

FIBRONECTIN AND C-REACTIVE PROTEIN IN PREGNANCY INDUCED HYPERTENSION

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Summary: Hypertension is the most common medical complication in pregnancy. Of the varying forms of hypertension that can effect pregnancy pre-eclampsia is the one specific to pregnant women. The differential diagnosis between pre-eclampsia and pregnancy induced hypertension (PIH) is essential to proper management of pregnancy. The aim of this study was to examine the effect of hypertension on plasma fibronectin and C-reactive protein (CRP) during gestation. The examined groups comprised 37 patients with normal pregnancy and 30 with PIH between 24 and 36 weeks of gestation. Plasma fibronectin and CRP were both assayed by nephelometric method. The obtained results for both examined parameters were significantly higher in PIH group than in controls ($p < 0.05$). A positive correlation was found between fibronectin, CRP and weeks of gestation ($p < 0.05$). Therefore, we can conclude that plasmatic fibronectin and CRP are among useful screening parameters for estimation of the endothelial injury in hypertensive disorders of pregnancy.

Key words: fibronectin, C-reactive protein, pregnancy induced hypertension

Introduction

Pre-eclampsia remains the major cause of maternal and perinatal morbidity and mortality. It is a loosely defined set of clinical signs that are neither exclusive nor precise. The hallmark of pre-eclampsia is hypertension (1).

The aetiology of pre-eclampsia and eclampsia is unknown. Pre-eclampsia develops in 5% of pregnant women, usually in primigravidas and in women with pre-existing hypertension or vascular disease. If untreated, pre-eclampsia characteristically smolders for a certain time, then suddenly progresses to eclampsia. Eclampsia develops in 1 of 200 patients with pre-eclampsia and is usually fatal if untreated. A major complication of pre-eclampsia is abortio placentae apparently caused by vascular disease (2). The pre-

eclampsia eclampsia syndrom is a vasospastic disorder and probably has a placental origin. The diminished placental perfusion probably creates endothelial damage. This damage has several effects: decreased prostaglandin production, activated coagulation cascade, stimulated fibrin aggregation and increased vascular permeability. One of the difficulties in studying the hypertensive disease of pregnancy is that hypertension and clinically evident multisystem failure are late manifestations of a disease process that was probably initiated early in pregnancy (3). Laboratory tests performed in order to predict pre-eclampsia essentially cover the entire range of clinically available and research-related laboratory determinations in pregnant women. This includes measurements of maternal concentrations of various placenta-derived hormones and enzymes, minerals and electrolytes, coagulation factors and blood components (4, 5). Some reports have demonstrated, by comparison with healthy pregnancies, that pre-eclampsia is associated with plasma fibronectin changes.

Plasma fibronectin is derived primarily from the liver and endothelial cells. As fibronectin occurs in vas-

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cular basement membrane, circulating fibronectin levels may serve as a marker for endothelial damage or disruption (6-8).

C-reactive protein (CRP) has traditionally been used as an acute phase marker of tissue injury, infection and inflammation. CRP may also increase macrophage production of tissue factor, the coagulation initiation responsible for occlusive thromboembolic events (9).

Among apparently healthy men, elevated levels of CRP are a predict risk of myocardial infarction. Whether increased levels of CRP are also associated with development of symptomatic peripheral arterial disease is unknown (10).

The aim of this article was to study the levels of plasma fibronectin and CRP in pregnancy-induced hypertension and to follow-up their concentrations during the gestational period.

Material and Methods

The study involved 37 normotensive and 30 hypertensive women. All the examined patients were between 24 and 36 weeks of gestation. Maternal blood samples were collected with EDTA, plasma separated by centrifugation at 3000 rpm and kept at -20°C until the assay. Fibronectin was measured by nephelometry (Behring Nephelometer Analyzer) considering values between 0.250 g/L and 0.400 g/L as normal. The plasma C-reactive protein was also assayed by nephelometric method. Reference ranges were from 0 to 5 mg/L. Differences between the two groups were analyzed statistically by Mann-Whitney's U-test. Spearman correlation test was used in order to establish the correlation between fibronectin and CRP concentrations and weeks of gestation.

Results and Discussion

The results we have obtained for fibronectin concentration in plasma of normotensive and hypertensive gravidas are presented in *Figure 1*.

Concentrations of fibronectin in the group of hypertensive patients compared to normotensive pregnant women were significantly higher ($p < 0.05$). This is in agreement with literature data proving that fibronectin increases in pregnancy even before the clinical manifestation of hypertension. Oslund and coworkers (11) studied 177 patients with suspected pre-eclampsia and found fibronectin values significantly higher than in the normal population.

In the same studied groups the concentration of CRP was assayed and results are presented in *Figure 2*.

The obtained values for CRP in pregnancy induced hypertensive women were also significantly higher compared to normotensive gravidas ($p < 0.05$). C-

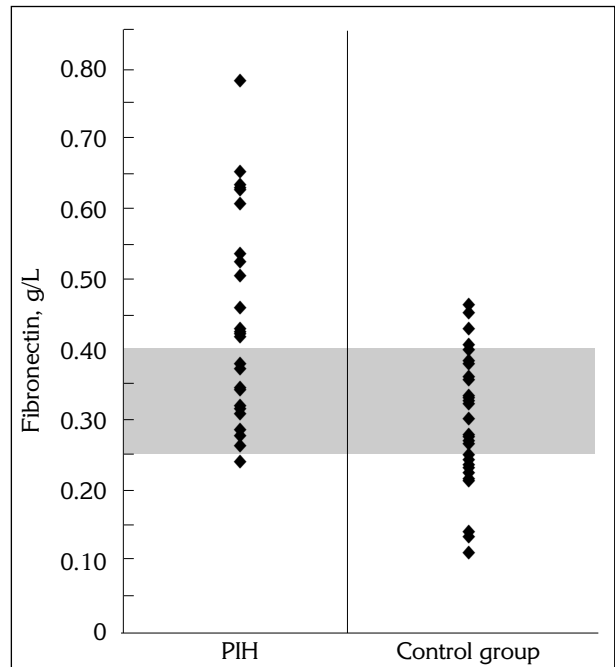


Figure 1. Concentrations of plasma fibronectin in pregnancy induced hypertension (PIH) and normotensive pregnant women (control group). \square reference values: 0.250-0.400 g/L.

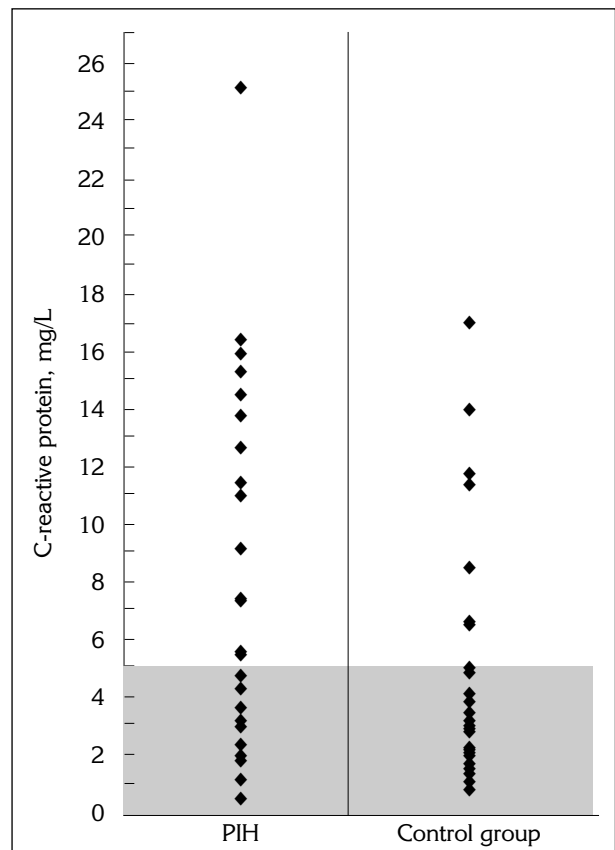


Figure 2. C-reactive protein in pregnancy induced hypertension (PIH) and normotensive gravidas (control group). \square reference values: 0-5 mg/L.

Table I Correlation between fibronectin and C-reactive protein (CRP) and weeks of gestation (mean \pm SD)

Weeks of gestation	Fibronectin, g/L	CRP, mg/L
< 24	0.382 \pm 0.039	9.2 \pm 0.157
24 28	0.334 \pm 0.077	3.9 \pm 0.141
30 32	0.501 \pm 0.071	5.6 \pm 0.139
34 36	0.465 \pm 0.085	3.7 \pm 0.153
> 36	0.375 \pm 0.073	8.9 \pm 0.165
p	< 0.05	< 0.05

reactive protein levels are also affected by interleukin-6, steroids, estrogen, insulin resistance, and changes in fat mass. Thus, the CRP change in pregnancy is not just pathological; it may be physiological and related to hormones and metabolism. At the same time, the levels of inflammatory markers are not high enough to explain the massive endothelial dysfunction that causes pre-eclampsia. Elevated levels may be more dangerous at an advanced stage of pregnancy (12).

The concentrations of both fibronectin and CRP were followed-up during the gestational period and results are presented in *Table I*.

By Spearman correlation test in PIH group we found a positive correlation between plasmatic fibronectin and weeks of gestation ($p < 0.05$). The

concentration of fibronectin starts to increase in the 26 weeks of gestation reaching the maximum at 30 weeks. Our results are in agreement with those published by Gredmark et al. (13). They found that changes in fibronectin levels between 26 and 34 weeks of gestation were the only variable that remained statistically associated with pre-eclampsia. We also found that CRP concentration correlated with the weeks of gestation ($p < 0.05$).

Hypertension during pregnancy causes a metabolic disturbance leading to changes in coagulation system. Measuring of plasma fibronectin (as a marker of endothelial damage) can reveal any pre-eclamptic process overlapping the vasoconstriction due to essential hypertension before there is any evidence of activation of coagulation cascade. Evaluation of the mean concentration of cellular fibronectin during the midtrimester is consistent with the hypothesis that endothelial cell injury is a specific lesion that occurs early in the course of pre-eclampsia, before clinical signs and symptoms (14). These data suggest that cellular fibronectin can also be used as a prediction test in women with risk for developing pre-eclampsia.

According to the results obtained in this study, plasma fibronectin and CRP levels seem to be useful in the differential diagnosis of pre-eclampsia and chronic hypertension, thus enabling a more suitable monitoring and treatment of these patients.

FIBRONEKTIN I C-REAKTIVNI PROTEIN KOD TRUDNOĆOM IZAZVANE HIPERTENZIJE

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Kratak sadržaj: Hipertenzija je jedna od najčešćih komplikacija u trudnoći. Od svih oblika hipertenzije najspecifičnija je pre-eklampsija. Za adekvatan tretman trudnica neophodno je postaviti diferencijalnu dijagnozu između pre-eklampsije i hipertenzije uzrokovane trudnoćom. Cilj ovog rada bio je ispitivanje uticaja hipertenzije na nivo plazmatskog fibronektina i C-reaktivnog proteina (CRP) tokom trudnoće. Ispitivane grupe sastojale su se od 37 pacijentkinja sa normalnom trudnoćom i 30 hipertenzivnih trudnica, između 24 i 36 nedelje gestacije. Koncentracije plazmatskog fibronektina i CRP-a određivane su nefelometrijskom metodom. Rezultati dobijeni za fibronektin i CRP bili su statistički značajno povišeni u grupi hipertenzivnih trudnica u poređenju sa normotenzivnim ($p < 0,05$). Ispitivanjem uticaja nedelja gestacije na koncentracije fibronektina i CRP-a utvrđena je pozitivna korelacija između koncentracija fibronektina i CRP-a i nedelja gestacije ($p < 0,05$). Na osnovu dobijenih rezultata potvrđeno je da su plazmatski fibronektin i CRP korisni parametri u proceni oštećenja endotela kod hipertenzivnih poremećaja u trudnoći.

Ključne reči: fibronektin, C-reaktivni protein, trudnoćom izazvana hipertenzija

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