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Full Length Research Paper

Comparison between Maternal Serum Leptin in Normotensive Pregnancy and Preeclampsia

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Abstract
Purpose to evaluate the value of maternal serum leptin as biomarker for prediction of pre-eclampsia, its onset and severity. This case control study was done among 90 pregnant women. They were divided into two groups (control and study) according to the absence or presence of clinical parameters of preeclampsia. Leptin was measured for both groups. Leptin levels were found to be significantly higher among all preeclampsia patients when compared to the control group. The mean value of serum leptin in normal group is (7.37 ± 3.39 ng/ml) versus (17.32 ± 1.57 ng/ml) in mild pre-eclampsia and (28.46 ± 3.19 ng/ml) in sever pre-eclampsia. The ROC curve analysis has shown that the cut-off value is (14.1 ng/ml) can be used to detect the pre-eclampsia with sensitivity of (91.3%) , specificity (65%) while the cut-off value is (21.55 ng/ml) can be used to detect the severity of pre-eclampsia with sensitivity of (85.2%) specificity (70%). Serum leptin increases significantly with occurrence of preeclampsia compared to normal pregnancy and even it is more increased with severe form of disease. It is a significant marker of both occurrence and severity of preeclampsia.

Keywords: *Pre-eclampsia- leptin-normotensive.*

Introduction

Pre-eclampsia is a complex and unpredictable disorder that may occur during pregnancy. Its presentation ranges from mild to severe, and the condition may lead to the death of the mother and/or the baby in extreme cases and remains a high cause of maternal and fetal morbidity and mortality in the developing world. The earlier the disorder is detected and managed, the better the outcome (Phipps et al., 2016). Leptin is primarily produced in adipose tissue but is also expressed in many other tissues, including the placenta, mammary gland, testes, ovary, endometrium, stomach, hypothalamus, pituitary, and others (Coppari and Bjorboek et al.,2012).In normal pregnancy, leptin supports implantation, human chorionic gonadotropin production, placental growth, amino acid uptake and lactation (Engl et al.,2012).Circulating leptin levels in pregnant women reach 2-3 fold higher concentrations as compared to non-pregnant conditions. During pregnancy the maternal plasma leptin concentrations rise in the first and second trimesters and peak during the third trimester and then return to normal after delivery (Vazque et al., 2015).

Patients and Methods

This case-control study was done in the department of obstetrics and gynecology- Al-Azhar University, New Damietta during the period from October 2016 to October 2017 and included 90 singleton pregnant women at age 25-30 years old with no risk factors of pre-eclampsia and were divided in to two groups :Group I (Control) : 30 normotensive pregnant women and Group II (Patient) : 60 preeclampsia pregnant women who were subdivided into 30 mild preeclampsia pregnant women and 30 sever preeclampsia pregnant women. Multiple pregnancy women or at age less than 20 years or more than 35 years or with preexisting chronic hypertension, preexisting diabetes mellitus, gestational diabetes, any chronic illness which may affect the results (renal disease, cardiac diseases or hepatic diseases), known history of peripheral vascular disease or obese patients (BMI $\geq$ 30) were excluded from the study. An informed written consent was obtained from all studied patients. Thorough obstetric history, complete general and obstetric examination was done. Ultrasound was performed in all patients to document fetal viability, evaluate gestational age, and fetal biometry, placental location, amniotic fluid volume and exclude multiple pregnancy.Dipstick urine test was done to detect proteinuria

in association with full laboratory investigations (CBC, ABO, RH, RBS, Urine analysis, ALT, AST, serum creatinine and uric acid). Leptin assay was done by obtaining 5 ml of peripheral venous blood from both groups under strict aseptic measures. Each sample was labeled with patient's name and identification number. Blood samples were transferred immediately to chilled siliconized glass tubes containing Na2EDTA (1 mg/ml) which was centrifuged and then stored at -20 co until assayed.Total circulating leptin concentration was measured by radioimmunoassay (RIA). Serum leptin levels were measured by enzyme linked immunosorbent assay (ELISA). Kit , EK-003-12 (from Phoenix Pharmaceuticals, INC) (U.K).

Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 15 for Windows® (SPSS Inc, Chicago, IL, USA).Quantitative data were presented as mean ± SD while qualitative data were expressed as numbers and percentages (%). Student t test was used to test significance of difference for quantitative variables and Chi Square was used to test significance of difference for qualitative variables; analysis of variance (ANOVA) test was used to compare quantitative variables among the three groups. Receiver operating characteristic (ROC) curve was used to identify a cut-off value for serum leptin levels to detect presence and severity of preeclampsia.A probability value (p value) 0.05 was considered statistically significant. Data were analyzed and appropriately presented in tables and figures.

Results

Table (1): Demographic data of studied groups

Character	Normal (control) group (N=30)	Pre-eclampsia (patient) groups (N=60)		P-value
		Mild (N=30)	Sever (N=30)	
Maternal age (years)	26.13 ± 3.32	26.30 ± 4.34	27.20 ± 4.56	P >0.05
Residency:	14	14	15	P >0.05
-urban	16	16	15	
-rural				
Work	14	15	13	
-employed	16	15	17	P >0.05
-not employed				
Education :	11	14	13	
-University				
-Read &Write	5	5	6	
-School	10	7	7	P >0.05
-Illiterate	4	4	4	
Body Mass Index(Kg / m^2	25.93 ± 1.58	26.17 ± 1.55	26.13 ± 1.65	P >0.05
Gestational age (weeks)	38.17 ± 1.46	37.80 ± 1.34	37.83 ± 1.52	P >0.05
Parity:	8	7	10	
-Primi	22	23	20	P >0.05
-Mult				
Blood Pressure:	11.33 ± 7.76	144.67 ± 5.07	177.00 ±12.91	
-Systolic				P<0.001*
-Diastolic	72.00 ± 7.61	95.00 ± 5.09	115.33 ± 12.52	

The comparison between normal and pre-eclampsia groups shows no statistical difference in Maternal age, Residency, Work, Education, Body Mass Index, Gestational age and Parity with P-value>0.05 while shows high statistical difference in Systolic Blood Pressure and Diastolic Blood Pressure with P-value <0.001.

Table (2): Laboratory investigations in studied groups

Parameter	Normal (control) group (N=30)	Pre-eclampsia (patient) groups (N=60)		P-value
		Mild (N=30)	Sever (N=30)	
Hemoglobin Hb%(g/dL)	10.88 ± 0.86	10.48 ± 0.96	10.30 ± 1.19	P >0.05
Platelet PLT(mm^3)	223.90 ± 48.01	210.27 ± 49.61	199.77 ± 55.89	P >0.05
Proteinuria:				
-Absent	29	6	0	

+1	+2	1	13	0	P<0.001*
+3	+4	0	11	2	
		0	0	20	
		0	0	8	

The comparison between normal and pre-eclampsia groups shows no statistical difference in Hemoglobin and Platelet with P-value>0.05. While shows high statistical difference in Proteinuria with P-value <0.001.

Table (3): Laboratory investigations in Pre-eclampsia groups

Parameter		Pre-eclampsia (patient) groups (N=60)		P-value
		Mild (N=30)	Sever (N=30)	
Liver functions:				
-AST (IU/L)	**-ALT**	**15.90 ±3.87**	**24.67 ± 8.47**	**P<0.001***
(IU/L)		**16.73 ± 4.05**	**25.47 ± 7.85**	
Serum Creatinine(mg/dL)		**0.63 ± 0.12**	**1.30 ± 0.23**	**P<0.001***
Uric Acid (mg/dL)		**17.93 ± 2.66**	**29.83 ± 11.82**	**P<0.001***

The present study showed statistically high significant differences in Serum Creatinine, Uric Acid, Alanine Transferase (ALT) and Aspartate Transferase (AST) in mild versus sever preeclampsia groups where P-value <0.001.

Table (4): Serum leptin in studied groups:

Parameter	Normal (control) group (N=30)	Pre-eclampsia (patient) groups (N=60)		P-value
		Mild (N=30)	Sever (N=30)	
Serum Leptin **(ng/ml)**	**7.37 ± 3.39**	**17.32 ± 1.57**	**28.46 ± 3.19**	**P<0.001***

The mean value of Serum Leptin in the Control groupwas (7.37 ng/ml); The mean value of Serum Leptin in the Mild group was (17.32 ng/ml); The mean value of Serum Leptin in the Sever group was (28.46 ng/ml); The comparison revealed statistically highly significant difference p- value<0.001.

Table (5): Accuracy of serum leptin as a biomarker of Pre-eclampsia

	S.leptin
Cut off point	14.1ng/ml
Sensitivity	91.3%
Specificity	65%
Positive predictive value (PPV)	100%
Negative predictive value (NPV)	70%
P value	< 0.001*

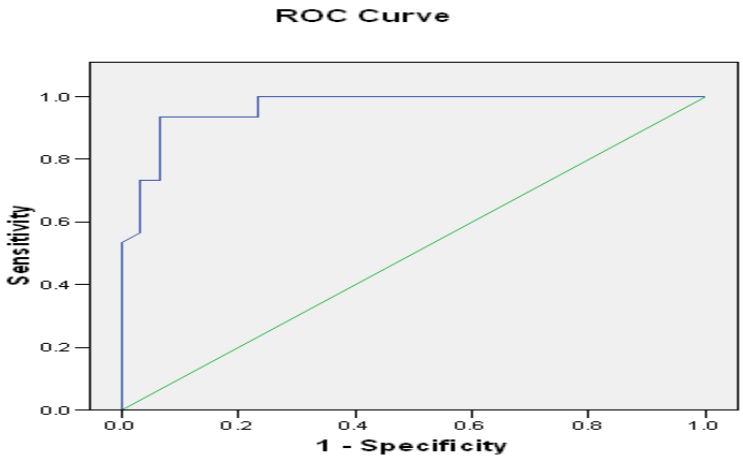

Fig (1): ROC curve of serum leptin as a biomarker of Pre-eclampsia.

The present study showed that the mean value of serum leptin in normal group is (7.37± 3.39 ng/ml) versus (17.32 ± 1.57 ng/ml) in mild pre-eclampsia and (28.46± 3.19 ng/ml) in sever preeclampsia respectively in comparison statistically high significant where P-value <0.001 and indicates that serum leptin increases with the severity of pre-eclampsia. The ROC curve analysis has shown that the cut-off value is (14.1 ng/ml) can be used to detect the pre-eclampsia with sensitivity of (91.3%) , specificity (65%), PPV (100%) and

PNV (70%) ,while the cut-off value is (21.55 ng/ml) can be used to detect the severity of pre-eclampsia with sensitivity of (85.2%), specificity (70%) , PPV (90%) and PNV (60.2%).

Table (6): Accuracy of serum leptin as a biomarker of severity of Pre-eclampsia

	S.leptin
Cut off point	21.55 ng/ml
Sensitivity	85.2%
Specificity	70%
Positive predictive value (PPV)	90%
Negative predictive value (NPV)	60.2%
P value	< 0.001*

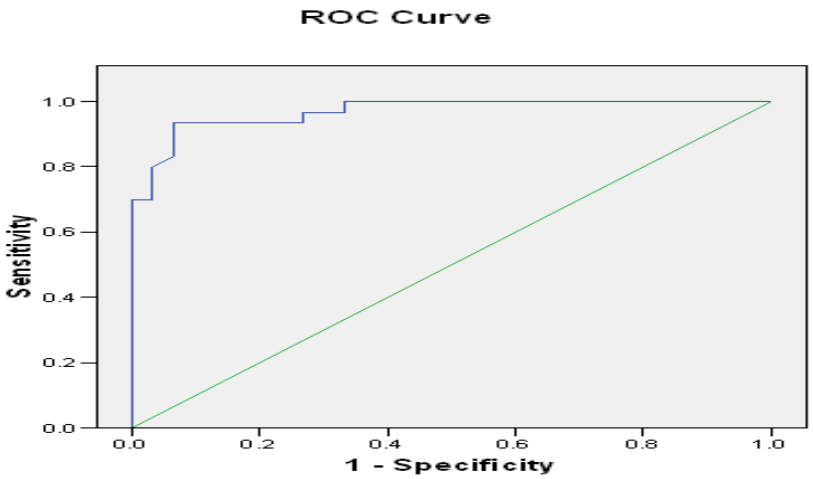

Fig (2): ROC curve of serum leptin as a biomarker of severity of Pre-eclampsia.

Discussion

The present study showed that the mean value of serum leptin in normal group is (7.37 ± 3.39 ng/ml) versus (17.32 ± 1.57 ng/ml) in mild pre-eclampsia and (28.46 ± 3.19 ng/ml) in sever preeclampsia respectively in comparison statistically high significant where P-value <0.001which indicates that serum leptin increases with the severity of pre-eclampsia. Our results agreed with Yingna Song et al., 2016, Kharb S, et al.,2016, Taylor,et al.,2015, Yusrawati.,et al.,2015, Salimi et al.,2014, Khosrowbeygi et al.,2013, Sucak et al.,2010,Chappell et al.,2002, Mise et al.,2003, Muy-rivera et al.,2005, Chan et al.,2006 andFirdous Mumtazet al.,2008 .who found that maternal serum leptin levels were significantly higher in preeclampsia group than in control group and in severe group than in mild group and control group as well as what we have found in the present study.On the other hand, other studies have shown inconsistent results and have reported that serum leptin levels were similar in preeclampsia and control pregnant women as Hassan et al., 2015, Kim et al., 2003, Laml et al., 2001, Nesa et al., 2011 and Martinez-Abundis et al., 2000.

Conclusion and Recommendations

Serum leptin increases significantly with occurrence ofpreeclampsia compared to normal pregnancy and even it ismore increased with severe form of disease. It is a significantmarker of both occurrence and severity ofpreeclampsia.Serum leptin can be used as a marker of prediction of preeclampsia and to differentiate patients with mild preeclampsia from those with severe disease.A future study should be carried out on alarge population to assess the value of leptin as amarker in monitoring, early detection of pre-eclampsia .

References

Chan TF, Su JH, Chung YF, et al (2006): Elevated amniotic fluid leptin levels in pregnant women who are destined to develop preeclampsia. Acta obstet Gynecol scand ; 85 (2) : 171- 4.

Chappell L C, seed PT, briley A, et al (2002): A longitudinal study of biochemical variables in women at risk of preeclampsia. Am J Obstet Gynecol 187:127-136.

Coppari R and Bjorboek C(2012): Leptin revisited: its mechanism of action and potential for treating diabetes. Nat Rev Drug Discov.; 11:692-708.

Engl, N (2012):Pregnancy in a Woman with a Leptin-Receptor Mutation. Journal Of Meditional Chemistry., 366:1064-1065.

Firdous Mumtaz A, Abdul Razaq Memon B , Sajida Yousfani S M, et al (2008):Role of serum leptin level as a marker of severity of pre-eclampsia. J Ayub Med Coll, 85:13-15.

Hassan MA, Ahmed SM, Elhassan EM, Elbashir LM, Gasim GI, et al. (2015):Maternal and Umbilical Cord Blood Level of Leptin and C - reactive protein in Preeclamptic Sudanese Women. J Womens Health, Issues Care 4:3.
Kharb S, Panjeta P, Ghalaut VS, Bala J, Nanda S (2016): Maternal Factors Affecting Serum Leptin Levels in Preeclampsia and Normotensive Pregnant Women and Outcome of Pregnancy. J Preg Child Health 3: 223.
Khosrowbeygi A, Ahmadvand H(2013):Leptin to Adiponectin Ratio in Preeclampsia. Bangladesh Med Res Counc Bull. 39: 18-21.
Kim MH, Cho YK, Ko JK, Kang WS, Park KH, Lee CM, Choi H, Kim BR, Lee HK (2003): Study on umbilical cord plasma leptin inpreeclampsia and normal pregnant women. Korean J. Obstet .Gynecol .46(12):2366–2372.
Laml T., Preyer O., Hartmann B.W, Rucklinger E., Soeregi G., Wagenbichler P. (2001): Decreased maternal serum leptin in pregnancies complicated by preeclampsia, J. Soc. Gynecol. Investig. 8:89–93.
Martinez-Abundis E, Gonzalez-Ortiz M, Pascoe-Gonzalez S (2000): Serum Leptin levels and the severity of preeclampsia. Arch Gynecol.Obstet. 264, 2: 71-73.
Mise H, Sagawa N, Matsumoto T, et al (2003):Augmented placental production of leptin in pre-eclampsia: Possible involvement of placental hypoxia. J. Clin. Endocrinol. Metab., 83, 3225 – 3229.
Muy-rivera M, ning Y , frederick1 IO, et al (2005):Leptin, Soluble Leptin Receptor and Leptin Gene Polymorphism in Relation to Preeclampsia Risk Am J Obstet Gynecol Vol. 54 pp 168-175.
Nesa Asnafi., Majid Sharbatdaran., Karimollah Hajian et al. (2011): Comparison of maternal and neonatal serum leptin levels in preeclampsia and normal pregnancy.Iranian J of Reproductive Medicine.9.(2): 131-134.
Phipps E, Prasanna D, Brima W, Jim B (2016):Preeclampsia: Updates in Pathogenesis, Definitions, and Guidelines. Clinical Journal of the American Society of Nephrology: CJASN.6; 11(6):1102-1113.
Salimi S., Farajian-Mashhadi F., Naghavi A., et al.,(2014) : Different profile of serum leptin between early onset and late onset preeclampsia, Dis. Markers.1-7.
Sucak A, Kanat-Pektas M, Gungor T, et al (2010): Leptin levels and antihypertensive treatment in preeclampsia. Singapore Med J; 51(1): 39-43.
Taylor B.D., Ness R.B., Olsen J., et al.,(2015): Serum leptin measured in early pregnancy is higher in women with preeclampsia compared with normotensive pregnant women, Hypertension 65 ;594–599.
Vazquez MJ., Romero-Ruiz A & Tena-Sempere M (2015):Roles of leptin in reproduction, pregnancy and polycystic ovary syndrome: consensus knowledge and recent developments.Metabolism, 1,79-91.
Yingna Song, Jinsong Gao, Yimin Qub, ShuWang, Xi Wang, Juntao Liu (2016):Serum levels of leptin, adiponectin and resistin in relation to clinical characteristics in normal pregnancy and preeclampsia.Clinica Chimica Acta.458:133–137.
Yusrawati, Ratna Lestari Habibah, Rizanda Machmud (2015): Differences in Maternal Leptin Serum Levels between Normal Pregnancy and Preeclampsia. Leptin Levels Differences between Normal Pregnancy and Preeclampsia .Indones Biomed J. 7(1): 37-42.