MATERNAL SERUM LEVELS OF ADIPONECTIN IN PREECLAMPSIA

Ali Khosrowbeygi, Hassan Ahmadvand

Department of Biochemistry, School of Medicine, Lorestan University of Medical Sciences, Khorramabad, Iran.

Background: The results of the serum levels of adiponectin in preeclamptic patients are conflicting. **Objective:** The aim of the present study was to assess serum levels of adiponectin in women with preeclampsia compared with healthy pregnant women. Methods: A cross-sectional study was designed. The case group consisted of women with preeclampsia (n=30). The control group consisted of 30 matched normal pregnant women. Serum levels of adiponectin were assessed using enzyme-linked immunosorbent assay method. **Results:** Serum levels of adiponectin were significantly higher in the preeclamptic group than those in the normal control group. In the preeclamptic patients serum levels of adiponectin showed a significant negative correlation with body mass index while no correlation was found in the normal pregnant women. In women with preeclampsia, levels of adiponectin were decreased significantly in the overweight women compared with normal weight women, while in the control group no significant difference was observed. **Conclusion:** In conclusion, elevation of adiponectin levels might be a physiological feedback response to minimize endothelial dysfunction in preeclamptic patients.

Keywords: Serum, Adiponectin, Preeclampsia, Pregnancy, BMI, ELISA.

INTRODUCTION

Preeclampsia, a pregnancy specific syndrome, is a major cause of maternal and perinatal morbidity and mortality.[1,2] Preeclampsia is characterized by the onset of hypertension and proteinuria after 20 weeks of gestation in a previously normotensive pregnant woman.[3–5] The exact mechanism underlying etiology of preeclampsia remains elusive.[6–8] There are many theories about the etiology and pathogenesis of preeclampsia including endothelial dysfunction, inflammation and angiogenesis. Adiponectin, a specific adipocyte derived hormone, has been considered to improve insulin sensitivity, inhibit vascular inflammation and atherogenesis. Thus, it has been hypothesized that adiponectin may be involved in the pathophysiology of preeclampsia.[9] The findings of the circulating levels of adiponectin in preeclamptic women are conflicting. Some studies have shown that serum levels of adiponectin are higher in women with preeclampsia than those in normal healthy pregnant women.[3,6,7,10–13] Low serum levels of adiponectin have also been reported in preeclampsia.[8,9,14,15] It also has been shown that there is no difference in circulating concentrations of adiponectin between pregnant women with and without preeclampsia.[16,17] Therefore, we designed a cross-sectional study to examine the serum levels of adiponectin in preeclamptic women.

MATERIALS AND METHODS

A cross-sectional study was designed. The study was approved by Institutional Ethical Review Board, and informed consent was obtained from each pregnant woman enrolled in this study. The case group consisted of women with preeclampsia (n=30). The control group consisted of 30 age, gestational week, and body mass index (BMI) matched normal pregnant women. Preeclampsia was defined as blood pressure equal to or higher than 140/90 mmHg with proteinuria of either higher than 100 mg/dl by urine analysis or higher than 300 mg in a 24 hours urine collection. Severe preeclampsia was defined as blood pressure equal to or higher than 160/110 mmHg.[3]

Exclusion criteria were smoking, multiple gestation, diabetes mellitus, chronic hypertension, heart failure, inflammatory or infective disorders, and infectious disease.[9]

Blood samples were collected from preeclamptic patients at the time of acceptance to the hospital shortly after the preeclampsia diagnosis was confirmed. Serum samples were stored at -70 °C until examination.

The concentration of total adiponectin was measured using enzyme-linked immunosorbent assay (ELISA) method. We used commercially available human adiponectin ELISA method (BioVendor Laboratory Medicine, Inc. Czech Republic).[18] The procedure for the ELISA method was according to the instructions provided by the manufacturer. The sample volume that used was 10 µl. Absorbance was measured at a wavelength of 405 ηm using ELISA reader (STAT FAX 2100, USA). The levels of adiponectin are presented as µg/ml. The intra-assay coefficient of variation was <10%. The sensitivity and specificity of the adiponectin assay were 26 ηg/ml and 100%, respectively (BioVendor Laboratory Medicine, Inc. Czech Republic).

Based on a literature review, using an α value of 0.05 and a β value of 0.2 (80% power), the minimum sample size required was calculated 30 samples per group. Differences between case and control groups were assessed using Mann-Whitney U test. Coefficients of correlation were calculated using Spearman's correlation analysis. All hypothesis tests

were two-tailed with statistical significance assessed at the *p*-value <0.05 level with 95% confidence intervals. The data are expressed as the Mean±SEM. Statistical computations were calculated using SPSS 11.5 for windows software (SPSS Inc, Chicago, IL, USA).

RESULTS

Characteristics of normal pregnant women and preeclamptic patients are shown in Table-1.

Table-1: Characteristics of Normal Pregnancy and Preeclamtic Women

Parameter	Normal pregnancy (n=30)	Preeclampsia (n=30)	*p*
Age (Year)	31.07±0.35	32.27±0.69	0.2
Gestational age (Weeks)	39.10±0.23	38.50±0.24	0.09
BMI before pregnancy (Kg/m^2)	21.95±0.50	23.65±0.75	0.08
Third trimester BMI (Kg/m^2)	26.23±0.51	27.88±0.78	0.1
Systolic blood pressure (mm Hg)	109.00±1.11	150.67±1.91	0.001
Diastolic blood pressure (mm Hg)	66.33±1.31	95.67±2.23	0.001
Adiponectin (µg/ml)	11.60±1.04	15.36±0.92	0.003

Results are presented as mean±SEM. BMI= Body Mass Index

There were no significant differences in age, gestational age, BMI before pregnancy, and third trimester BMI between the preeclamptic and control groups. Women with preeclampsia had a higher mean systolic and diastolic blood pressure than the normal pregnant women. As shown in Table-1, serum levels of adiponectin were significantly higher in the preeclamptic group than in the normal control group. Patients were then stratified to mild and severe preeclampsia. There was no significant difference in the serum levels of adiponectin between women with mild and severe preeclampsia (16.54±1.35 vs 13.81±1.08 µg/ml, $p> 0.05$). We also examined the relationship of adiponectin concentrations with BMI. In the preeclamptic patients serum levels of adiponectin showed a significant negative correlation with BMI before pregnancy (r= -0.62, $p= 0.001$) and third trimester BMI (r= -0.49, $p= 0.006$). However, no correlation was found between serum levels of adiponectin and BMI in the normal pregnant women.

Then, we subdivided the normal pregnant women and preeclamptic patients to normal weight (BMI <25 kg/m^2) and overweight (BMI >25 Kg/m^2) (15). In women with preeclampsia, serum levels of adiponectin were decreased significantly in the overweight women compared with normal weight women (14.18±0.94 vs 18.12±1.92 µg/ml, $p= 0.04$). In women with severe preeclampsia, serum levels of adiponectin were decreased significantly in the overweight women compared with normal weight women (12.61±0.63 vs 20.42±4.17 µg/ml, $p= 0.003$). There was no significant difference in the serum levels of adiponectin between the overweight and normal weight of women with mild preeclampsia and the control group. In normal weight women with preeclampsia serum levels of adiponectin were slightly increased compared with normal weight control group (18.12±1.92 vs 12.77±1.71 µg/ml, $p= 0.06$).

DISCUSSION

The most relevant findings of this study were (i) a significant increase in serum levels of adiponectin in preeclamptic subjects than those from normal pregnant women (ii) a significant negative correlation between serum levels of adiponectin and BMI in preeclamptic patients, and (iii) a significant decrease in serum levels of adiponectin in overweight preeclamptic women compared with normal weight subjects.

Our data confirm the results obtained by Nakatsukasa *et al*[3], Lu *et al*[6], Takemura *et al*[7], Ramsay *et al*[10], Kajantie *et al*[11], Naruse *et al*[12] and Nien *et al*[13], who observed that circulating levels of adiponectin are significantly higher in preeclamptic patients than in normal pregnant women. However, our findings do not agree with those of Ouyang *et al*[8], Ouyang *et al*[9], Mazaki-Tovi *et al*[14], and Herse *et al*[15], studies who observed that preeclamptic women have lower circulating concentrations of adiponectin than healthy pregnant women.

Adiponectin is a hormone produced exclusively by adipocytes. Circulating levels of adiponectin are relatively high. The levels of adiponectin are inversely correlated with insulin resistance, obesity, and hypertention. Adiponectin has antiatherogenic properties. It suppresses transformation of the macrophages to foam cells and inhibits the expression and function of the class A scavenger receptors in macrophages. Adiponectin also have anti-inflammatory properties, including suppression of macrophage production of cytokines, tumor necrosis factor-alpha (TNF-α), interferon-gamma (INF-γ), and interleukin-6 (IL-6).[13,19]

Ramsay *et al*[10] first reported elevation of circulating adiponectin levels in preeclamptic patients compared with normal pregnant women. These authors proposed that exaggerated release of adiponectin by adipocytes is one possible mechanism for the elevation.

Naruse *et al*[12], study observed that adiponectin levels are significantly increased in women with preeclampsia than healthy pregnant women. Haemoconentration is a main characteristic of preeclamptic women, but Naruse *et al*, study showed that adiponectin levels still are higher after correcting for haematocrit. These authors suggest that

adiponectin may act as an inhibitor of inflammatory cytokine production in preeclamptic patients.

Hendler *et al*[16] found that there is no difference in the concentrations of adiponectin between women with preeclampsia and normal pregnant women. Their study also showed that in women with severe preeclampsia, adiponectin levels are decreased in overweight compared with normal weight women. Hendler *et al* also found that there is no difference in the levels of adiponectin between overweight and normal weight women when compared within mild preeclampsia and normal healthy women. Their study also showed that in normal weight women, adiponectin levels are increased in preeclamptic patients compared with normal pregnant women. When our study subjects were stratified to normal weight and overweight women, the results were very similar to Hendler *et al* study findings. It was proposed that production of adiponectin is increased as a physiological response by adipocytes in preeclamptic women. Increased adiponectin levels in women with preeclampsia could minimize the excess fat accumulation in tissues. The increased circulating levels of adiponectin may also block the expression of adhesion molecules in vascular endothelial cells and cytokine production from macrophages. Therefore, elevation of adiponectin concentrations could inhibit the inflammatory events that are proposed the major etiology of preeclampsia.

Nien *et al*[13], studied circulating levels of adiponectin in women with severe preeclampsia compared with healthy pregnant women. They observed that, circulating levels of adiponectin are significantly higher in women with severe preeclampsia than normal control group. This result was confirmed by our study. Nien *et al.* study also showed that adiponectin levels of normal pregnant women correlate negatively with BMI. Unlike Nien *et al.* study, we observed the correlation in women with preeclampsia. Nien *et al.* also observed that overweight normal pregnant women have lower adiponectin levels than those who are normal weight while overweight and normal weight preeclamtic patients have similar adiponectin concentrations. In contrast to Nien *et al.* in our study overweight preeclamtic women had lower adiponectin levels than those who are normal weight.

Lu *et al*[6], study showed that women with preeclampsia have higher concentrations of circulating adiponectin than healthy pregnant women. Although adiponectin has anti-inflammatory and endothelial cells protecting properties, but excessive inflammation and endothelial dysfunction are characteristics of preeclampsia. Therefore, when pathological characteristics of preeclampsia and elevation of circulating levels of adiponectin are considered together, it is obvious that the role of adiponectin in the pathogenesis of preeclamsia is difficult to understand.

CONCLUSION

In summary, according to present study circulating levels of adiponectin is increased in preeclamptic patients compared with normal pregnant women. Elevation of adiponectin levels might be a physiological feedback response to minimize endothelial dysfunction in preeclamptic patients.

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Address for Correspondence:

Dr. Ali Khosrowbeygi, Department of Biochemistry, School of Medicine, Lorestan University of Medical Sciences (Pardis Kamalvand), Broujerd Road, Khorramabad, Lorestan, Iran. PO Box: 381351698. **Tel:** +98-6616200133
E-mail: khosrowbeygi@yahoo.com, khosrobigi.a@lums.ac.ir