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Leptin to adiponectin ratio in preeclampsia

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Abstract

The aim of the present study was to assess leptin/adiponectin ratio in preeclamptic patients compared with normal pregnant women. A cross-sectional study was designed. The study population consisted of 30 preeclamptic patients and 30 healthy pregnant women. Serum levels of total leptin and adiponectin were assessed using commercially available enzyme-linked immunosorbent assay methods. The one-way ANOVA and Student's *t* tests and Pearson's correlation analysis were used for statistical calculations. Levels of leptin and adiponectin were also adjusted for BMI. A *p*-value <0.05 was considered statistically significant. The leptin/adiponectin ratio was increased significantly in preeclamptic patients. The leptin/adiponectin ratio was significantly higher in severe preeclamptic patient than in mild preeclampsia. Adjusted leptin/adiponectin ratio was also significantly increased in preeclamptic patients than in normal pregnant women. The findings of the present study suggest that the leptin/adiponectin ratio was increased in preeclamsia and imbalance between the adipocytokines could be involved in the pathogenesis of preeclampsia.

Introduction

Preeclampsia is a pregnancy specific syndrome and it is a major cause of maternal and perinatal morbidity and mortality[1-5]. The exact etiology of preeclampsia remains unknown[2,6]. Studies have shown a relationship between preeclampsia and increased risk of maternal coronary heart disease and metabolic syndrome in later life[7,8].

Leptin is a cytokine that was originally thought to be secreted only by white adipose tissue with a role in the regulation energy homeostasis. However, the hormone is now known to be produced by human placental trophoblasts regulating fetal growth and development. Leptin is also thought plays a role in the regulation of insulin sensitivity[7]. Adiponectin is an adipokine produced almost exclusively in adipose tissue. The hormone has been considered to sensitize other organs to the effects of insulin, inhibit vascular inflammation and atherogenesis, and protect against atherosclerosis[7,9].

The findings of leptin and adiponectin serum levels[7,8,10-12] and leptin/adiponectin ratio[7,11] in preeclamptic women are conflicting. Therefore, the aims of the present study were to determine (i) maternal circulating levels of leptin and adiponectin and (ii) leptin/adiponectin ratio in preeclamptic women compared with normal pregnant 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. Sixty pregnant women attending the Women's Hospital of Lorestan University of Medical Sciences were included in the present study. Of these 30 women were preeclamptic patients and 30 age-, gestational week-, and body mass index (BMI) - matched were as normal group. 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-h urine collection. Severe preeclampsia was defined as blood pressure equal to or higher than 160/110 mmHg or a proteinuria greater than 2.0g in a 24-h urine collection. Exclusion criteria were smoking, multiple gestation, diabetes mellitus, chronic hypertension, heart failure, inflammatory or infective disorders, and infectious disease[13-16]. 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 concentrations of total leptin and adiponectin were measured using commercially available enzyme-linked immunosorbent assay (ELISA) methods (BioVendor Laboratory Medicine, Inc. Czech Republic). The procedures for the methods were according to the instructions provided by the manufacturer. Absorbances were measured at a wavelength of 405 nm using ELISA reader (STAT FAX 2100, USA). The levels of leptin and adiponectin are presented as ng/ml and µg/ml, respectively. Data were analyzed using one-way ANOVA and unpaired Student's *t* tests.

Coefficients of correlation were calculated using Pearson'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)[13-15].

Results

Clinical characteristics of normal pregnant women and preeclamptic patients are shown in Table I. There were no significant differences in age, gestational age, and BMI between the study and normal pregnant women. Women with preeclampsia had a higher mean systolic (p=0.001) and diastolic (p=0.001) blood pressures than the normal pregnant women.

The comparison of leptin, adiponectin and leptin/adiponectin ratio in preeclamptic and normal pregnant women are presented in Table II. Serum levels of both leptin and adiponectin were significantly higher in preeclamptic group than in normal control group (p=0.001). The leptin/adiponectin ratio was increased significantly in preeclamptic patients (p=0.02).

Patients were then stratified to mild (n=16) and severe (n=14) preeclampsia (Table III). Women with mild and severe preeclampsia showed significant increasing in the serum levels of both leptin and adiponectin compared with normal control group (p=0.01). No significant difference was observed between mild and severe preeclampsia. Women with severe preeclampsia showed significant increasing in leptin/adiponectin ratio compared with control group (p=0.01) and mild preeclamptic women (p=0.03). The leptin/adiponectin ratio showed no significant differences between mild preeclampsia and normal pregnant women.

The leptin/adiponectin ratio showed a significant positive correlation with diastolic blood pressure values in patient group (r=0.41, p=0.03) (Fig. 1). When both normal pregnant women and preeclamptic patients were pooled (n=60), the ratio showed a significant positive correlation with both systolic (r=0.34, p=0.01) (Fig. 2) and diastolic (r=0.38, p=0.01) (Fig. 3) blood pressures. In pooled sample, levels of both leptin and adiponectin showed a significant positive correlation with systolic (r=0.49, p=0.000; r=0.49, p=0.000, respectively) and diastolic (r=0.49, p=0.000; r=0.35, p=0.001, respectively) blood pressures (data not shown). Levels of both leptin and adiponectin showed a significant relationship with BMI. Therefore, levels of leptin and adiponectin were adjusted for BMI. Adjusted leptin values were slightly higher in preeclamptic group than in normal control group (20.86±0.45; 19.88±0.25 ng/ml, respectively; p=0.06), while adiponectin levels were significantly decreased (13.29±0.18; 14.00±0.13 µg/ml, respectively; p=0.01). Adjusted leptin/adiponectin ratio were significantly increased in preeclamptic patients than in normal pregnant women (1.62±0.05; 1.40±0.03, respectively; p=0.03).

Table I: Characteristics of preeclamtic and normal pregnant women

Parameter	Normal pregnant (n=30)	Preeclamptic (n=30)	*p*
Age (years)	31.57±0.33	32.53±0.47	0.2
Gestational age (weeks)	39.10±0.23	38.50±0.23	0.09
BMI before pregnancy (kg/m^2)	21.95±0.50	23.65±0.75	0.08
Third trimester BMI (kg/m^2)	26.22±0.51	27.88±0.78	0.1
Systolic blood pressure(mm Hg)	109.33±1.26	154.00±1.48	0.001
Diastolic blood pressure(mm Hg)	68.67±1.41	98.00±2.06	0.001

Data were analyzed using unpaired Student's *t* test and presented as mean±SEM, BMI=body mass index.

Table II: Serum leptin and adiponectin levels of preeclamtic and normal pregnant women

Parameter	Normal pregnant (n=30)	Preeclamptic (n=30)	*p*
Leptin (ng/ml)	16.61±1.45	24.14±0.60	0.001
Adiponectin (µg/ml)	10.96±0.78	16.36±0.79	0.001
Leptin/adiponectin ratio	1.23±0.11	1.54±0.06	0.02

Data were analyzed using unpaired Student's *t* test and presented as mean ± SEM.

Table III: Maternal serum levels of leptin and adiponectin in mild and severe preeclampsia (PE) compared with normal pregnancy

Parameter	Normal (n=30)	Mild PE (n=16)	Severe PE (n=14)	*p* [a]	*p* [b]	*p* [c]
Leptin (ng/ml)	16.61±1.45	23.62±0.82	24.73±0.89	0.00	0.00	0.37
Adiponectin (µg/ml)	10.96±0.78	15.87±1.30	16.79±0.97	0.00	0.00	0.57
Leptin/adiponectin ratio	1.23±0.11	1.43±0.07	1.69±0.09	0.27	0.00	0.03

Results were analyzed using one-way ANOVA test and presented as mean±SEM.
[a]Mild PE compared with normal pregnancy; [b]Severe PE compared with normal pregnancy; [c]Comparison between mild and severe PE.

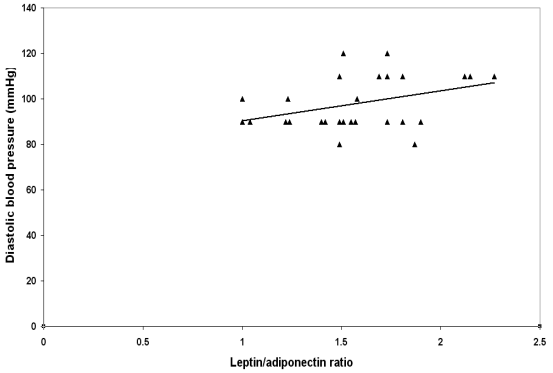

Figure 1: Correlation between leptin/adiponectin ratio and diastolic blood pressure in the patients with preeclampsia (n=30) (r=0.41, p=0.03). Coefficient of correlation was calculated using Pearson's correlation analysis.

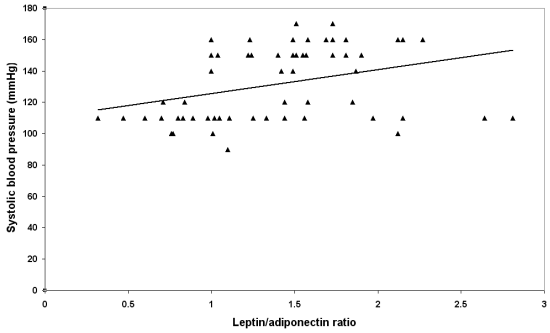

Figure-2: Correlation between leptin/adiponectin ratio and systolic blood pressure in entire 30 preeclamptic and 30 normal pregnant women (r=0.34, *p*=0.01). Coefficient of correlation was calculated using Pearson's correlation analysis.

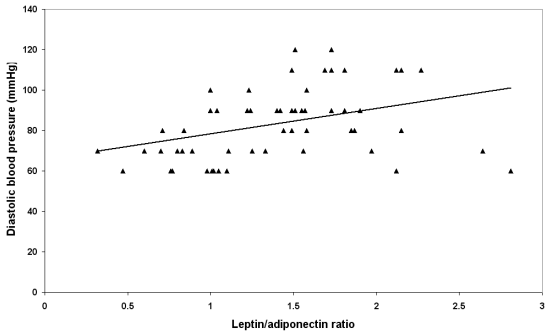

Figure-3: Correlation between leptin/adiponectin ratio and diastolic blood pressure in entire 30 preeclamptic and 30 normal pregnant women (r=0.38, *p*=0.01). Coefficient of correlation was calculated using Pearson's correlation analysis.

Discussion

The most relevant finding of this study was a significant increasing of the leptin/adiponectin ratio in the preeclamptic patients compared with normal pregnant women.

The present study findings are agree with results obtained by others who observed that circulating levels of leptin are significantly higher in preeclampsia than in normal pregnancy[7,8,10-12,17-22] However, our finding was not agree with the result of Laml et al[23] study who reported that the levels of leptin are decreased in preeclamptic women. In contrast to our study Martínez-Abundis et al[24] observed that there is no significant difference in serum leptin levels between women with preeclampsia and normotensive healthy pregnant women.

The results of the present study were in line with the studies reporting the increased circulating levels of adiponectin in preeclamptic patients compared with normal pregnant women[11,12,20,25-28]. However, the present study findings do not agree with studies that showed studies who showed preeclamptic women have lower circulating concentrations of adiponectin than healthy pregnant women[7,8,22,29].

Ouyang et al[7] first reported the leptin/adiponectin ratio in preeclamptic patients. They observed a significant increasing of the ratio in preeclampsia compared with normal pregnancy that confirmed by the present study. However our data were not agreed with Nakatsukasa et al[11] study that showed there is no significant difference in leptin/adiponectin ratio between preeclamptic patients and healthy pregnant women. The leptin/adiponectin ratio is more informative parameter of insulin resistance than leptin and adiponectin alone. Insulin resistance is characteristic of normal pregnancy and preeclampsia that associates with metabolic changes[7,11].

Haemoconentration is a main characteristic of preeclamptic women. However, Naruse et al[12] study showed that leptin levels are significantly higher in preeclamptic women before and after correcting for haematocrit than in normal pregnant women.

In the present study maternal circulating levels of leptin and adiponectin were adjusted for BMI[1,14,15,30]. Adjusted leptin values were slightly increased in preeclamptic group, while adjusted adiponectin levels were significantly decreased. However, adjusted leptin/adiponectin ratio was significantly higher in preeclamptic patients than in normal pregnant women. It could be concluded that the ratio does not depend on adjusting the levels of leptin and adiponectin for BMI.

The leptin/adiponectin ratio could be used as a serologic biomarker of preeclampsia progression and severity. It might have important diagnostic and therapeutic implications[7]. However, the limited data available are contradictory. On the other hand, longitudinal studies assessing this biomarker are scarce. Therefore, it should be explored in future research with higher sample size.

The findings of the present study suggest that the leptin/adiponectin ratio, a parameter of insulin resistance, was increased in preeclamsia. Therefore, perturbation of the adipocytokines and insulin resistance could be involved in the pathogenesis of preeclampsia. The authors also concluded that the leptin/adiponectin ratio may be more informative than leptin and adiponectin alone in preeclampsia.

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