Original Article

Uric Acid, Creatinine and Proteinuria: Do They Have any Relationship with Leptin During Pre-Eclampsia?

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ABSTRACT

Objective: To determine the relationship between serum leptin, uric acid, creatinine and proteinuria during pre-eclampsia.

Study Design: Comparative cross-sectional study.

Place and Duration of Study: This study was carried out in the department of physiology, Basic Medical Sciences Institute, JPMC, in collaboration with the department of Gynaecology and Obstetric, JPMC from Jan 2007 to Dec 2007.

Materials and Methods: For this purpose 45 primigravidas with normal pregnancy and 45 primigravidas with pre-eclamptic pregnancy were selected who were in their third trimester. All the subjects were of the same maternal age, gestational age, height and weight. Serum leptin levels were determined by immunoenzymometric assay and total lipid profile was determined by enzymatic colorimetric method. Serum uric acid and serum creatinine were determined by uricase method and jaffe's method by photometric system. To perform the dipstick urine analysis, multistix URS-10 test strips were used.

Results: The study included 90 patients, divided into two groups. Serum uric acid was found to be significant in pre-eclamptic group ($p<0.001$) but there was no difference between serum creatinine of the two groups. No significant correlation was found between serum leptin, uric acid and creatinine. It was found that the level of leptin rises with the level of proteinuria.

Conclusion: From this study, it was concluded that serum leptin levels during pre-eclampsia were not strongly associated with serum uric acid and creatinine but relation with proteinuria was found to be significant.

Key Words: Leptin, Pre-eclampsia, Uric acid , Creatinine, Proteinuria

INTRODUCTION

Leptin is a versatile 16kDa peptide with a tertiary structure resembling the long chain helical cytokine family. It is mainly produced by adipocytes and was originally thought to act only as satiety factor[1]. It has been observed that leptin functions in a variety of other physiological processes including immune and reproductive functions, hematopoiesis and glucose homeostasis[2].

Leptin is also synthesized by placenta and cross-sectional studies suggest that leptin concentration peaks in the 2nd trimester and remains elevated until parturition[3]. Maternal circulating leptin concentration is significantly higher in pregnancies complicated by pre-eclampsia than gestational age matched controls[4]. Pre-eclampsia (PE) is a multisystem disorder of 2nd half of pregnancy characterized by generalized endothelial dysfunction and oxidative stress[5]. Leptin has also been reported to induce oxidative stress in cultured endothelial cells[6]. Leptin may contribute to increase uric acid concentration as plasma uric acid concentrations are increased by oxidative stress[7]. Impaired renal function is a pathophysiological component of PE and may effect creatinine clearance, also measured increase in plasma leptin concentration may reflect reduced renal clearance[8].

Therefore the present study was designed to assess whether any relationship exists between serum leptin and uric acid, creatinine and proteinuria during pre-eclampsia.

MATERIALS AND METHODS

This study was carried out in the department of Physiology, Basic Medical Sciences Institute, JPMC, in collaboration with the department of Gynaecology and Obstetrics, JPMC.

The study was performed on 90 pregnant women of age ranging between 16-32 years and gestational age between 28-38 weeks. All the subjects were briefed about the nature of the study and an informed consent was taken.

Inclusion Criteria:

- 45 normotensive women with singleton pregnancies were taken as control without any previous history of hospitalization or any medical complication.
- 45 Obstetric patients with singleton pregnancies were diagnosed as having PE according to ISSHP (International society for the study of

hypertension) when they presented with blood pressure ≥ 140/90mmHg on 2 separate occasions 4hrs apart or a single recording of a diastolic blood pressure of 110mmHg in association with proteinuria ≥ 2+ on dipstick testing.

Exclusion Criteria:

- Pre-existing chronic hypertension.
- Pre-existing diabetes.
- Gestational diabetes.
- Diseases involving kidneys.
- Diseases involving liver.
- Known history of any peripheral vascular disease.
- Twin pregnancy.
- Smoking or any drug addiction.

All the subjects included in the study were primigravidas with same maternal age, gestational age, height and weight. A detailed general physical examination was done and history was taken.

The blood samples were collected under strict aseptic measures. Each sample was labelled with patient's name and identification number. Samples were analyzed in one run at the end of the study. Serum leptin was determine by immunoenzymometric assay. Serum uric acid and serum creatinine were determined by uricase method and jaffe's method respectively by photometric system. To perform the dipstick urine analysis, multistix URS-10 test strips were used.

Data analysis was done on computer package SPSS (Statistical Package for Social Sciences) version 10.0. The Statistical significance of difference between the mean values of two groups was evaluated by the student's "t" test. The difference in the mean values of the two groups was regarded as statistically significant, if the P-Value was less than 0.05 and it was taken as highly significant, if P-Value was less than 0.001**.** Correlation Coefficient was detected using Pearson Coefficient of Correlation SPSS-10.0.

RESULTS

In this study 90 women were included. Among which 45 were normotensive primigravidas and 45 were PE primigravidas. The pre-eclamptic group was again divided according to severity of the disease into mild PE (n=28) and severe PE (n=17). Maternal serum leptin levels were significantly higher in PE group than in control group.

Results are summarized in table1-3. Table 1 shows the comparison of serum uric acid and creatinine between control group and PE. Serum uric acid shows a statistically significant increase (P<0.001) in PE group as compared to controls whereas serum creatinine shows a non-significant change between the two groups. On correlating serum uric acid and serum creatinine with serum leptin (table2), a non-significant correlation was found. Table 3 shows serum leptin levels according to the level of proteinuria. Proteinuria of 1^+ and 2^+ were not found to be significant in relation to leptin but proteinuria of 3^+ was found to be significantly associated (P<0.001) with serum leptin.

Table No.1: Serum uric acid and serum creatinine in normal pregnant women (controls) and in pre-eclamptics

(All the values are expressed in Mean±S.D)

Variables	Group A Control (n=45) Mean ±S.D	Group B Pre-eclamptic (n=45) Mean ±S.D
Serum uric acid (mg/dl)	3.01±0.55	5.56±0.92*
Serum creatinine (mg/dl)	0.64±0.10	0.68±0.12

*P<0.001 when compared to control.

Table No.2: Correlation coefficient (r) of serum uric and serum creatinine vs serum leptin in normal pregnant women (controls) and in pre-eclamptics

Variables	Group A (control (n=45) Serum leptin	Group B (Pre-eclamptic) (n=45) Serum leptin
Serum uric acid (mg/dl)	r =-0.06	r=-0.06
Serum creatinine (mg/dl)	r =-0.22	r =0.22

Table No.3: Serum leptin levels according to proteinuria in pre-eclampsia

Proteinuria	No of subjects	Serum leptin (ng/ml) in P.E (n=45) Mean ± S.D
1+	18	52.1±4.23
2+	13	52.0±5.56
3+	11	86.1±5.58*
4+	3	77.6±13.38

* Significantly higher as compared to 1+ and 2+ (p< 0.001)

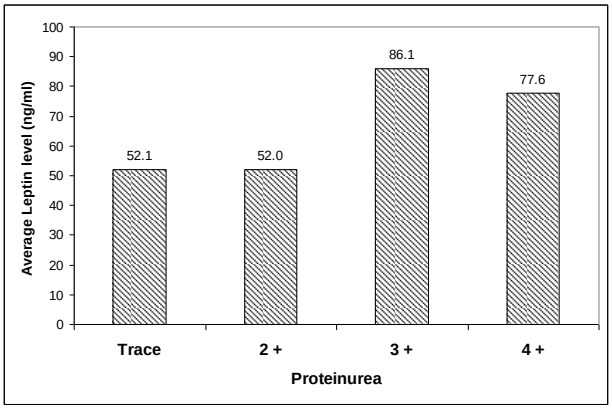

Figure No.1: Serum leptin level according to proteinuria in pre-eclampsia

DISCUSSION

PE is a complex polygenetic trait in which maternal and fetal genes, as well as environmental factors are involved[9]. The cause remains largely unknown but oxidative stress and generalized inflammatory state are features of the maternal syndrome[10]. Release of proinflammatory cytokines such as TNF-α and reactive O_2 species from ischemic placenta in PE may also contribute directly to oxidative stress[5].

It has demonstrated that leptin increases in situations associated with higher levels of cytokines as in PE[11]. Changes in plasma leptin concentration in PE correlates with uric acid concentration[12]. Both uric acid and leptin may be the markers of PE[13]. Contrary to these findings, the results of our study do not find any positive correlation between between serum leptin and uric acid but uric acid levels were found to be significantly associated with PE.

Our findings do not reveal any difference in the serum creatinine level between the two groups studied nor it finds any correlation between serum leptin and creatinine during PE which are in agreement with the findings of Sebiha Ozkan et al[8], and Anim-Nyame et al[12]. Thus it seems unlikely that hemoconcentration or impaired renal function which are pathophysiological components of PE, contribute to high leptin observed in the disease. When the level of proteinuria was observed in relation to leptin, it was found that as proteinuria increases, the level of leptin also increases. The leptin level were found to be significantly associated with proteinuria.

CONCLUSION

From this comparative cross-sectional study it is concluded that leptin levels during PE are not found to be associated with uric acid and creatinine but a significant association was found between serum leptin and proteinuria. The mechanism responsible for this and the role played by leptin requires further study on a larger scale.

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