Correlation between Serum & Urinary Placental Protein (Pp13) in Pre-eclamptic Women at their Third Trimester

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Abstract

Background: Preeclampsia (PE) consider as one of the most One of the most serious complications of pregnancy, and the chief reasons of

Objectives: Study the correlation between serum &urinary placental protein (pp13) in pre-eclamptic women at their third trimester

Materials and Method: Case control study was achieved from August 2018 to January 2019. A total of 100 women involved in this research, 50preeclampsia pregnant women and 50 apparently normal pregnant women as control, for all the subjects in the research serum and urine sample were collected for placental protein 13(pp13) estimation by using ELISA technique.

Results: Results indicated that a highly significant decreased in serum and urine pp13 in preeclamptic women compared to healthy women pregnant

Conclusion: Maternal serum PP13 at their 3rd. Trimester has evidences to be a credible biomarker for preeclampsia risk evaluation: the specificity and sensitivity of pp13 provided the highest diagnostic for preeclampsia

Keywords: *third trimester, preeclampsia, PP13.*

Introduction

Preeclampsias (PE) consider as one of main pregnancy disorders that has worldwide incidence rates about 5–8% [1]. The delivery of the placenta is the only acknowledged cure. PE is the major reason of the premature birth in developed countries, generally physically shown for the assistance of the mother [2].

PE is capable of being separated into two major kinds, the early and the late onset PE. This classification is depending either on the onset period or the identification of the syndrome [3]. The late onset PE comprises the majority (>80%) of preeclamptic. In the early onset type, the clinical symptoms appear prior to33weeks of gestational, while regarding late onset kind they happen following 34 weeks. The early-onset type that is accountable for most of the high maternal and fetal mortality and morbidity rates [1].

The American College of Obstetrics and Gynecology defined the clinical diagnosis of PE which involves blood pressures more than 140/90 mm Hg on 2 occasions joined with excretion of protein in urine more than 300 mg/d. The word Edema, considered as a classic characteristic of this disorder, it is not yet regarded as a detection sign due to absence of validity indicators the eclampsia could be existing in 20 percent of patients without previous protein uria or hypertension, suggestive of the presently using biomarkers for diagnosis are not ideal [4].

Placental protein 13 (PP13) is a 32 kDa dimer protein which is produced just in the placenta also it is believed to be included in maternal artery remodeling and usual placentation. It was found by Nicolaides et al. [5] that a remarkable decrease of serum PP13 values at 11 to 13

gestational weeks in the women whom consequently resulted the early type of preeclampsia, which was then validated by Spencer et al. [6].

Galectins (GAL) are many purposely controllers of primary cellular methods. They are as well included in natural and adaptive immune responsiveness and achievement aoperative role in the immune endocrine crosstalk. A number of GAL have invited interest in the reproductive knowledge for the reason that they are very much expressed at the maternal fetal line, their purposeful importance in eutherian pregnancies, and their unregulated illustration is detected in the "huge obstetrical disorders." Those GAL; could function as significant proteins included in maternal fetal connections. The examiner of these GAL can progress the predictive, detection, and therapy of the pregnancy women difficulties [7].

Methods

A case control study was carried out on 100 pregnant women over a period of seven months from August 2018 till January 2019. The participants in this research were collected from different hospitals in Baghdad city; the Al-Elweyia, Al-Hakeem, and Al- Imamain alkadhimain medical city. The practical fraction was accomplished at Research Laboratories in the Department of Chemistry and Biochemistry, College of Medicine/Al Nahrain University.

All subjects who included in the research were subjected by their physician to physical examination, blood pressure measurement, and laboratory investigations including serum and urinary pp13.

Inclusion criteria: All pregnant women included in this study were chronic hypertension pregnant women at their third trimester, gestational hypertension, renal and liver diseases, diabetes mellitus, smokers, fetal structural anomalies, multiple pregnancy, intrauterine fetal growth restriction from other causes, heart failure, inflammatory disorders, elderly pregnant, infectious disease, endocrine disease, HELLP syndrome and collagen vascular disorder were all expelled from the study.

Five milliliters (ml) venous blood had been withdrawn from all pregnant women by the use of disposable syringes in the sitting situation. Then it was discharged gradually in disposable test tubes without anticoagulant. And waited for clotting at 37˚C for 10 to15 minutes, then centrifugation at 1000 xg for about 10-15 minutes. Their serum was stored eppendorf tubes at -80˚C until analysis of pp13.

Random urine sample was collected in asterilecup for urine collection. Pregnant women who participate were informed to throw away the initial20-25ml of urine and have a collection ofapproximately60 mL urine of mid stream and stored in at -80˚C until analysis of placental protein 13(pp13).

Results

The mean ± SE of maternal age for control group and PE groups (mild and severe cases) were 29.28±1.08 years, 29.84±1.70years, 29.85±1.27 respectively. No significant difference (P= 0.931) was found between them.

Table (1) the mean ±SE of maternal age, control group and PE groups (mild and severe cases) at 3rd trimester.

Type	Control	Mild	Sever	P value
	Mean ±SE	Mean ±SE	Mean ±SE	
Age	29.28±1.08	29.84 ±1.70	29.85 ± 1.27	0.931NS

*Ns not significant, SE standard error

The mean ± standard error of mean of serum pp13 for control group and PE groups (mild and severe cases) at 3rd trimester afterbirth were 67.06± 3.296 pg/ml, 54.29± 3.129 pg/ml, 54.33 ±4.312 pg/ml, 54.25 ±4.64 pg/ml respectively.

There was highly significant increased (P=0.006) in mean of serum pp13 between control versus patient group

Also, high significant decreased (p=0.026) was found between mild preeclamptic group versus control group, while a highly significant decreased (P=0.035) was found between severe preeclamptic group versus control pregnant (Table1-2), but no significant difference (P=0.990) was found between mild against sever group.

The mean ± standard error of mean of urine pp13 for control group and PE groups mild and severe cases

at 3rd trimester after birth were 51.84±2.601 pg/ml, 38.39±2.717 pg/ml 43.44± 4.914 pg/ml, 33.34 ±1.863 pg/ml, respectively.

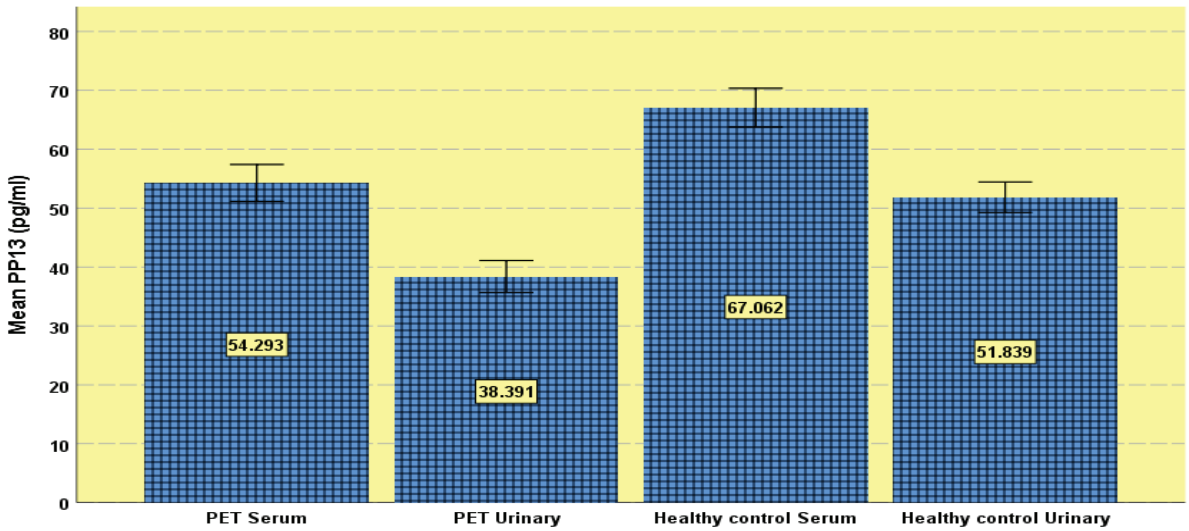
There was a highly significant decreased (P=0.001) in mean of serum pp13 between patient versus controls group. Also, high significant decreased (p=0.022) was found between mild preeclamptic group versus control pregnant group also, there was highly significant decreased (P=0.002) between severe preeclamptic group versus control pregnant (Table1-2). But no significant difference (P=0.062) between mild against sever group showed Table (1-2).

Table 2: The results of the serum placental protein 13 (pp13), urine placental protein 13 (pp13) for both control group and PE groups (mild and severe cases) at 3rd trimester.

		Mean ± SE	P value	Control vs Mild	Control vs Sever	Mild vs Sever
Serum pp13 (pg/ml)	Control	67.06±3.296	0.006*	0.036*	0.035*	0.900 NS
	PET	54.29±3.129				
	Mild	54.33±4.312				
	Sever	54.25±4.648				
Urine pp13 (pg/ml)	Control	51.84±2.601	0.001*	0.022*	0.002*	0.062 NS
	PET	38.39±2.717				
	Mild	43.44±4.914				
	Sever	33.34±1.863				

Table 1.3 showed comparison between placental protein 13 urinary and serum among preeclamptic and control women, the mean ±SE of serum levels preeclamptic and control were 54.29±3.129 pg/ml, 67.06±3.296 pg/ml respectively while the mean ±SE of urine levels for preeclamptic and control 38.39±2.717 pg /ml 51.84± 2.601 pg/ml when compared with serum pp13 between patients and control showed high significant (p=0.006). Also, patients compared urine pp13 was found with very high significant decreased (p=0.001)

Placental protein 13 urine and serum was measured in sera samples patients and healthy was presented in figure (3.2)



(Figure 1) serum and urinary pp13 level in different study group

Table (3) Correlation of serum placental protein 13 pg/ml with all of the studied parameters in control pregnant group, mild and severe preeclamptic group.

	Serum pp13 (pg/ml)		
	Control pregnant	**Mild preeclampsia**	**Severe preeclampsia**
Age	-0.496**	0.096	-0.332
Urine pp13 (pg/ml)	-0.008	0.320	0.019
pp13 ratio	0.694**	0.344	0.806**

Regarding the correlation of the serum pp13 concentration with all of the studied parameters in control, mild, and severe PE groups ; in severe PE, serum pp13 values showed very high positive significant correlation (P<0.001) with pp13 ratio(r=0.806). And positive correlation with urine pp13 (r= 0.019). On the other hand, in mild PE, positive correlation with age (r=0.096) In the control group, the highest level of significance (P<0.001) were observed in correlation of PP13 with age (r=- 496), and pp13 Ratio(r= 0.694). Also it showed significant negative correlation (P<0.01) with age, urine pp13.

Regarding ROC study between patients and control: Receiver operating characteristic curve (ROC) analyses of serum PP13 reveals the capacity of this biomarker to distinguish normal pregnancies from preeclamptic (Figure 3.5). The cut-off value = 50.43ng / ml of PP13 optimally identified patients with preeclampsia; at the sensitivity was 64% and specificity was 82.5 % and the area under curve (AUC) was 0.70 P = 0.002 .ROC study between patients and control : Receiver operating characteristic curve (ROC) analyses of serum PP13 reveal the ability of this marker to differentiate preeclamptic from normal pregnancies (Figure 3.5). The cut-off value = 50.43ng / ml of PP13 optimally identified patients with preeclampsia; at the sensitivity was 64% and specificity was 82.5 % and the area under curve (AUC) was 0.746 P = 0.002.

Table (4) Test Result Variable

Test Result Variable(s)	**Area**	**cutoff**	**Sensitive**	**Specific**	**P value**
Serum PP13 (pg/ml)	0.700	50,43	64%	82%	0.002*
Urine PP13 (pg/ml)	0.746	50,43	64%	82,5%	0.0001*

Discussion

Preeclampsia influences about 2 to 5 percent of women at pregnancy, causative to the fetal, neonatal and maternal mortality and morbidity, whilst the disorder noticeable at the 3rd trimester, the main placental function disturbances starts to a great extent in pregnancy earlier. Placental protein 13 (PP13) is a 32 kDa which is a dimmer protein that is present just in the placenta and is consider to be included in maternal artery remodeling and usual placentation.

The results of current research shown that there was no significant difference (P<0.05) in means of maternal age in the cases groups (mild and severe preeclampsia) when compared with control group, also there was no significant difference (P<0.05) between mild and severe preeclampsia groups(Table 1.1), these findings agreed with Aggarwal et al. (2011); Stepan et al. (2013) ; Magna and Sitikantha, (2013) who showed no significant

differences in the mean age of preeclampsia group and control normotensive

In the current study, the maternal values of the placental protein 13 in serum were found highly significant in pre-eclamptic cases groups (mild and severe preeclampsia) as compared to controls group and showed decrease in the results of pp13 levels in preeclampsia disorder.

The result conducted by Fahmy there was low in pp13 levels in pre-eclampsia groups, this agreement with our study appeared there was decreases in pp13 levels in preeclampsia groups as compared with control pregnant group Perhaps, (Fahmy et. al. 2018).

And in agreement with Berthold Huppertz observation in patient with Preeclampsia the pp13 serum levels were increased compared with control pregnant individuals. (Berthold Huppertzetal, 2008)

And the study by Farina conclude that variations in PP13 in preeclampsia be able to be measured revealing a pathophysiological alter of PP13 in pregnancy very early. It stays to be observed if the decreased value of PP13 in pregnancy early is an essential reason or an outcome of the placentation disturbance (Farina et al., 2010).

Conflict of Interest – Nil

Source of Funding- Self

Ethical Clearance – Not required

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