular disease [2]Major cause of Pre-eclampsia is the failure to develop an adequate blood supply to the placenta , leading to placental oxidative stress and results in the excess release of the placental factors such as syncytiotrophoblast debris or soluble fms-like tyrosine kinase -1(sFl1-1) in to the maternal circulation.[3] . Procalcitonin is an inflammatory marker which is raised in Pre-eclampsia , It is the 116 aminoacid polypeptide precursor of calcitonin , which is a calcium regulatory hormone and as marker in bacterial infection and sepsis[4] . There are only a few published data on PCT in pregnancy , Although no clear biological role for PCT has been explained , it has been suggested that it plays an

important role in the pathogenesis of the sepsis and non-infectious systemic inflammation [5,6]. It is known that human pregnancy goes together with profound changes in the hemostatic system toward a procoagulant and hypofibrinolytic state.[7] Tissue type plasminogen activator cleaves fibrin to produce fibrin degradation products , usually assayed as cross linked fibrin fragments (D-Dimer) . Normal pregnancy causes the maternal plasma D-Dimer level to increase progressively from conception until delivery. [8] It is accepted that the hemostatic2 system is disturbed in Pre-eclamptic patients , but the effect or relationship with D-Dimer level and Pre-eclampsia remains to elucidate .The maternal syndrome of Pre-eclampsia results from a systemic inflammatory response that involves the entire inflammatory network of the circulation , including the endothelium . [9] The diagnosis of pre-eclampsia is based on traditional but somewhat unreliable and non-specific clinical markers such as blood pressure ,urine protein excretion , and symptoms . For example , more than 20% of women who have eclampsia will fail to meet the common diagnostic criteria of preeclampsia prior to their event , making the prediction of this adverse outcome extremely difficult .[10] Pre-eclampsia is new hypertension presenting after 20 weeks with significant proteinuria .

Severe pre-eclampsia is pre-eclampsia with severe hypertension (160/110mmHg) and /or with symptoms , and / or biochemical and / or haematological impairment . [11]

Epidemiology and risk factors

Preeclampsia is the 2nd leading cause of maternal mortality in UK and US after thromboembolic disease. [12] The incidence of preeclampsia in the united states is estimated to range from 2-6%in healthy nulliparous woman [13,14], in the developing world to be 4-18% [15,16]. The disease is mild 75%of cases and severe in 25%. [17] In all cases of preeclampsia 10% occur in pregnancy of less than 34-week gestation. [11] The incidence of hypertensive disorders in pregnancy is estimated to range between 3% and 10% among all pregnancies. Worldwide, preeclampsia and related conditions are among the leading causes of maternal mortality.[18] While maternal death due to preeclampsia is less common in developed countries, preeclampsia-related maternal morbidity is high and remains a major contributor to intensive care unit admissions during pregnancy[19]. Approximately 12–25% of growth-restricted fetuses and small-forgestational- age infants as well as 15–20% of all preterm births are attributable to preeclampsia; the associated complications of prematurity are substantial and include neonatal deaths and serious long-term neonatal morbidity.[20] Despite major medical advances, the only known cure for preeclampsia remains delivery of the fetus and placenta.One-quarter of stillbirths and neonatal deaths in developing countries are associated with preeclampsia/eclampsia. Infant mortality associated with preeclampsia is three times higher in lower source settings than in high-income countries, largely due to the lack of neonatal intensive care facilities.[21] Women who had pre- eclampsia in any pregnancy after their first one had a mortality risk that was two- to fivefold higher over the next 35 years.[22]

D-dimer is a fibrin degradation product (or FDP), a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis. It is so named because it contains two crosslinked D fragments of the fibrin protein , D-dimer concentration may be determined by a blood test to help diagnose thrombosis. Since its introduction in the 1990s, it has become an important test performed in patients suspected of thrombotic disorders. While a negative result practically rules out thrombosis, a positive result can indicate[23]

Patints & Methods

Prospective case control study of eighty pregnant patients (fourty patients with approved diagnosis of pre-eclampsia and fourty normotensive pregnant women as a control group) presented to the department of obstetrics and gynecology / Baghdad Teaching Hospital / Medical city / Baghdad / Iraq in the period from May 2013 May 2014.Consents were obtained from all subjects. All the pregnant women enrolled in the study had similar demographic backgrounds.Fourty healthy normotensive third trimester women who were chosen in out patients clinic and who received regular follow up served as control group.

Methods

Getsational age was calculated considering last menstrual period and confirmed by first trimester or early second trimester ultrasonography finding. In both study groups, blood samples were collected when the patients first presented for the evaluation and before initiation of any treatment, such as magnesium sulfate, betamethasone, or labor induction.Blood sample(3ml) was drawn from antecubital vein or from the dorsum of the hand of each patient without using tourniquet using a serum separator tube and left the samples to clot for two hours at toom temperature or overnight at 4˚C before centrifugation for 15 minutes at 1000 xg then frozen at 20˚C and keep till the time of testing when serum procalcitonin level was measured by ELISA using CUSABIO pct. ELISA kit according to the manufacturer's instructions.
Plasma D-Dimer was measured using D-Di test a rapid latex agglutination slide test, the samples were collected in tubes with trisodium citrate anticoagulant and centrifuged for 15 minutes at 2000 – 2500 xg within 3 hours of blood samples collection, then frozen at -20˚C and kept till the time of testing.

Pre-eclampsia group

This group was subdivided into two subgroups **first subgroup** included 20 patients diagnosed with sever pre-eclampia with blood pressure ≥ 160 / 110 mmHg and proteinunia of 3+ or more on two random urine samples collected at least 4 hours apart.

Second group included 20 patients diagnosed with mild pre-eclampsia with blood pressure ≥ 140 /90 mmHg but less than 160 / 110mmHg and without signs and symptoms that are associated with sever pre-eclampsia while proteinuria in this group was 1+ or 2+.

Control group.

The control group included 40 pregnant women, all of whom were monitored at the department of obstetrics and gynecology of our hospital from the 1th trimester and who have an uncomplicated antenatal course blood pressure measurements in this group were normal – control patients were matched for gestational age and had no history of illness, hypertention, diabetes or renal disease.

Statistical analysis:

By using the statistical package for social sciences (SPSS) software version 21, data were entered and analyzed with appropriate statistical tests. Data were presented as mean, standard deviation. Analysis of ariances (ANOVA) test was used to compare means of any variable according to the studied group. Logistic regression (curve estimation model) was used to assess the correlation between PCT and D-dimer.
Pearson’s correlation test was used to analyze the inter-correlation between PCT, D-dimer and MAP. The correlation coefficient (r)was calculated which usually ranged between 0 – 1, the higher r value indicated the stronger correlation , furthermore by

using the multiple logistic regression test (linear model) for the analysis of predictors, and the odds ratio was calculated, the larger significant odds ratio indicated the higher prediction value and that the specified variable is more predictor.Receiver operating characteristics curve (ROC) was used to assess the validity of PCT and D-dimer in prediction of severity of PET, the area under the curve (AUC) indicated the accuracy of the test, the larger AUC indicated the higher accuracy. Sensitivity, specificity, accuracy, positive predictive value and negative predictive value then calculated depending the results of ROC analysis. Level of significance (P.value) less than 0.05 considered significant difference or correlation. Results and findings presented in tables and figures with an explanatory paragraphs.

Results

A total of 40 women with pre-eclampsia (sub groups; 20 women with mild PET and 20 women with severe PET) in addition to 40 healthy women as control group were enrolled in this study.

Demographic characteristics of PET and control groups:

Table 1 summarizes the demographic characteristics of the studied groups, No significant differences had been found in mean age, mean BMI or mean gestational age in neither between the PET groups and controls nor between the PET subgroups, P>0.05.

The mean systolic blood pressure (SBP) of severe PET group was significantly (P<0.001) higher than that of mild PET group and controls; 142.2 ± 9.8 vs. 139.4 ± 7.3 and 119.0 ± 11.0, respectively. On the other hand the mean SBP of mild PET group was significantly higher than that of controls. No significant difference had been found in mean SBP between PET sub groups (P>0.05).Similarly, the diastolic blood pressure and mean Arterial pressure was significantly higher in both PET groups (P<0.001) than controls with no significant difference between PET sub groups (P>0.05).

Table1: Demographic characteristics of PET patients and controls.

Characteristic	**Mild PET patients (N=20)**	**Severe PET patients (N=20)**	**Control (N=40)**	**P.value**
	Mean± SD Median (range)	**Mean± SD Median (range)**	**Mean± SD Median (range)**	
Age	26.9 ± 5.3	25.4 ± 4.4	28.0 ± 5.2	0.11
	19-35	19 – 33	27.3 (19 – 36)	
BMI	27.2 ± 6.2	28.4 ± 7.0	26.9 ± 6.6	0.83
	20.8 – 38.2	19.7 – 43	20.9 – 42.3	
Gestational age(weeks)	32.9 ± 3.2	33.6 ± 3.6	36.2 ± 3.7	0.23
	28 – 39	28 – 39	32 – 40	
SBP*	139.4 ± 7.3	142.2 ± 9.8	119.0 ± 11.0	**<0.001**
	128 – 154	131 – 160	100 – 138	
DBP*	95.4 ± 2.5	104.8 ± 6.3	80.5 ± 6.2	**<0.001**
	91 – 99	95 – 115	70 – 89	
MAP*	111.1 ± 3.1	117.2 ± 6.3	93.3 ± 5.4	**<0.001**
	103 – 116	107 – 128	83 – 105	

* P.value of difference between mild and severe PET groups was insignificant (P>0.05).

Procalcitonin and D-Dimer

As it is shown in table 2, Both severe pre-eclampsia and mild preeclampsia groups showed significantly higher PCT values when compared with healthy control group (p<0.001). Also, severe pre-eclampsia group showed significantly higher PCT values when compared with mild pre-eclampsia group (P=0.012).

Similar trends are found regarding the D-dimer, where severe pre-eclampsia and mild pre-eclampsia groups showed significantly higher D-Dimer values than healthy controls and the severe PET group had significantly higher DDimer than the mild PET group, (P=0.031)

Table2: Comparison of PCT and D-Dimer among the studied groups

Parameter		Mild PET patients (N=20)	Severe PET patients (N=20)	Control (N=40)	P.value
Procalcitonon (ng/ml)	Mean± SD	0.33 ± 0.054	0.77 ± 0.1*	0.14 ± 0.07	<0.001
	Range	0.050 – 1.10	2.5 – 4.0	0.06 – 0.30	
D-Dimer (mg/l)	Mean± SD	4.6 ± 0.5	6.9 ± 0.7**	1.6 ± 0.9	<0.001
	Range	4 - 5.5 6	6 – 8	0.5 – 3.6	

* P=0.012, between severe and mild PET groups.

** P= 0.031, between severe and mild PET groups.

Correlation between PCT and D- Dimer

Figure 3.1. (A and B) shows the correlation between PCT and D- Dimer in PET patients and controls. A significant direct (positive) correlation had been found between PCT and D-Dimer in both PET patients and controls, however the correlation was stronger and more significant in PET patients (R=0.88,P<0.001) than in controls (R = 0.38, P=0.017).

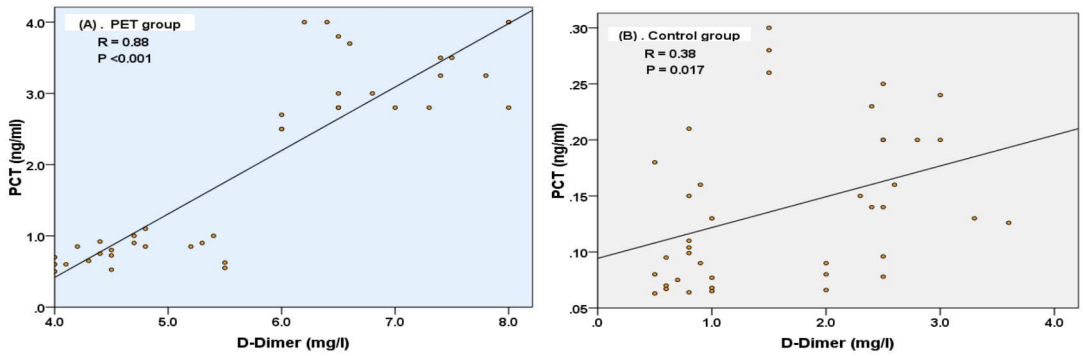


Figure 3.1. The correlation between PCT and D-Dimer , (A) in PET patients,(B) in controls

Predictors of PET

By using the multiple logistic regression tests, adjusting for the age, body mass index (BMI) and gestational age, the finding of regression test revealed that higher PCT and higher D-Dimer are risk factors and predictor of severe PET. (OR was 6.12 and 4.14) respectively, (P<0.001) , table 3.

Table3: Multiple logistic regression analysis findings for the predictors of PET risk factors

Parameter	Odds ratio (OR)	95% CI	P.value
Age	**1.32**	**0.71-3.60**	**0.42 *NS***
BMI > 30	**1.48**	**0.87 – 4.10**	**0.28 *NS***
Gestational age < 34	**1.61**	**0.93 – 5.40**	**0.12 *NS***
PCT > 0.07	**6.12**	**3.30-13.50**	**< 0.001 *sig***
D-Dimer > 1.5	**4.41**	**2.8-9.8**	**<0.001 sig**

Correlation between Markers and mean arterial pressure (MAP):

The bivariate correlation tests (Pearson's correlation test) revealed significant correlations between PCT, D-Dimer and MAP, (P<0.001)

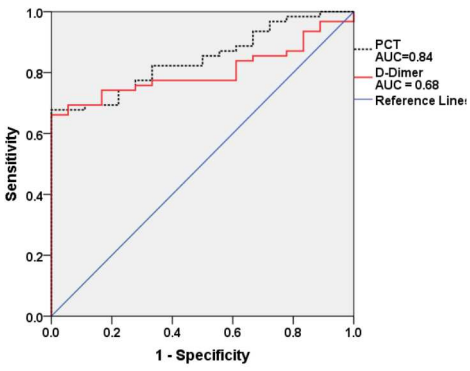
Table 4: Correlation between PCT, D-Dimer and MAP:D-Dimer MAP

	D-Dimer	MAP
PCT	0.87*	0.75*
D-Dimer		0.83*

* values represented correlation coefficient (R), P<0.001

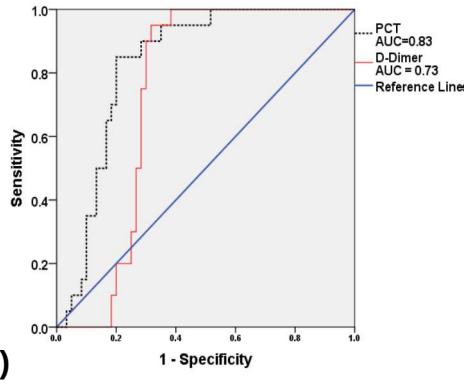
* Receiver operating characteristic curve (ROC) analysis

By using the ROC curve analysis between the PET and control groups are shown in figure3. 2, according to these figures, it had been found that the area under the curve (AUC) for prediction of severe PET, it had been significantly found that higher PCT and D-Dimer are good predictors for severe PET and their sensitivity, specificity, accuracy, positive predictive value and negative predictive values are shown in the same figures.



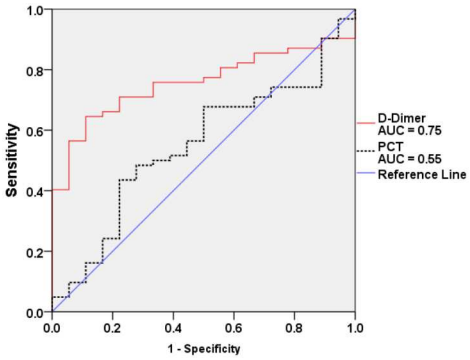
(a)

Sensitivity (82%)
Specificity (75%)
PPV (78.5%)
NPV (89%)
Accuracy (80%)



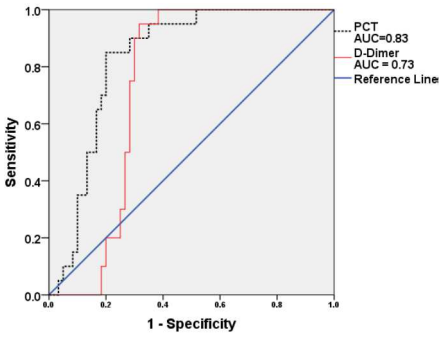
(b)

Sensitivity (87%)
Specificity (90%)
PPV (88%)
NPV (92%)
Accuracy (88.5%)



(c)

Sensitivity (66%)
Specificity (85%)
PPV (79%)
NPV (85%)
Accuracy (75.5%)



(d)

Sensitivity (89%)
Specificity (82.5%)
PPV (84%)
NPV (89%)
Accuracy (85.7%)

Figure 3.2. Receiver operating characteristics curve (ROC) analysis of the positive relationship between increasing PCT and D-Dimer and the study groups. (a) between controls and PET patients (total PET patients), (b) between controls and severe PET groups, (c) between Severe and Mild PET groups, (d) between controls and mild groups.(AUC; area under the curve)

Discussion

Preeclampsia remains a major cause of maternal and prenatal mortality and morbidity. Despite progress towards understanding the cause of preeclampsia and contributing circulating factors, the etiology of preeclampsia remains unclear [24].Present study found significant higher means of serum procalcitonin among preeclampsia patients and higher among severe PE than mild PE ($p<0.001$). Serum procalcitonin is a new marker in pregnant women population. Procalcitonin levels do not change with pregnancyrelated conditions (type of birth, time of birth, type of anesthesia and the stress of childbirth), but are affected by premature rupture of membranes and infectious conditions, such as group B streptococcal colonization.[25,26] Montagnana et al. showed that serum procalcitonin was associated with preeclampsia. Following this study, Can et al. found that there was a significant correlation between severe preeclampsia and procalcitonin levels [27]. Another study published recently showed that serum procalcitonin, CRP and D-dimer was significantly associated with preeclampsia [28]. Serum procalcitonin level has still been studied in urinary tract infections and a significant correlation between the grade 3 vesico-urethral reflux and procalcitonin was shown in the children. In the same study, serum procalcitonin levels which were higher than 0.5 ng/ml were associated with an increased risk of recurrent urinary tract infection [29].

D-Dimer means in our study were higher among PE patients and higher among severe PE than mild PE ($p<0.001$). Kucukgoz GU, et al study in Turkey concluded that D-dimer and procalcitonin were significantly higher among PE and can be used to predict severity of PE [30].

In PE, there is a deterioration of maternal renal function with the possibility of a rise in serum creatinine to more than 0.9 g/L, liver involvement with elevated liver enzymes, pulmonary edema (particularly in cases of severe preeclampsia), hematological disorders including thrombocytopenia, hemolysis and disseminated

intravascular coagulation, neurological involvement with visual disturbances, severe headaches and hyperreflexia, and intrauterine growth restriction [31,32] . As well, women with preeclampsia in the 3rd trimester showed significantly higher levels of serum procalcitonin, C-reactive protein (CRP), and plasma D-dimer levels, and these hematological indices were significantly higher in patients with severe as compared to mild preeclampsia [33].

Procalcitonin and D-dimer were correlated significantly to each others in all study participants. This finding is consistent with results of Kaya B, et al study in Turkey[34]. Many studies have confirmed that procalcitonin is a biomarker of inflammatory host response to microbial infections and increased in surgical pathologies such as ileus and pancreatitis. There is also a proportional increase in PCT levels with the severity of the infection. D-dimer is a degradation product of fibrin dissolution. Local fibrin formation and lysis are common events during inflammatory response [34,35] .

A significant correlation was observed in present study between mean arterial blood pressure and both procalcitonin and D-dimer ($p<0.001$). This finding is agreed with results of Jaimes F, et al study in Colombia [36] and Kucukgoz GU, et al study in Turkey[30]. Present study revealed mean age of patients with mild preeclampsia was 26.9 ± 5.3 years and with severe preeclampsia was 25.4 ± 4.4 years. This finding is indicating younger ages of preeclampsia patients which is close to results of Bilir F, et al study in Turkey [36] .that reported mean age of 26.9±4.6 years. Although no significant ifference in means of BMI between preeclampsia patients and controls, BMI means of preeclampsia patients were higher than controls and mean BMI of severe preeclampsia patients was higher than that of mild preeclampsia. Direkvand-Moghadam A, et al study in Iran [37]. reported no significant association between BMI and preeclampsia. Reys LM, et al study in Colombia [38] concluded that high BMI is a significant risk factor for development and severity of preeclampsia among pregnant women.

In present study, no significant difference was observed in gestational age between patients and controls. This finding is not agreed with results of Magnussen EB, et al study in Norway [39] , that found low gestational age of pregnant women was a significant risk factor of pr-eeclampsia.Blood pressure (systolic and diastolic) of women in this study was significantly higher among preeclampsia than controls and it was significantly higher among women with severe preeclampsia ($p<0.001$).

This finding is agreed with results of Hakim J, et al study in Canada[37] , that reported significant association between gestational hypertension with preeclampsia development and severity. Several different mechanisms have been linked to endothelial dysfunction in preeclampsia. Those include hypoxia, excessive oxidative stress, the renin-aldosteroneangiotensin II axis, and more recently imbalance of placental angiogenic factors, favoring antiangiogenic-soluble form of the type 1 receptor of vascular endothelial growth factor (sVEGFR-1 or sFlt1), which binds and thus neutralizes proangiogenic VEGF and placental growth factor [40]. Ensuing endothelial dysfunction may further be worsened by several vasoactive markers that are elevated in preeclampsia, such as cellular fibronectin, endothelin, platelet-derived growth factor, soluble E-selectin, soluble tissue factor, and von Willebrand factor. In vitro experiments have shown endothelial dysfunction after incubation with serum from women with preeclampsia. Several studies have evaluated short- and long-term endothelial function after preeclampsia, demonstrating ongoing vascular dysfunction measurable from 6 to 12 months to 5 to 6 years and even up to 15–25 years postpartum [41].

In current clinical practice, the use of mercury sphygmomanometers remains the gold standard for noninvasive BP monitoring, but there are concerns for both the clinical performance and safety of these instruments. These problems have been largely overcome by the use of automated BP devices, but so far only 1 of these has been validated for use both in pregnancy and in PE [42,43]. ROC curve analysis confirmed the use of procalcitonin and Ddimer for screening of PET (sensitivity (82%) and specificity (75%), severe PET (sensitivity 87% and specificity 90%) and mild PET (sensitivity 89% and specificity 82.5%). These findings are close to results of da Silva-Costa F, et al study in Australia 60 and Bilir F,et al study in Turkey[28] , Despite great research efforts, in 2004, the World Health Organization concluded that no single test was yet available to provide accurate screening for PE. Since then, there has been growing interest in the combination of markers for PE screening.Recently, this was reviewed by Giguère et al. [44] who concluded that the combination of biochemical and ultrasonographic markers improves prediction of PE. However, the authors did not systematically evaluate the contribution of maternal history and MAP to combined screening.

Limitations of study

1. Restriction in time and financial resources, additionally, unavailability and high cost of these tests, PCT and D-dimer, in our country lead restriction in the sample size. These tests performed depending on the researcher private expenditure.
2. This study conducted at a tertiary center, so that findings of the study cannot be generalized on Iraqi population.
3. As other case-control studies, recall bias couldn't be excluded.

Conclusions

1. Procalcitonin level and D-dimer level are good predictors for preeclampsia among pregnant women.
2. Procalcitonin level and D-dimer level are good predictors for severity of preeclampsia among pregnant women with preeclampsia.
3. Procalcitonin level and D-dimer level had good sensitivity ,specificity and accuracy and could be used as screening tests for detection and severity of pre-eclampsia .

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