Leptin Values in Maternal and Umbilical Cord Blood in Pregnant Women with Preeclampsia

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Abstract

Background: Leptin is a protein product of obesity gene and is synthesized mainly by adipose tissue.

Objective: The aim of this study was to determine maternal and neonatal serum leptin levels in preeclamptic and normal pregnancies.

Patient and Methods: This corss sectional study was performed on 45 preeclamptic and 45 normotensive pregnant women without other disease.Serum level of leptin was measured in all of pregnant mothers and after delivery,measured in umbilical cord of their neonates. This study was performed in Hospitals of Suez Canal University.

Results: In this study, when comparing the serum leptin levels between normal pregnancies and pregnancies complicated with both mild and sever preeclampsia there was a highly statistically significant deference in between ($p< 0.01$). plasmaleptin concentrations were significantly greater in women with pre-eclampsia than in normal controls.Umbilical cord leptin concentrations were significantly greater in women with pre-eclampsia than in normal controls. Cord blood leptin in the present study showed that there is significant positive correlation with severity of pre-eclampsia.

Conclusion: According to the results, we detected an increase in maternal plasma and umbilical cord leptin in preeclamticgroup.There was a highly statistically significant deference in between preeclamtic group and the matched control group

Keywords: Leptin, Pre-eclampsia, Umbilical Cord

Introduction

Leptin is a 16KD polypeptide hormone and the protein product of obesity gene,issynthesised and secreted mainly by adipose tissue (1). Under the supervision of the obesity gene,the adipocytes and placental trophoblasts secrete leptin which decreases the body weight by acting through its hypothalamic receptors and reducing the food intake.Leptin also act as ametabolic signal for the neuroendocrine and reproductive systems (2). Trophoblasts are responsible for the significantly increased plasma concentrations of leptin during the first two trimesters of normal pregnancy.This marked increase in synthesis of leptin is attributed to the prominent alterations of maternal weight,energy expenditure and hormonal status (3). The expression of leptin by the human trophoblasts significantly increased when cultured under hypoxic conditions.Placentalischaemia could therefor explain the rapid increase in leptin concentrations during late third trimester in preeclampsia(4). Processes associated with preeclampsia,includ-

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ing placental hypoxia lead to increased leptin levels for a compensatory mechanism to increase nutrient delivery to the fetus,by stimulating placental angiogenesis, aminoaciduptake and inhibiting apoptosis(5). Leptin levels are higher among women than men because women have abody mass index with relative higher content of fat and serum leptin level proportional to adiposity.Maternal serum leptin levels during pregnancy higher than those non pregnant women (6). Umbilical cord blood leptin is derived from fetal tissue.It is detectable by gestational week 18 but only increases to significant level after 34 weeks.Whereas much maternal leptinproduced by the placenta,most cord leptin is produced by fetal adipose tissue(7). Leptin levels in umbilical cord at term are correlated with birth weight(8).

Preeclampsia is a pregnancy-specific, multisystem disorder that is characterized by the development of hypertension more 140/90mmHg and proteiurea>300mg/day after 20 weeks of gestation in a woman with previously normal blood pressure(9). Preeclampsia is a common and serious complication of human pregnancy, affecting 5-7% of primigravid women and about 10-15% of all pregnant women(10). Preeclampsia can be subclassified into early onset, arrising before 34 weeks gestation, or late onset, arrising at or after 34 weeks gestation. Early onset preeclampsia carries a significantly greater risk of maternal and fetal morbidity and mortality due to larger and longer placental under-perfusion and prematurity (11). Preeclampsia may occur due to incomplete trophoblastic invasion and diffuse endothelial dysfunctions lead to hypoxic state and enhance leptin production (12). The exact aetiology of preeclampsia remains unknown, numerous biochemical, biophysical and clinical tests have been proposed for prediction, evaluation and assessement of aetiology, pathogenesis, courseand severity of this disease. However, it is unknown whether elevated leptin levels are the causes or consequences of preeclampsia (13).

Patient and Methods

This prospective case control study was carried out on 90 pregnant women in their third trimester of singleton pregnancies recruited from the obstetric department of Suez Canal University Hospital between April 2014 and April 2015. Divided into two equal groups. Consent was taken from each patient before investigation and management. 45 preeclamptic patients between 28-40weeks gestation subdivided into two groups, including 22 cases of mild preeclampsia and 23 cases of severe preeclampsia . 45 pregnant ladies with normal pregnancies without any symptoms or signs of preeclampsia.The inclusion criteria for the preeclampsia group were a blood pressure of 140/90mmHg or more and 300 mg or more protein in 24 hour urine sample ,or ++2 proteinuria dipstick finding in a random urine sample.preeclamptic patients wih these criteria who had not received any medications were included in the study.No medications was given to these patients before blood was taken for leptin levels and other routine tests.Patients with any of the following disorders were excluded:

1. Diabetes mellitus.
2. Essential hypertension.
3. Multifetal gestation.
4. Polyhydramnios.
5. Patient with any known medical diseases affecting the results as renal , cardiac and autoimmune diseases.
6. Body Mass Index > 27.

Sample preparation

Ten mL Blood were collected by sterile veniopuncture with 18 gauge needle from the patient before any treatment. 5 mL were transferred to test tube labelled with the name and number of the patient. The test tube was then centrifuged in cold centrifuge for 20 minutes. Serum was then separated and stored frozen at -70○C till the assay of leptin. The remaning 5 mL were similarly centrifuged, serum separated and transferred to assay of the remaning tests.5 ml blood were collected by sterile veniopuncture with 18 gauge needle from the umbilical cord after delivery and transferred to test tube labelled with the name and number of the patient to assay serum cord leptin.The maternal and umbilical cord blood leptin concentrations of preeclamptic group (n=45) were compared with those of normal pregnancies (n=45)who have similar BMI and gestational age matched.

Statistical Analysis

The clinical and laboratory data were recorded on a “investigative report form”. The data were analyzed statistically using statistical software package

"SPSS", version 9.05, EchoSoft Corp., USA, 1998. The following stastical tests were used:

I. Descriptive statistics: Mean (X), standard deviation (SD) Minimum and maximum values (range)

II. Student "t" test: to compare between independent means of parametric data.

The results were evaluated at the 95% confidence interval, and $p<0.05$ significance level.

Results

In this study, 90 patients were analysed. Amoong which 45 were normotensive and 45 preeclampticpatients.Out of 45 preeclamptic, 22 were with mild preeclampsia and 23 were having sever preeclampsia.There was a significant statistical high level of maternalleptin in severe pre-eclampsia(48.96 ± 5.53ng/ml.) when compared to mild pre-eclampsia(28.05 ± 5.7ng/ml.) which in turn shows higher levels of leptin when compared to control group(26.18 ± 3.37ng/ml). Thus, the difference between the pre-eclamptic groups as a whole and the control normotensive group was statistically significant (table 1).There was a significant statistical high level of umbilical cord leptin in severe pre-eclampsia (6.65 ±1.11ng/ml.) when compared to mild pre-eclampsia (4.45 ± 0.86ng/ml.) which in turn shows higher levels of leptin when compared to control group (4.04 ±1.10ng/ml.). Thus, the difference between the pre-eclamptic groups as a whole and the control normotensive group was statistically significant(table 2).The age of mild pre-eclamptic group ranged from 21-40 years with a mean of 27.45±6.29 years.

The age of severe pre¬-eclamptic group ranged from 20-38 years with a mean of 27.13±5.91 years. The age of control group ranged from 20-40 years with a mean of 27.1±5.98 years.There was no statistical significant difference between the three studied groups regarding the age.

There was statistically significant difference between the three studied groups regarding the gestational age, blood pressure, blood picture, renal function, liver function and proteinuria. The results are summarized in table (3).

Table (1): Maternalleptin among the studied groups.

	Maternal leptin			ANOVA	
	Range	Mean ±	SD	f	P-value
Group A1 (Mild P.)*	22 - 35	28.05 ±	5.7	48.9	<0.01
Group A2 (severe P.)	38 - 60	48.96 ±	5.53		
Group B (control)	20 - 33	26.18 ±	3.37		
Tukey's test					
A1 & A2	**A1 & B**			**A2 & B**	
<0.01	<0.05			<0.01	

*P : preeclampsia

Table (2): Umbilical Cord leptin among the studied groups.

	Cord leptin			ANOVA	
	Range	Mean ±	SD	f	P-value
Group A1 (Mild P.)*	3 - 8	4.45 ±	0.86	48.3	<0.01
Group A2 (severe P.)	5 - 9	6.65 ±	1.11		
Group B (control)	3 - 7	4.04 ±	1.10		
Tukey's test					
A1 & A2	**A1 & B**			**A2 & B**	
<0.01	<0.05			<0.01	

Table (3): Statistical comparison of studied parameters between studied groups.

parameters	Mild Preeclampsia N=22 Mean±SD	Severe Preeclampsia N=23 Mean±SD	Control N=45 Mean±SD	Anova(F) test	Anova(F) test
Gestational age	35.78±1.73	31.83±2.64	37.05±1.86	41.4	<0.01
Systolic Bl.Pr.	145.45±5.10	186.96±17.95	114.70±5.05	198.3	<0.01
Diastolic Bl.Pr.	94.55±5.10	111.30±7.57	74.90±5.06	112.9	<0.05
Haemoglobin	10.35±0.61	9.85±0.55	10.9±0.62	3.9	<0.05
Platelet Count	194.32±33.00	181.22±21.04	224.42±49.35	10.1	<0.01
Urea	25.09±5.29	30.91±7.58	22.84±3.37	18.4	<0.01
Creatinine	1.05±0.13	1.12±0.12	1.00±1.00	16.3	<0.01
Uric Acid	4.15±0.54	4.76±0.89	3.72±0.60	18.3	<0.01
SGPT	18.23±2.09	38.17±7.19	16.11±2.55	22.6	<0.01
SGOT	19.42±3.02	37.92±6.99	17.2±1.99	26.4	<0.01
Protinuria	429.0±65.3	2707.2±485.7	<300	10.99	<0.01
Prothrombine	90.59±3.80	87.30±3.90	92.71±4.02	12.4	<0.01

There was positive correlation between maternal leptin and umbilical cord leptin, systolic and diastolic blood pressure, urea, uric acid,creatinine, SGOT, SGPT and protinuria (table 4).Also,there was positive correlation between cord leptin and maternal leptin, systolic and diastolic blood pressure, urea, uric acid, creatinine, SGOT, SGPT and protinuria (table 5). Cut off between Group A (pre-eclampsia) and Group B (control) as regard maternal leptin = 39 by sensitivity = 88.6, specifity =100.0, positive predictive value =100.0, negative predictive value =71.4 by accuracy = 0.957.

Cut off between Group A (pre-eclampsia) and Group B (control) as regard cord leptin = 5.5 by sensitivity = 87, specifity =60.0, positive predictive value =88.6, negative predictive value =60.0 by accuracy = 0.730

Table (4): Correlation between maternal leptin and studied variable

	Maternal leptin	
	r	**P.value**
Age	-0.090	>0.05
Gestational age	-0.536	<0.01
Systolic blpr	0.741	<0.01
Diastolic blPr	0.641	<0.01
Hg	-0.332	<0.05
Platelets	-0.222	>0.05
Sgpt	0.88	<0.01
Sgot	0.87	<0.01
Urea	0.262	>0.05
Creatinine	0.391	<0.01
Uric acid	0.294	0.05
Prthrombin activity	-0.427	<0.01
Umbilical cord leptin	0.602	<0.01
protinuria	0.739	<0.01

Table (5): Correlation between cord leptin and studied variable

	Umbilical cordleptin	
	r	**P.value**
Age	-0.113	>0.05
Gestational age	-0.511	<0.01
Systolic blpr	0.66	<0.01
Diastolic blPr	0.639	<0.01
Hg	-0.052	>0.05
Platelets	-0.318	<0.01
Sgpt	0.7	<0.01
Sgot	0.69	<0.01
Urea	0.482	<0.01
Creatinine	0.291	<0.01
Uric acid	0.455	<0.01
Prthrombin activity	-0.397	<0.01
Maternal leptin	0.602	<0.01
protinuria	0.739	<0.01

Discussion

Preeclampsia may be mild or severe depending on the degree of blood pressure elevation, degree of proteinuria, extent of edema and the presence of signs and symptoms, including epigastric pain, severe headache and blurred vision. However severe pre-eclampsia can result in bleeding disorders and death (14).

The present study demonstrated that maternal plasma leptin is increased in women with pre-eclampsia compared to normal pregnant woman. Furthermore, maternal plasma leptin concentration in pre-eclampticspositivily correlates with fetal cord concentrations. This is only present in pre-eclamptic woman but not in healthy pregnant woman.

In a longitudinal study done by Kolyingit et al. (15) showed that increased plasma leptin level with severity of pre-eclampsia could be taken as a marker of placental hypoxia in severe pre-eclampsia.

In the current study, the mean value of plasma leptin level in control group (normotensive pregnant women) was 26.18 ± 3.37ng/ml, in mild preeclamptic group it was 28.05 ± 5.7ng/ml and in sever preeclamptic group it was 48.96 ± 5.53ng/ml.

In the current study, according to Receiver Operating Characteristic (ROC) curve of serum leptin and preeclampsia, the best cutoff value was 39ng/ml which gives a sensitivity of 88% and specificity of 100 %.

In this study, when comparing the serum leptin levels between controls and pregnancies complicated with both mild and sever preeclampsia there was a highly statistically significant deference in between ($p< 0.01$). This in correspondence with the study by Anim-Nyame et al. (16)in whichCirculating concentrationsof leptin were measured (19 women with pre-eclampsia and 13 normal pregnantcontrols) In this study, plasma leptin concentrationswere significantly greater in women with pre-eclampsia thanin normal controls. This study confirmed thatplasma leptin concentrations are increased in established pre-eclampsia.

Also, the results of the study is in agreements with another study done by Donghong et al. (17)which was carried out to determine the changes in serum levels of adiponectin, leptin and soluble leptin receptor, and in the free leptin index in women with pre-eclampsia.

The result of the present work showed that maternal plasma leptin concentration reflects accurately the severity of hypertension in pre-eclamptic women. This is evidence by the significant positive correlation between leptin values and blood pressure measurements.This finding is consistent with finding of Donghong et al. (17)who found that maternal plasma leptin levels reflect the severity of hypertension in woman suffering from EPH Gestosis as they reported that there was a significant difference in leptin levels between those with severe EPH Gestosis as compared to mild or control and there was a significant positive correlation between leptin values and values of blood pressure.

Cord blood leptin in the present study showed

that there is significant positive correlation with severity of pre-eclampsia. the mean value of cord leptin level in control group (normotensive pregnant women) was 4.04 ± 1.10ng/ml, in mild preeclamptic group was 4.45 ± 0.86ng/ml and in sever preeclamptic group was 6.65 ± 1.11ng/ml. This is consistent with the study of Salvatores et al. (18), Acromite et al. (19),Kocyigit et al. (20) and Akerman et al. (21)who's study included 40 normotensive pregnant women and 80 women with pre-eclampsia measuring the concentration of leptin in the umblical cord and reported that the level of cord leptin increased with the severity of pre-eclampsia.

Many studies measured the concentration of leptin in umbilical cord and reported that the level of cord leptin varies between 2.5-10 ng/ml (19,22) and this correlates with the present study which ranged from 3-9 ng/ml.

Conclusion

Maternal serum leptin is increased in preeclamptic women and more in sever than mild preeclampsia. From previous data, it coud be concluded that serum levels of leptin may be used as a marker of severity of preeclampsia.Umbilical cord leptinincreased inpreeclamptic women than normal pregnancies.

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