

## ROLE OF SERUM LEPTIN LEVEL AS A MARKER OF SEVERITY OF PRE ECLAMPSIA

Firdous Mumtaz, Abdul Razaq Memon\*, Sajida Yousfani, S. M. Tahir\*, Imdad Khushk\*\*, Mumtaz Memon\*\*\*, Amna Memon

Department of Obstetrics and Gynaecology, \*Department of Surgery, \*\*Senior Research Officer, \*\*\*Department of Physiology, Liaquat University of Health & Medical Sciences, Jamshoro, Pakistan

**Background:** To explore the possibility of serum leptin being a marker of severity of pre-eclampsia, so that risk of imminent eclampsia and eclampsia can be reduced. **Methods:** This observational study was conducted at a private hospital of Hyderabad from 31<sup>st</sup> July to 1<sup>st</sup> December 2007. Forty primipara with same age, body mass indices and gestational age were included in this study. Twenty women had raised blood pressure in third trimester of pregnancy and 20 women with a normal blood pressure in third trimester of pregnancy. The exclusion criteria included history of diabetes, twin pregnancy, chronic hypertension, liver or renal disease. After counselling and affordability of laboratory testing their blood sample was taken for serum leptin, uric acid, serum creatinine and urine for albumin. The serum leptin level was measured by radio-immunoassay (RIA) kits. All data was filled in a pre-designed proforma after taking detailed history and examination. Statistical analysis was performed on SPSS. Student's t-test was applied where applicable. **Results:** Mean systolic and diastolic blood pressure between pre-eclamptic and control group showed a marked difference ( $p < 0.001$ ) ranging from  $149.50 \pm 3.44$  and  $104.40 \pm 3.03$  as compared to control  $107 \pm 1.56$  and  $74.50 \pm 1.49$  respectively, similarly proteinuria was present in 20 (100%) cases of pre-eclampsia and 07 (35%) of normotensive women. Mean serum leptin level was significantly high in pre-eclamptic ( $79.380 \pm 3.287$ ), when compared with a control group ( $27.825 \pm 1.050$ ). Mean serum uric acid in pre-eclamptic ( $5.040 \pm 0.147$ ) showed significant changes than control ( $3.600 \pm 0.141$ ), while serum creatinine level was insignificant in both groups. It has been observed that Mean  $\pm$  SEM value of serum leptin level was much higher in severe pre-eclampsics ( $76.418 \pm 5.056$ ) than in women with mild pre-eclampsia ( $40.856 \pm 2.807$ ). All the parameters correlated positively and significantly with increased blood pressure. **Conclusion:** Elevated plasma leptin concentration appears to be a marker of pre-eclampsia independently or along with other parameters of pre-eclampsia could be used to reduce the severity of pre-eclampsia thus avoiding risk effects of pre-eclampsia to mother and foetus. This study still needs more research work to prove our results.

**Key Words:** Pregnancy, Leptin, Pre-eclampsia prevention.

### INTRODUCTION

Pre-eclampsia is a major cause of maternal morbidity and mortality, complicating 7–10% of pregnancies.<sup>1</sup> Every year almost 600,000 women die because of various causes related to pregnancy, delivery and puerperal diseases.<sup>2</sup> Obstetrics haemorrhages, eclampsia and puerperal sepsis are commonly reported direct causes of maternal deaths<sup>3</sup> in Pakistan as well as other parts of the globe.

Pre-eclampsia is a syndrome defined as the onset of hypertension and proteinuria after 20 weeks of gestation in previously normotensive and non-proteinuric women. Although the precise mechanism of disorder remained elusive but according to new emerging consensus it is a complex polygenetic trait in which maternal and foetal genes as well as environmental factors are involved.<sup>4</sup>

Though pathogenesis is not yet clear, several theoretical mechanisms have been proposed which result in uteroplacental insufficiency,<sup>5</sup> this may result because of endothelial dysfunction which may be a final pathway between metabolic preturbance to clinical

manifestations and is responsible for formation of various cascades for example increased procoagulant production responsible for microthrombi and formation of free oxidative radicals, leads to maternal vascular dysfunction and leucocytes activation,<sup>6</sup> especially neutrophils which releases superoxide and various cytokines. All these are responsible for placental hypoxia and increase in plasma leptin concentration<sup>7</sup> along with there is associated insulin resistance which is greatly influenced by adipocytokines characterizes pre-eclampsia maternal leptin rise.<sup>8</sup>

Leptin is a product of ob/ob gene produced by adipose tissue and is synthesized by placenta during pregnancy<sup>9</sup> resulting in increased serum leptin level with increasing gestational age particularly in pre-eclampsia and level declines in post partum period.<sup>9</sup>

Anim-Nayame N *et al*,<sup>10</sup> in his longitudinal study had shown that plasma leptin level in early gestational age precedes the significant risk of pre-eclampsia with rise in maternal serum leptin concentration and can be used as a marker of pre-eclampsia, while Ning Y *et al*<sup>11</sup> observed a strong

linear component of trend in pre-eclampsia with increased maternal plasma leptin concentration, as per him each 10 ng/ml increase in leptin concentration was associated with 30% increase in pre-eclampsia risk.<sup>10,11</sup>

The exact role of placental leptin production is not known but in cases in which there is reduction in placental circulation, it serves as a gestational hormone, for regulating growth of foetus and placenta<sup>1</sup>, and can be taken as a marker for severity of pre-eclampsia and intrauterine growth restriction (IUGR).<sup>12</sup>

**MATERIAL AND METHODS**

This observational study was conducted at a private hospital of Hyderabad from 31<sup>st</sup> July to 1<sup>st</sup> December 2007. A total number of 40 primipara were included in this study. All of them were of same age, height, weight and gestational age. A detailed obstetrical and medical history was taken, and they were divided into 2 groups. Group A with normal blood pressure without any history of prior hospitalization and Group B had 20 primipara with pregnancy induced hypertension.

The exclusion criteria included pre-existing chronic hypertension, diabetes, multiple pregnancies and any chronic renal or liver disease.

After counselling and affordability of investigations their blood sample were drawn for serum leptin along with serum uric acid, creatinine and urine for albumin. Serum leptin level was measured by radio-immunoassay (RIA) Kits. All these results were documented by predesigned proforma after obtaining informed consent. Statistical analysis was performed on SPSS. Student's *t*-test was applied where applicable.

**RESULTS**

A total 40 primipara of same age group ranging from (20–32 years), gestational age (28–38 weeks) with same height and weight were included in this study. There were no significant differences between two groups (Table-1). Proteinuria was present in 20 (100%) cases of pre-eclampsia and 7 (35%) of normotensive women's. Figure-1 provides illustrative explanation of observation. Mean systolic and diastolic blood pressure between pre-eclamptic and control group showed a marked difference ( $p < 0.001$ ) ranging from 149.50±3.44 and 104.40±3.03 as compared to control 107±1.56 and 74.50±1.49 respectively (Table-2). The result showed that mean serum leptin level was positively correlated with increase in blood pressure (79.380±3.287) than control (27.825±79.380), similarly mean serum uric acid level also showed significant difference (5.040±0.147) than control (3.600±0.141). While mean serum creatinine was insignificant in both groups (Table-2). It was observed from our study that mean serum leptin level was high in severe pre-eclampsia then mild pre-eclampsia. Mean±SEM value of serum leptin level was (76.418±5.056) in severe pre-eclampsia than in women

with mild pre-eclampsia (40.856±2.807) Table-3. All the parameters correlated positively and significantly with increased blood pressure (Figure-2).

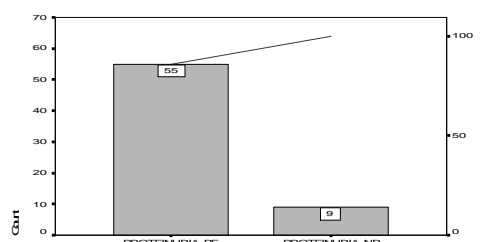
Figure-2 shows graphical representation of mean serum leptin level in both systolic and diastolic blood pressures and there was a strong correlation with increased serum leptin level with severity of pre-eclampsia suggesting 20-25% contribution of serum leptin in elevating systolic and diastolic arterial pressures respectively.

**Table-1: Maternal age, gestational age, height and weight in normal pregnant controls and Pre-eclamptics**

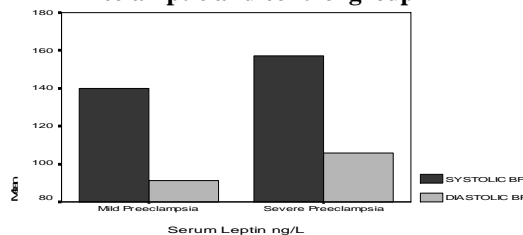
Variable	Control (n=20) Mean±SEM	Pre-eclamptic (n=20) Mean±SEM	p Value
Age (Years)	25.0±0.40	27.75±0.856	0.029
Gestational age (Weeks)	32.60±0.73	34.05±0.60	0.145
Height (m)	1.56±0.81	1.55±1.01	0.332
Weight (Kg)	64.80±0.97	67.10±1.54	0.182

**Table-2: Comparison of systolic and diastolic BP, serum leptin, serum uric acid, serum creatinine in normal pregnant controls and Pre-eclamptics**

Variables	Control (n=20) Mean±SEM	Pre-eclamptic (n=20) Mean±SEM	p Value
Systolic BP (mm Hg)	107±1.56	149.50±3.44	<0.001
Diastolic BP (mm Hg)	74.50±1.49	104.40±3.03	<0.001
Serum leptin (ng/ml)	27.825±1.05	79.380±3.287	<0.001
Serum uric acid (mg/ml)	3.600±0.141	5.040±0.147	<0.001
Serum creatinine (mg/ml)	0.645±2.76	0.655±2.633	0.748



**Figure-1: Variation of proteinuria between pre-eclamptic and control group**



**Figure-2: Variation of serum leptin level with severity of pre-eclampsia**

**Table-3: Severity of serum leptin level according to severity of pre-eclampsia**

Variable	Pre-eclamptic = 20	
	Severe pre-elcampia Mean±SD	Mild pre-elcampia Mean±SD
Serum leptin mg/ml	76.418 ± 5.056	40.856 ± 2.907

## DISCUSSION

Pre-eclampsia continues to be an important cause of maternal morbidity and mortality globally. The cause of hypertensive disease is not yet clear; it includes immunological, genetic, environmental and placental abnormalities. The final result of all these is endothelial dysfunction, characteristic of pre-eclampsia.<sup>13</sup>

In a longitudinal study done by Kolyingit *et al*<sup>14</sup> in 2004 showed increased plasma leptin level with severity of pre-eclampsia could be taken as a marker of placental hypoxia in severe pre-eclampsia, and the same was noticed in a study done by Sattar N, *et al*, 1998.<sup>8</sup>

The current study was done to compare and confirm the reported increase in pre-eclampsia and to investigate the possibility of serum leptin being a marker of severity of pre-eclampsia.

The results of our study suggested that serum leptin level increases with increase in blood pressure both systolic and diastolic. Similar findings were seen in a study done by Anim-Nyame N<sup>10</sup>, however Martinez-Abundis *et al*<sup>15</sup> contradicts our study and according to them serum leptin levels were similar in the patients with different grades of pre-eclampsia and normotensive pregnant women. High leptin level may be increased in women with increased gestational age because not only adipose tissue is a source of leptin, but also in pregnancy foetus, placenta, amniotic fluid, increase in plasma volume and extra vascular fluid accumulation leads to increase in maternal weight and also the body mass index (BMI) is responsible for increase in serum leptin level.<sup>16</sup> Our study suggested that BMI value has no significant impact on serum leptin levels, but in pregnancy induced hypertension, placental ischemia is responsible for increase in leptin level with increase in inflammatory cytokines such as TNF alpha IL-6<sup>17</sup> along with increased in serum uric acid.

Though there is correlation between serum leptin levels and serum lipid levels<sup>14</sup> but we did not include this parameter in our study.

Our study had some limitations such as smaller sample size, lacking some parameters hence our finding still needs some more interpretation for further study.

## CONCLUSION

It has been concluded from our study that plasma leptin level is increased in pre-eclampsia with increased gestational age. It can be taken independently or along with other parameters as a marker for severity of pre-

eclampsia. Hence avoiding risk effects of pre-eclampsia to mother and foetus.

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## Address for Correspondence:

**Dr. Firdous Mumtaz**, Associate Professor, Department of Obstetrics and Gynaecology, Liaquat University of Health & Medical Sciences, Jamshoro (Sindh) Pakistan. Tel: +92-302-3990239

**Email:** drfirdous@hotmail.com