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Plasma pentraxin 3 levels in preeclamptic patients

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Summary

The authors evaluated plasma pentraxin 3 (PTX 3) levels in preeclamptic patients and determined the relationship between albuminuria and plasma PTX 3 levels. During a period of one year, 29 patients with severe or mild preeclampsia and 49 healthy pregnant women were included in the cross-sectional study. The two groups were compared each other with PTX 3 levels. The relationship between PTX 3 levels and urea, creatinine, AST, ALT, CRP, LDH, platelet count, and spot urine protein/creatinine rate were evaluated. PTX 3 level was significantly high in the preeclamptic group ($p < 0.05$). No significant correlation was found between serum PTX 3 level and urea, creatinine, AST, ALT, CRP, LDH, platelet, and spot urine protein/creatinine rate ($p > 0.05$). PTX 3 is a biochemical parameter that shows endothelial dysfunction. The authors believe that PTX 3 can be a valuable parameter to predict preeclampsia according to the significantly high PTX 3 levels in preeclamptic patients.

Key words: Pentraxin 3; Preeclampsia; Albuminuria.

Introduction

The etiology of preeclampsia remains unclear despite its association with significant maternal and fetal morbidity. Disorders of trophoblastic development, endothelial dysfunction, angiogenesis, and abnormal oxidative stress may contribute to the pathophysiology of preeclampsia [1]. The maternal serum markers related to these mechanisms have been evaluated for the early identification of women at high risk developing preeclampsia [2].

Pentraxin 3 (PTX 3), which belongs to the same family as C-reactive protein (CRP), is expressed in response to inflammatory stimuli by a variety of cells, including endothelial cells, monocytes, macrophages, and fibroblasts [3]. Previous studies have shown that maternal PTX 3 levels are significantly higher in women with preeclampsia when compared to those in normal pregnancies [4]. As PTX 3 is expressed from inflammatory tissue, it is mainly related to endothelial dysfunction [5].

The aim of this study was to evaluate PTX 3 levels at preeclamptic patients and to show the relationship between proteinuria and PTX 3 levels as being the marker of endothelial dysfunction.

Materials and Methods

This cross-sectional study was carried out in women with preeclampsia and healthy pregnant women. They were recruited 12 months from the maternal–fetal medicine services at the present hospital. The study group consisted of 29 women with mild or severe preeclampsia at third trimester. The control group was made up of 49 women with uncomplicated pregnancies at third trimester, selected by simple random sampling using a table of random numbers.

The study protocol conformed to the Helsinki Committee requirements and was approved by the Ethics Committee of the present hospital. Written informed consent was also obtained from all subjects before the study

All participants were non-smokers, had not received any medication, and had no clinical evidence of cardiovascular, metabolic, or inflammatory diseases. Exclusion criteria were smokers, confirmed diabetes mellitus, chronic hypertension, renal diseases, connective tissue diseases, inflammatory or infective disorders, and heart diseases, as well as treatment with aspirin and nonsteroidal anti-inflammatory drugs.

The two groups were compared to each other with PTX 3 levels, urea, creatinine, AST, ALT, CRP, LDH, platelet count, and spot urine protein/creatinine rate. The relationship between PTX 3 levels and mentioned biochemical parameters were evaluated.

Maternal age, gestational age, gravid, parity, and systolic and diastolic blood pressure were recorded. Mild preeclampsia was defined as a systolic blood pressure of at least 140 mmHg or a diastolic blood pressure (BP) of at least 90 mmHg recorded on two occasions at least six hours apart, in association with new onset proteinuria. Proteinuria was defined as +1 or greater on dipstick on at least two occasions. The present authors defined severe preeclampsia as having a BP of at least 160 mmHg systolic or at least 110 mmHg diastolic on at least six hours apart or if proteinuria of five grams or more in 24 hours. Women with symptoms of end-organ involvement (persistent headache, disturbance in vision, protracted nausea and vomiting, or epigastric pain) were considered to have severe disease. The present definition of severe preeclampsia also included those with laboratory abnormalities of complete or limited hemolysis, elevated liver enzymes, low platelets (HELLP) syndrome (total bilirubin of 1.2 mg/dl or more, lactate dehydrogenase (LDH) of 600 U/l or more, aspartate aminotransferase (AST) of 72 U/l or more, or platelet

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Table 1. — *Maternal demographic characteristics and pregnancy outcomes in the study groups.*

		All cases n or median		Normal n or median		PE n or median		p^1
Age		27.17 ± 5.90		26.73 ± 5.89		27.90 ± 6.43		*0.404*
Gestational age (weeks)		34.67 ± 3.86		34.20 ± 3.39		35.45 ± 4.50		*0.171*
Gravid		1.99 ± 1.33 (2)		1.94 ± 0.96 (2)		2.07 ± 1.81 (1)		*0.385*[2]
Parity		0.79 ± 1.13 (0.5)		0.80 ± 0.84 (1)		0.79 ± 1.52 (0)		*0.211*[2]
		n	%	n	%	n	%	*p*
Previous Preeclampsia history	Positive	2	2,6	1	2.0	1	3,4	*1.000*[3]
	Negative	76	97.4	48	98.0	28	96.6	
Parity	Nulliparous	37	47.4	20	40.8	17	58.6	*0.198*[3]
	Parous	41	52.6	29	59.2	12	41.4	

[1]*Student T Test;* [2]*Mann Whitney U test;* [3]*Fisher's Exact test.*

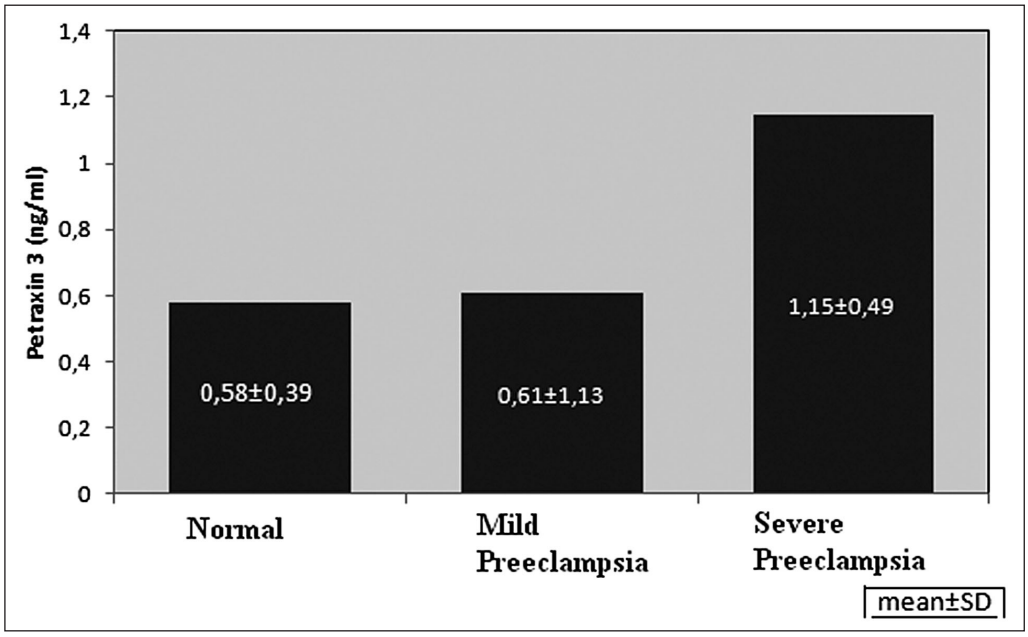

Figure 1. — PTX 3 levels among study groups.

count of no more than 100,000/mm3) [6]. Eclampsia was considered as the occurrence of convulsion in preeclamptic cases, not attributable to other causes.

Biochemical Analyses

After maternal blood samples were collected, they were centrifuged and serum was stored at -80°C to record their urea, creatinine, AST, alanine aminotransferase (ALT), CRP, LDH, platelet count. Sandwich enzyme-linked immunosorbent assay (ELISA) for PTX 3 was performed. The PTX 3 ELİSA system had a detection limit of 0.02 ng/ml with an intra-assay and inter-assay coefficient of variation (CV) of % 4-6 and % 8-10, respectively. Serum levels of CRP were measured using the ultrasensitive latex immunoassay CRP Vario with the intra- and inter-assay CV both <10%. Spot urine protein and creatinine were analyzed. Spot urine protein/creatinine rate was calculated.

Statistical analyses

All data were analyzed with Number Cruncher Statistical System (NCSS) 2007 and Power Analysis and Sample Size (PASS) 2008 Statistical Software. Descriptive statistics are reported as mean ±SD and percentage. Unpaired Student's t test, Mann–Whitney U test, v2 test, or Fisher's exact test was used for intergroup comparisons. Statistical significance was defined as $p < 0.05$. Correlations between variables were evaluated with Pearson's correlation coefficient.

Results

All 29 women (100%) in the preeclampsia group met the criteria for the diagnosis of severe preeclampsia. Of those women, seven women had developed severe preeclampsia. Demographic and pregnancy characteristics are shown in Table 1. Serum urea, creatinine, LDH, AST, and protein/creatinine rate were found significantly high at the preeclamptic group ($p < 0.05$). The present authors also found PTX 3 levels significantly high in the preeclamptic group (1.01 ± 1.00 ng/ml vs. 0.58 ± 0.39 ng/ml) ($p < 0.05$). The level of

PTX3 in women with severe preeclampsia was higher than women with mild preeclampsia ($p < 0.05$, Figure 1). No significant correlation was found between serum PTX 3 level and urea, creatinine, platelet, LDH, AST, ALT, CRP, and spot urine protein/creatinine rate ($p > 0.05$).

Discussion

PTX3 is a member of the pentraxin family, which includes CRP and serum amyloid P component (SAP). The cross-species evolutionary conservation of PTX3, in contrast to CRP and SAP, suggests an important role for this molecule. PTX3 appears to have a major role in resistance against selected pathogens by acting as a predecessor of antibodies, recognizing microbes, activating complement, and facilitating pathogen recognition by phagocytes. The abnormal pro-inflammatory maternal status, pre-existing endothelial damage, and excess of oxidized LDL seen in women who subsequently develop preeclampsia may all induce PTX3 elevation [6, 7]. Vascular endothelial growth factor (VEGF) has the major role in the microcirculation of the renal glomerulus. It is shown that VEGF is excreted from both glomeruli endothelium and podocytes. Any abnormality of the excretion of the VEGF causes fenestration loss and proteinuria [8]. PTX 3 reduces excretion of VEGF by inhibiting FGF2, therefore PTX3 causes antiangiogenic situation and damages microcirculation at the glomerular endothelium [9].

Zhou *et al*. searched the expression of PTX3 in placentas from patients with severe preeclampsia and evaluate the relationship between PTX3 and the pathogenesis of severe preeclampsia. They found that PTX 3 level was higher in severe preeclamptic patients [10]. Hamad *et al.* searched endothelial function in relation to anti-angiogenic biomarkers and the inflammatory process in preeclampsia [11]. They found that PTX3 was higher in women with preeclampsia especially in women with early-onset preeclampsia. In the present study, the authors found PTX3 levels in preeclamptic group higher than control group, especially in severe preeclamptic patients.

Durnwald *et al.* found that there was no significant correlation between protein/creatinine rate in spot urine and proteinuria in 24-hour urine. They found that looking for proteinuria in 24-hour urine is much more significant [12]. However, Kuang *et al.* evaluated the clinical application of protein/creatinine rate in spot urine samples in order to check whether it can replace urine protein excretion in 24-hour collections for the diagnosis and screening of preeclampsia. They found that the protein/creatinine in spot urine samples can replace urinary protein excretion in 24-hour collections [13]. In the present study no significant correlation was found between PTX3 levels and proteinuria. The reason of this uncorrelation may be detecting proteinuria by calculating protein/creatinine rate in spot urine instead of proteinuria in 24-hour urine.

Caterino *et al.* searched acute phase proteins in preeclampsia.They found the concentrations of CRP is significantly higher in preeclamptic patients [14]. Kucukoz *et al.* also found that CRP and D-dimer levels were significantly higher in preeclamptic patients in their study [15]. In the present study the authors found no significant difference in CRP levels between control group and preeclamptic patients. CRP levels were normal in both groups and also no significant correlation between PTX3 and CRP levels was found in this study. The authors believe that the reason of low CRP levels in preeclamptic patients is due to the very limited amount of severe preeclamptic patients in this study. Jaiswar *et al.* evaluated LDH as a biochemical marker of preeclampsia in their research [16]. They found LDH significantly higher in preeclamptic patients. In the present study, LDH levels were also significantly higher in preeclamptic patients. However, there was no significant correlation between LDH and PTX3 levels. The authors believe that this uncorrelation is because of the limited number of severe preeclamptic patients. Sibai determined that with severe preeclampsia/eclampsia, elevated liver enzymes are seen because of the fibrin deposits at hepatic sinusoids according to the endothelial dysfunction [17]. In the present study, similar elevated AST levels were found in preeclamptic patients.

The small amount of the severe preeclamptic patients is one of the limitations of the present study. Another limitation of this study is that the population of the study included only the patients in their third trimester. It would have been better if the patients were selected from the beginning of the pregnancy for early prediction of preeclampsia. Another limitation was the determining of proteinuria in preeclampsia by calculating protein/creatinine rate in spot urine instead of proteinuria in 24-hour urine. However there is no significant consensus for the spot urine protein/creatinine ratio to determine proteinuria, hence further studies should be designed with 24-hour urine collection for proteinuria.

As a conclusion, PTX3 level is higher in preeclamptic patients. PTX3 can be used to predict preeclampsia due to its evidence of endothelial dysfunction. The present authors can recommend to clinicians that PTX3 can be a valuable parameter to predict preeclampsia.

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