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Serum Leptin Level in Severe Preeclampsia

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Abstract

Background Preeclampsia is a major cause of maternal morbidity and mortality with unknown aetiology. Placental hypoperfusion and diffuse endothelial cell injury are considered the central pathological process. Many adipocyte hormones like leptin play an important role in the inflammatory and atherosclerotic process and may be used as a marker for preeclampsia.

Objective To find the role of serum leptin measurement in pregnant women as a marker of preeclampsia.

Methods Seventy six primigravida women in their 3rd trimester of pregnancy were studied; 44 of them with severe preeclampsia, while the other 32 women with normal blood pressure without any history of previous diseases. Blood samples were taken for serum leptin, uric acid and creatinine levels, urine samples were collected for albumin. Serum leptin level was measured by ELISA kits.

Result Serum leptin and uric acid levels but not the creatinine was different in eclamptic group than control group. Mean age, height and weight were not different between the two groups. The systolic and diastolic blood pressures were also different between the two groups. 26 cases (59.1%) had proteinuria of 3+ albumin and 18 cases (40.9%) with 4+.

Conclusion Elevated serum leptin level can be used as a marker in the assessment of preeclampsia.

Key words Primigravida, preeclampsia, serum lipten.

Introduction

Preeclampsia is a systemic disease characterized by hypertension and proteinuria; and it continues to be an important cause of maternal morbidity and mortality. The cause is not yet clear; it includes immunological, genetic, environmental and placental abnormality. The final result of all of these is endothelial dysfunction, characteristic of preeclampsia [(1)]. Preeclampsia refers to the onset of hypertension and proteinuria after 20 weeks of gestation in a previously normotensive woman.

The clinical manifestations of preeclampsia can appear anytime from the second trimester to the first few weeks postpartum; however, the initial pathological changes begin in the late first trimester and consist of abnormal remodeling of the spiral arteries [(2)]. Because the only cure is delivery, preeclampsia is associated with a high maternal and neonatal morbidity and mortality, so preeclampsia is believed to account for 15% of premature delivery and 17.6% of maternal death worldwide [(3,4)]. Preeclampsia is the 3rd leading cause of maternal mortality and can complicate 3-14% of all pregnancies [(5,6)]. The disease is mild in 75% of cases and severe in 25% [(7-9)].

A good test for predicting women who will develop preeclampsia should be simple, rapid, noninvasive, inexpensive, and easy to perform and should not expose the patient to discomfort

or risk. Ideally, it should provide an opportunity for intervention to prevent development of the disease, or at least result in better maternal and/or fetal outcomes [10].

Leptin (from the Greek "leptos"; meaning thin) is a protein hormone with important effects in regulating body weight, metabolism and reproductive functions [11]. The protein has 167 amino acid sequence containing one disulphide bond, it's molecular weight is about 16 KDs and has four helix bundle with one very short strand segment and two relative intermitting loops [12]. In pregnant women, leptin is synthesized in and secreted from placental trophoblast into maternal circulation at a considerable amount comparable with those in non pregnant woman [13]. Leptin is also produced by a culture of human choriocarcinoma cell line. Plasma leptin level is also markedly elevated in patient with Hydatidiform mole and choriocarcinoma, indicating that gestational trophoblastic neoplasms are leptin producing tumors. It has been demonstrated that placental production of leptin is augmented in women with severe preeclampsia [14].

Ouyang *et al*. [15] did a case control study between women with severe preeclampsia and normotensive women regarding serum leptin and found a significant elevation of serum leptin in women with severe preeclampsia. This finding pointed to the importance of leptin in the pathophysiology of preeclampsia and their involvement in the pathogenesis of the disease. As leptin causes oxidative stress in endothelial cells and has a calcifying effect on these cells, it has been suggested that leptin promote atherogenesis.

So, in pregnancy induced hypertension, placental ischemia is responsible for increased leptin level with increase in the inflammatory cytokines such as TNF alpha and IL-6 [16]. The aim of this work is to study the correlation between serum Leptin and severe preeclampsia.

Methods

This cross-sectional age-control study was done in the Department of Obstetrics and Gynecology/Baghdad Teaching Hospital-Medical City during the period from January 2010 to August 2010. A total number of 76 primipara in their third trimester where included in this study. Women with preexisting chronic hypertension, Diabetes mellitus, multiple pregnancies, chronic renal disease, chronic liver disease, and those with history of hyperuricemia were excluded from the study.

After taking detailed obstetrical and medical history 32 patients were having normal blood pressure without any history of prior hospitalization; while other 44 patients were presented with severe hypertension; diagnosed as systolic blood pressure of 160 mmHg and more and diastolic blood pressure of 110 mmHg and more, with a marked proteinuria on dipstick test in a random urine samples. After counseling and affordability of investigation, their blood samples were drawn for serum creatinine and uric acid.

Other samples were collected to obtain and clarify sera. Those samples were left to stand at room temperature for at least 30 minutes to allow the blood to clot, then centrifuged for 5 minutes, frozen at (-20 °C) and kept there without thawing till the day of testing. Then, serum leptin was measured using ELISA sandwich kits with the range of the assay from 0 to 100 ng/dl, also urine samples were taken for proteinuria by dipstick.

Results

Table 1a & b show that there was no statistically significant differences regarding body mass index between the two groups, while there were statistically significant differences regarding systolic and diastolic blood pressure ($P < 0.0001$). Their albumin in urine dipsticks on random urine samples show proteinuria in all cases of severe PET group (100%), while it was nil in all cases of the control group (100%).

There is statistically significant difference regarding serum leptin and serum uric acid between the two groups ($P = 0.0001$) While serum creatinine show mean±SD of 0.92 ± 0.18 in the severe PET group which is the upper

normal value, and of 0.86 ± 0.15 in the controls group which shows no statistical significant difference between them (Table 2).

Table 3 shows the correlation between serum leptin and serum uric acid in the severe PET group (r = 0.511). In addition, there was correlation between serum leptin and serum creatinine in the severe PET group (r = 0.724).

Table 1a. The Demographic Criteria of Patients with Severe Preeclampsia and the Control Group

Parameter		PET	Control group
Age (years)		23.95 ± 3.24	23.78 ± 3.23
BMI (Kg/m2)		30.33 ± 4.64	30.23 ± 4.96
Blood Pressure (mmHg)	Systolic BP	171.59 ± 14.3	111.72 ± 7.68*
	Diastolic BP	119.55 ± 8.88	68.44 ± 7.98*

* = $P < 0.0001$

Table 1b. The Demographic Criteria of Patients with Severe Preeclampsia and the Control Group

		PET		Control	
Parameter		Number	%	Number	%
Age (years)	< 20	6	13.6	5	15.6
	20-24	18	40.9	13	40.6
	25-29	20	45.5	14	43.8
Albumin	Nil	-	-	32	100
	+	-	-	-	-
	+++	26	59.1	-	-
	++++	18	40.9	-	-

Table 2. The distribution of Serum Leptin, Creatinine and uric acid in Severe Preeclamtic Group and the Control group

Parameter	PET		Control group	
	Mean±SD	Range	Mean±SD	Range
Leptin (ng/dl)	73.65 ± 38.13	7.0 - 140.0	23.08 ± 13.87	6.9 - 48.0*
Creatinine (mg/dl)	0.92 ± 0.18	0.7 - 1.3	0.86 ± 0.15	0.7 - 1.1
Uric acid (mg/dl)	5.53 ± 0.95	3.7 - 7.0	3.85 ± 0.86	3.0 - 6.0*

* = $P < 0.0001$

Table 3. The Correlations of Serum Leptin with Different Parameters in Both Control and PET Group

Parameter	Leptin (ng/dl)		Level of Significance
	Control	PET	
Age (years)	0.604	0.451	r
	0.0001	0.002	*P*
BMI (Kg/m^2)	0.801	0.098	r
	0.0001	0.527	*P*
Systolic BP (mmHg)	0.016	0.267	r
	0.931	0.079	*P*
Diastolic BP (mmHg)	0.142	0.014	r
	0.438	0.929	*P*
Uric acid (mg/dl)	0.258	0.511	r
	0.154	0.0001	*P*
Creatinine (mg/dl)	0.397	0.724	r
	0.024	0.0001	*P*

Discussion

Our study shows that all patients with severe preeclampsia have upper normal creatinine level which may indicate that the patient start to have a defect in glomerular function; in that the serum creatinine level still does not exceed upper normal level, and this may explain why there is accumulation of serum uric acid and leptin which depend on glomerular filtration in spite of normal creatinine level.

This may be due to high sensitivity of leptin and uric acid to the early changes in glomerular function than serum creatinine [15], so leptin can be used possibly as an indicator of severity of preeclampsia, which indicates that the patient started to have affected glomerular filteration by severe preeclampsia. This is in agreement with the study done by Laivuori *et al*. [17], where they explain that as leptin is eliminated mainly through the kidney and preeclampsia can be accompanied at least by histological renal changes [18]. The correlation between serum leptin, serum creatinine and serum uric acid suggest an association, either direct or indirect, between elevated serum leptin and renal changes in preeclampsia. Finally it could be concluded that elevated serum leptin level can be used as a marker in the assessment of severe preeclampsia.

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