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Association of Serum Leptin Level with Preeclampsia

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Abstract

Introduction with Objective: *The aim of the present study was to assess the association of serum leptin level with preeclampsia.* ***Materials and Methods:*** *This cross-sectional study was conducted from March 2022 to February 2023 in the department of Laboratory Medicine, Fetomaternal Medicine and Obstetrics and Gynaecology, BSMMU. A total 80 cases were selected as study population as per inclusion and exclusion criteria. They were grouped as preeclamtic (group I) and normal pregnant women of more than 20 weeks of gestation (group II). After taking written informed consent, 2.0 ml of random venous blood and 24 hours urine for protein were collected. Serum leptin level was estimated in Laboratory Medicine department and 24 hours urinary protein measured in Biochemistry and Molecular Biology department. After data collection and processing, all statistical analysis were done by SPSS software windows version 26.* ***Result:*** *The mean serum leptin level was found 28.3±12.52 ng/ml in group I and 14.24±5.10 ng/ml in group II. The difference was statistically significant (p 0.001) between two groups in unpaired t-test. Mean 24 hours urinary protein was 0.33±0.03 gm and 0.12±0.13 gm in group I and II respectively and the difference was statistically significant (p in unpaired t-test. There was positive linear relationship between 24 hours urinary protein and serum leptin level (r=+0.225, p>0.05) found in Pearson's correlation co efficient test. In ROC curve analysis, cut off value of serum leptin was found 21 ng/ml with 80% sensitivity and 90% specificity. The area under curve (AUC) of serum leptin level was 0.904. In our study, 32 preeclampsia patients (80%) had serum leptin level was ≥21 ng/ml which considered positive This finding of the study revealed that increased serum leptin level was associated with preeclampsia.* ***Conclusion:*** *Serum leptin level was increased in preeclamptic study group compared to normal pregnancy. Serum leptin level may be used as a biomarker of preeclampsia to help the clinicians for diagnosis.*

Keywords: *Leptin, preeclampsia, proteinuria.*

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Introduction:

Preeclampsia is a multisystem disorder of unknown etiology and is associated with maternal and fetal mortality and morbidity. According to the new guideline of National Institute for Health and Care Excellence (NICE) 2019, Preeclampsia can be defined as new onset of hypertension (BP≥140/90 mm of Hg) after 20 weeks of pregnancy and associated with significant proteinuria or in absence of proteinuria with thrombocytopenia, impaired liver function, new development of renal insufficiency, pulmonary oedema or new onset of cerebral or visual

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disturbance. Pre-eclampsia was previously determined by oedema, proteinuria and hypertension; the term is now changed because of very high incidence of generalized oedema in healthy pregnant women[1]. Worldwide, the incidence of preeclampsia ranges from 2% to 10% of pregnancies[2]. Incidence of preeclampsia in Bangladesh is 4.3%. The pathogenesis of preeclampsia involves multiple systems like placental, genetic, immunologic, environmental factors[3]. Some established risk factors for preeclampsia is extreme of age (<18 or >35), primiparity, previous history of preeclampsia, twin pregnancy and family history of hypertension[4]. There is no single, reliable and cost-effective test is available in preeclampsia[5]. Routine screening for preeclampsia is measurement of blood pressure and urine analysis for protein. Various study of different countries showed association of increased level of serum leptin in preeclamptic patient[6]. In pregnancy, leptin is synthesized and secreted from placental trophoblast into maternal circulation in larger amount in comparison to non-pregnant women. Placental leptin exhibits metabolic and physiological functions in normal pregnancy such as regulation of fetal growth, placental growth, angiogenesis and immunomodulation. Thus, placenta is not only the source of leptin it is also the target of leptin action[7]. In preeclamptic placenta, leptin expression is increased that suggested a positive correlation between elevated serum leptin level and preeclampsia[8]. Elevation of leptin level is due to placental stress caused by hypoxia in preeclamptic placenta[9]. As leptin is a strong angiogenic factor, its level increases in preeclampsia to improve the placental blood supply by neovascularization. Leptin also regulates transport of nutrient through placenta so that elevated leptin level in preeclampsia is a compensatory response to enhance nutrient supply to the hypoxic or under perfused placenta of preeclampsia[10].

Materials & Methods:

This cross-sectional study was conducted from March 2022 to February 2023 in the department of Laboratory Medicine, Fetomaternal Medicine and Obstetrics and Gynaecology, BSMMU. Atotal 80 cases were selected as study population as per inclusion and exclusion criteria. They were grouped as preeclamtic (group I) and normal pregnant women of more than 20 weeks of gestation (group II). After taking written informed consent, 2.0 ml of random venous blood and 24 hours urine for protein were collected. Serum leptin level was estimated in Laboratory Medicine department and 24 hours urinary protein measured in Biochemistry and Molecular Biology department. After data collection and processing, all statistical analysis were done by SPSS software windows version 26 to assess the association of serum leptin level with preeclampsia. The study was approved by the institutional ethical committee.

Results:

In this study, the patients were divided into four age groups. The mean (±SD) age was 25.1±5.2 years and 24.9±4.9 years in preeclamptic and normal pregnant women respectively. The mean age difference was not statistically significant (p>0.05) between two groups in unpaired t-test. The results are shown in the table I.

Table I: Age distribution of the study subjects (N=80)

Age group (years)	Preeclampsia (n=40)		Normal pregnancy (n=40)		p-value
	N	%	N	%	
<20	12	30.0	10	25.0	
21-25	7	17.5	8	37.5	
26-30	15	37.5	16	22.5	
31-35	6	15.0	6	15.0	
Mean±SD	25.1±5.2		24.9±4.9		0.877ns
Range	(17-35)		(18-35)		

Unpaired t-test was performed to compare between two groups ns = not significant, Data were expressed as frequency, percentage and mean ±SD

The mean (±SD) of 24 hours urinary protein was 0.33±0.03 gm with ranged from 0.31 to 0.40 gm in preeclamptic group. In normal pregnant women the mean (±SD) of urinary 24 hours protein level was 0.12±0.13 gm with ranged from 0.04 to 0.80 gm. The mean 24hrs urinary protein difference was statistically significant (p<0.001) between two groups in unpaired t-test. The results are shown in the table-II.

Table II: Comparison of 24 hrs urinary protein between two groups (N=80)

Urinary protein (gm/24 hours)	Preeclampsia (n=40) Mean±SD	Normal pregnancy (n=40) Mean±SD	P value
Mean±SD	0.33±0.03	0.12±0.13	
Range	(0.31-0.40)	(0.04-0.80)	<0.001s

Unpaired t-test was performed to compare between two groups s = significant, Data were expressed as mean ±SD and range

The mean (±SD) serum leptin level was 28.3±12.52ng/ml with ranged from 11.75 to 67.7 ng/ml in preeclamptic group. In normal pregnancy, the mean (±SD) serum leptin level was 14.24±5.10ng/ml with ranged from 6.72 to 27.20 ng/ml. The mean serum leptin difference was statistically significant (p<0.001) between two groups in unpaired t-test. The results were shown in the table III.

Table III: Serum Leptin level of the study subjects (N=80)

Serum Leptin (ng/ml)	Preeclampsia (n=40) Mean±SD	Normal pregnancy (n=40) Mean±SD	P value
Mean±SD	28.3±12.52	14.24±5.10	<0.001[s]
Range	(11.75-67.70)	(6.72-27.20)	

Unpaired t-test was performed to compare between two groups s = significant, Data were expressed as mean ±SD and range

24 hours urinary protein of 40 pre-eclamptic women was measured as gm/24hrs and serum leptin level was measured in ng/ml. Negligible positive correlations were found between urinary protein and serum Leptin level. The values of Pearson's correlation coefficient was r= +0.225 which showed a negligible positive linear correlation between urinary protein and serum leptin level in preeclamptic group (Figure 1).

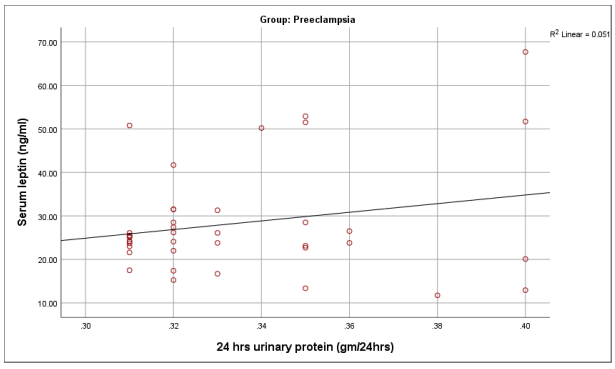

Figure-1: The scatter diagram showed positive relationship (r=0.225, p>0.05) in preeclamptic group.

In ROC curve analysis, cut off value of serum leptin was found 21 ng/ml with 80% sensitivity and 90% specificity. The area under curve (AUC) of serum leptin level was 0.904 (Figure-2).

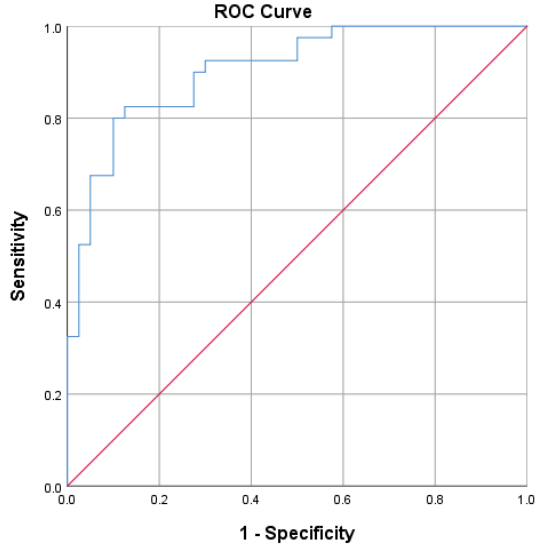

Figure-2: ROC curve analysis performed to measure the best cut off value of serum leptin for preeclampsia.

ROC curve analysis showed that a cutoff point of serum leptin 21 ng /ml can be used to diagnose preeclampsia with a sensitivity of 80%, specificity 90%, PPV 88.9%, NPV 81.8% and 85% accuracy (Table IV).

Table- IV: Diagnostic performance of serum leptin

Diagnostic validity test	Values
Sensitivity	80.0%
Specificity	90.0%
Positive Predictive Value	88.9%
Negative Predictive Value	81.8%
Accuracy	85.0%

Table V reveals that 32 preeclampsia patients had serum leptin level was ≥21 ng/ml which considered positive and 8 preeclampsia patients had serum leptin level was <21 ng/ml which considered negative. In normal pregnancy, 4 women had serum leptin level was ≥21 ng/ml which considered positive and 36 patients had serum leptin level was <21 ng/ml which considered negative.

Table-V: Diagnostic validity test of serum leptin with preeclampsia (N=80)

Serum leptin (ng/ml)	Group		Total (N=80)	p-value (χ2 test)
	Preeclampsia (n=40)	Normal pregnancy (n=40)		
Positive (≥21)	32(80.0%)	4(10.0%)	36(45.0%)	<0.001*
Negative(<21)	8(20.0%)	36(90.0%)	44(55.06%)	
Total	40(100.0%)	40(100.0%)	80(100.0%)	

Discussion:

The study subjects were divided into four age groups. In this study, the maximum number was found in the age group of 26-30 years in both groups. The mean (±SD) age was 25.1±5.2 years and 24.9±4.9 years in Group 1and Group 2 respectively and the difference was not statistically significant. Similarly, Ozkan S et al. (2005) study observed that mean age was 29.31±5.21 years in preeclamptic and 29.11±5.97 years in normal pregnant women and the difference was not statistically significant and was little higher than current study[11]. In this present study the mean 24 hours urinary protein was found 0.33±0.03 g/24 hours and 0.12±0.13 g/24 hours in preeclamptic and normal pregnancy respectively and p value was 0.001.This results were nearly consistent with Aradhana et al. (2019) study where they found 24 hours urinary protein 0.50±0.11 g/24 hours in preeclampsia and 0.19±0.43 g/24 hours in normal pregnant women with significant p value <0.0001[6]. In this study the serum leptin level was found ranged from 11.75 to 67.70 ng/ml in preeclampsia and 6.72-27.20 ng/ml in normal pregnant women. The mean serum leptin level was 28.3±12.52 ng/ml and 14.24±5.10 ng/ml in group-I and group-II respectively. The mean serum leptin level difference was statistically significant (p<0.001) between two groups. Taylor et al. (2014) reported serum leptin level were significantly (p=0.011) increased in women with preeclampsia where they found mean serum leptin level was 30.5 ng/ml in PE group compared with 20.9 ng/ml in normal group[12]. The area under the receiver operator characteristic (ROC) curves for serum leptin level was depicted in present study. The area under the curve (AUC) was 0.904. This ROC curves showed that the cut off value for serum leptin was 21 ng/ml which had 80% sensitivity and 90% specificity for prediction of preeclampsia. In Rao S et al. (2021) study found that cut off value of serum leptin was 23.3 ng/ml had 90% sensitivity and 88.3% specificity. Their results were nearly consistent with our study[13]. It was observed that serum leptin level significantly increased in patient with preeclampsia than normal pregnancy. There was a positive correlation of serum leptin level with preeclampsia. AUC suggested that serum leptin level has the discriminative ability in identification of preeclampsia.

Conclusion:

Serum leptin level was increased in preeclamptic study group compared to normal pregnancy. AUC showed fair predictive performance of serum leptin to differentiate preeclamptic patients from normal pregnant women. Serum leptin level may be used as a biomarker of preeclampsia to help the clinicians for diagnosis.

Conflict of Interest: None.

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References:

1. Murmu, A.K., Kumari, S., Sharan, A. and Baskey, et al. Correlation of Hypothyroidism with Pregnancy Outcome in Preeclampsia. IOSR J Dent Med Sci. 2018; 17:72-78.

2. Osungbade, K.O. and Ige, O.K. Public health perspectives of preeclampsia in developing countries: implication for health system strengthening. Journal of pregnancy, 2011.

https://doi.org/10.1155/2011/481095

PMid:21547090 PMCid:PMC3087154

3. Siddiquea, A., Sultana, A., Rahman, S.M.H., et al. Study on risk factors and pregnancy outcome in pre-eclampticpatients: A study in Sir Salimulah Medical College and Mitford Hospital, Dhaka, Bangladesh, Saudi Journal of Medical and Pharmaceutical Sciences. 2020; 6(2):232-241.

https://doi.org/10.36348/sjmps.2020.v06i02.015

4. Pérez-Pérez, A., Maymó, J., Dueñas, J.L., et al. Leptin prevents apoptosis of trophoblastic cells by activation of MAPK pathway. Archives of Biochemistry and Biophysics. 2008; 477(2):390-395.

https://doi.org/10.1016/j.abb.2008.06.015

PMid:18619412

5.Wagner, L.K. Diagnosis and management of preeclampsia. American family physician. 2004;70(12):2317-2324.

6. Aradhana, B., Ratnakumari, V. and Vani, N. Serum Leptin levels in normal pregnancy and in patients with preeclampsia-a comparative study. IOSR J Dent Med Sci. 2019; 18:1-6.

7. Laivuori, H., Kaaja, R., Koistinen, H., et al. Leptin during and after preeclamptic or normal pregnancy: its relation to serum insulin and insulin sensitivity. Metabolism. 2000; 49(2):259-263.

https://doi.org/10.1016/S0026-0495(00)91559-2

PMid:10690955

8. Song, Y., Gao, J., Qu, Y., et al. Serum levels of leptin, adiponectin and resistin in relation to clinical characteristics in normal pregnancy and preeclampsia. Clinica chimica acta. 2016; 458: 133-137.

https://doi.org/10.1016/j.cca.2016.04.036

PMid:27154800

9. Chrelias, G., Makris, G.M., Papanota, A.M., et al. Serum inhibin and leptin: risk factors for pre-eclampsia? Clinica Chimica Acta. 2016;463:84-87.

https://doi.org/10.1016/j.cca.2016.10.013

PMid:27737735

10. Ghantous, C.M., Azrak, Z., Hanache, S., et al. Differential role of leptin and adiponectin in cardiovascular system. International journal of endocrinology, 2015.

https://doi.org/10.1155/2015/534320

PMid:26064110 PMCid:PMC4433709

11. Özkan, S., Erel, C.T., Madazli, R. and Aydınlı, et al. Serum leptin levels in hypertensive disorder of pregnancy. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2005; 120(2):158-163.

https://doi.org/10.1016/j.ejogrb.2004.02.046

PMid:15925044

12. Taylor, B.D., Ness, R.B., Olsen, J., et al. Serum leptin measured in early pregnancy is higher in women with preeclampsia compared with normotensive pregnant women. Hypertension, 2015; 65(3):94-599.

https://doi.org/10.1161/HYPERTENSIONAHA.114.03979

PMid:25510827 PMCid:PMC4326535

13. Rao, S., Kumari, A., Sharma, M. and Kabi, et al. Predicting maternal serum adiponectin and leptin level as biomarkers of pre-eclampsia: A prospective study. The Journal of Obstetrics and Gynecology of India. 2021;71:58-65.

https://doi.org/10.1007/s13224-020-01378-6

PMid:33814800 PMCid:PMC7960875