

# Comparison of serum leptin concentration and electrolytes in pre-eclampsia and normal pregnancy

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## Abstract

**Background:** Preeclampsia is one of the leading causes of maternal as well as perinatal morbidity and mortality. Studies have shown that leptin has also been implicated in the pathogenesis of many of the maternal features of the disease. People with hypertension have electrolyte abnormalities when compared to normotensives. Screening pregnant women at high risk for PE with biochemical markers can reduce unnecessary suffering and health care costs by early detection and early management. **Aim:** To assess the level of serum leptin concentration and electrolytes in PE and normal pregnant women. **Material and Methods:** This study involved Group A (40 pre-eclamptic women) and Group B (40 normal pregnant). Serum Leptin was estimated by the DRG Leptin ELISA Kit and serum electrolytes concentration Na<sup>+</sup>, K<sup>+</sup> and Cl<sup>-</sup> were measured by EASYLYTE Analyser in both groups. **Results:** Mean serum leptin concentration was significantly higher in PE women compared to controls 28.85±7.2 ng/ml vs 24.80±6.5 ng/ml, p<0.01. The mean serum sodium level for pre-eclamptic women was found to be statistically elevated (p<0.03) than normal pregnant women. The serum levels of calcium (p<0.01) and potassium (p<0.003) in pre-eclamptic women was significantly lower than in normal pregnant women. However, chloride showed no significant changes in both groups. **Conclusion:** Leptin levels were significantly elevated in PE than in normal pregnant women. Serum leptin level was increased with the severity of pre-eclampsia. The results also showed significant increase in sodium level and a significant decrease in calcium and potassium levels in pre-eclampsia

**Key Word:** Pre-eclampsia, Normal pregnancy, Serum leptin, Serum electrolytes

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## INTRODUCTION

Pre-eclampsia (PE) is a medical condition characterized by high blood pressure and significant amounts of protein in the urine of a pregnant woman. If left untreated, it can develop into eclampsia, the life-threatening occurrence of seizures during pregnancy. It is a severe complication of human pregnancy with a worldwide incidence of 3-5%.<sup>1</sup> It is one of the leading causes of maternal as well as

perinatal morbidity and mortality, even in developed countries.<sup>2</sup> Human leptin, a circulating placental protein, plays role in normal pregnancy which include the regulation of conceptus growth and development, fetal/placental angiogenesis, embryonic hematopoiesis, and hormone biosynthesis within the maternal-fetoplacental unit. Studies have shown that leptin has also been implicated in the pathogenesis of many of the maternal features of the disease.<sup>3</sup> Cross-sectional studies have found a significantly higher plasma concentration of leptin in pre-eclamptic pregnancies when compared with normal pregnancies.<sup>4,5</sup> People with hypertension have electrolyte abnormalities when compared to normotensives. In PE, placental damage, in the form of hypoperfusion, leads to maternal vasoconstriction and pathological lesions in the liver, kidney and placental bed<sup>6</sup> and the subsequent renal lesion leads to retention of sodium and water, but most of the fluid accumulates in the tissues instead of in the vascular system. Screening pregnant women at high risk for PE with biochemical

markers can reduce unnecessary suffering and health care costs by early detection and early management. The present study was hence designed to assess the level of serum leptin concentration and electrolytes in PE and normal pregnant women.

## MATERIAL AND METHODS

This was a case control study which involved 40 pre-eclamptic (Group A) and 40 normal pregnant (Group B) women attending the Department of Obstetrics and Gynaecology of a tertiary care hospital. The Institutional Ethical and Research Committee approved the study protocol and informed consent was obtained from the controls and the patients before the collection of the blood samples. At the time of registration, a detailed obstetric and medical history was taken. General, Systemic and obstetric examination were carried out on the same day.

### Inclusion Criteria

- Group A consisted of 40 obstetric patients, diagnosed as having pre-eclampsia according to ISSHP (International society for the study of hypertension). Preeclamptic women were then divided according to the severity of the disease into mild preeclampsia (BP  $\geq$ 140/90 -159/110 mm Hg, and proteinuria  $\geq$  0.3-5.0 g/day) and severe preeclampsia (BP  $\geq$  160/110 mm Hg and proteinuria  $\geq$  5.0 g/day).
- Group B consisted of 40 healthy pregnant subjects having blood pressure  $\leq$ 120/80mmHg and no significant proteinuria, without any previous history of hospitalization or any medical complication and were considered as controls.

### Exclusion Criteria

- Pregnant women with Multifetal gestation, chronic hypertension, diabetes mellitus, autoimmune diseases, vascular diseases, renal disorder, maternal or fetal infection and fetal congenital anomaly.

### Measurement of BP

The arterial blood pressure in the brachial artery was measured by using a simple mercury sphygmomanometer on right arm in a comfortable sitting position after 10 minutes of rest. Blood pressure was measured using both palpatory and auscultatory methods. The reported values represent the mean of two readings taken at 5 minutes interval.

### Measurement of Proteinuria

UriTrace 2GP (Glucose and Protein) reagent strips for urinalysis based on the protein-error-of-indicator

principle. For this, freshly voided midstream urine sample was collected in a clean and dry container. The reagent area of the strip was immersed in the urine specimen and compared the result on the strip with the colour chart on the bottle label closely.

### Blood collection

Serum was used for the estimation of Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup> and Ca<sup>2+</sup> electrolyte levels. Remaining serum was stored at -20<sup>o</sup>C for analyzing leptin concentration.

### Estimation of Serum Leptin

Serum Leptin was estimated by The DRG Leptin ELISA Kit based on Enzyme immunoassay principle for quantitative determination. A 15  $\mu$ L of each standard, controls and samples was dispensed with new disposable tips into appropriate wells and 100  $\mu$ L Assay Buffer into each well and mixed for 10 seconds. Incubated for 120 minutes at room temperature. The wells were briskly shaken and rinsed 3 times with diluted wash solution (300  $\mu$ L per well). Added 100  $\mu$ L antiserum to each well. Incubated for 30 minutes at room temperature. After incubation, the wells were washed 3 times with washing buffer. A 100  $\mu$ L Enzyme Complex was dispensed into each well. Incubated for 30 minutes at room temperature and repeat step 3. Added 100  $\mu$ L of Substrate Solution to each well and then incubated for 15 minutes at room temperature. The enzymatic reaction was stopped by adding 50  $\mu$ L of Stop Solution to each well. The absorbance (OD) of each well was determined at 450nm with a microtiter plate reader.

### Estimation of Serum Electrolytes

The serum electrolytes concentration Na<sup>+</sup>, K<sup>+</sup> and Cl<sup>-</sup> were measured by EASYLYTE Analyser.

### Estimation of Serum Calcium

The serum calcium was measured by Modified OCPC (ortho-cresolphthalein) method.

### Statistical Analysis

Data analysis was done on computer package SPSS (Statistical Package for Social Sciences). The Statistical significance of difference between the mean values of two groups was evaluated by the student's "t" test. The values were expressed as mean  $\pm$  standard deviation. 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. For data feeding, the computer package Microsoft Excel was used.

## RESULTS

The two study groups were statistically similar in age and gestational age. As expected from the recruitment criteria, the preeclampsia group had significantly higher systolic and diastolic BP values ( $p < 0.0001$ ). Table 1 shows the biochemical parameters between normal pregnant women (group A) and preeclamptic women (group B).

**Table 1:** Anthropometric and Clinical Parameters of the Study Subjects

|                         | Group A (n=40)<br>(Pre-eclamptic) Mean±SD | Group B (n=40)<br>(Normal) Mean±SD | p value  |
|-------------------------|---|------------------------------------|----------|
| Age (years)             | 26.63±3.4                                 | 27.60±2.9                          | NS       |
| Gestational age (weeks) | 33.15±3.3                                 | 32.82±3.2                          | NS       |
| Systolic BP (mmHg)      | 156.5±12.4                                | 122.2±12.11                        | <0.0001* |
| Diastolic BP (mmHg)     | 102.2±8.3                                 | 79.20±4.6                          | <0.0001* |

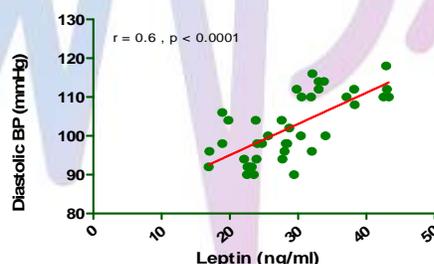
\* $p < 0.05$  was considered statistically significant.

Mean serum leptin concentration was significantly higher in PE women compared to controls  $28.85 \pm 7.2$  ng/ml vs.  $24.80 \pm 6.5$  ng/ml,  $p < 0.01$ . The mean serum sodium level for preeclamptic women was found to be statistically elevated ( $p < 0.03$ ) than normal pregnant women. The serum levels of calcium ( $p < 0.01$ ) and potassium ( $p < 0.003$ ) in pre-eclamptic women was significantly lower than in normal pregnant women. However, chloride showed no significant changes in both groups.

**Table 2:** Serum Biochemical Parameters of the Study Subjects

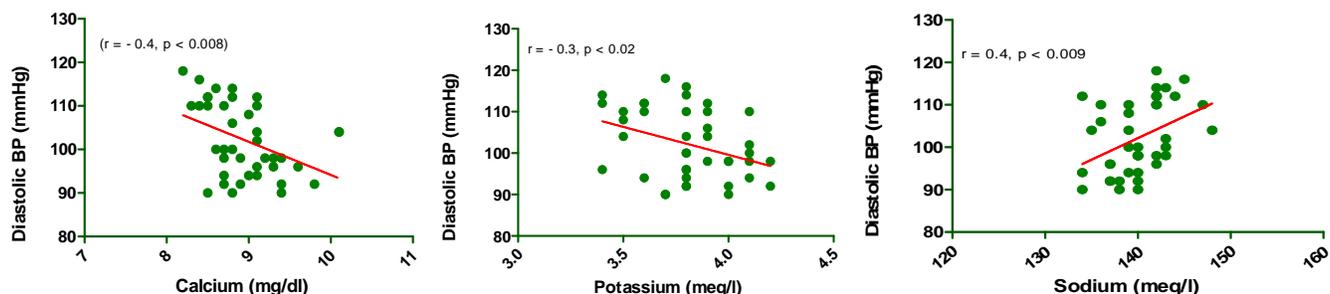
| Parameters       | Group A (n=40)<br>(Pre-eclamptic)<br>Mean±SD | Group B (n=40)<br>(Normal)<br>Mean±SD | P value |
|------------------|--|---------------------------------------|---------|
| Leptin(ng/ml)    | 28.85±7.2                                    | 24.80±6.5                             | <0.01*  |
| Sodium (meq/L)   | 140.0±3.3                                    | 138.7±2.1                             | <0.03*  |
| Potassium(meq/L) | 3.8±0.2                                      | 4.0±0.3                               | <0.003* |
| Calcium (mg/dl)  | 8.9±0.4                                      | 9.2±0.5                               | <0.01*  |
| Chloride(meq/L)  | 101.4±3.1                                    | 101.0±3.2                             | NS      |

\* $p < 0.05$  was considered statistically significant.



**Figure 1:** Correlation between Leptin and Diastolic BP In PE

A significant positive correlation ( $r = 0.6$ ,  $p < 0.0001$ ) was observed between serum leptin and diastolic blood pressure in pre-eclamptic women.



**Figure 2:** Correlation Between Electrolytes and Diastolic BP in PE

There was a significant negative correlation ( $r = -0.4$ ,  $p < 0.008$ ) between serum calcium and diastolic BP. There was also a significant negative correlation ( $r = -0.3$ ,  $p < 0.02$ ) between serum potassium and diastolic BP. However, positive correlation ( $r = 0.4$ ,  $p < 0.009$ ) was observed between serum sodium and diastolic BP in pre-eclamptic women.

## DISCUSSION

Preeclampsia is a disease that begins in the placenta and ends at the maternal endothelium and is a major cause of maternal morbidity and mortality in the developed countries.<sup>1</sup> It is significantly associated with alterations of maternal physiologic characteristics and metabolism manifesting itself primarily as hypertension with arteriolar vasoconstriction. The two study groups were statistically similar in age and gestational age as shown in Table 1. The mean systolic and diastolic blood pressure was higher in PE women than in normal pregnant women ( $p < 0.001$ ). Table 2 showed that plasma leptin levels were elevated significantly in PE women than normal pregnant women. There is cumulative evidence that PE is a systemic inflammatory disease.<sup>7,8</sup> The observed increase in the concentration of leptin in the present study may represent the abnormal cytokine responses in PE and its possible involvement in the pathogenesis of this maternal syndrome. The elevated leptin concentrations in preeclampsia may also be due to a compensatory response to increase nutrient delivery to the under perfused placenta.<sup>9</sup> Numerous studies have demonstrated that maternal peripheral leptin levels are enhanced during normal pregnancy and collectively suggest that leptin concentrations peak in the second trimester.<sup>10</sup> The plasma leptin levels in the severe PE group were significantly higher than those in the mild PE group. In severe PE, placental production of leptin is increased in response to hypoxia, thereby supporting the notion that augmented plasma leptin levels in severe PE reflect placental hypoperfusion and/or hypoxia. Because hypoxia induces a set of several placental genes in trophoblast, augmented placental production of leptin may represent one of the generalized hypoxic responses of trophoblasts in PE. These findings were also supported by Hauguel-de *et al*<sup>11</sup> who showed that placental leptin production is increased in choriocarcinoma, preeclampsia and type 1 diabetes. Estrogens, hypoxia and insulin have been suggested as positive regulators of placental leptin production. Therefore, leptin may serve as a placenta-derived marker of PE, possibly reflecting placental hypoxia associated with severe PE. A significant difference in blood pressure values between mild and severe preeclampsia group was observed. There was also a positive correlation between serum leptin and diastolic blood pressure values. It has been shown that intra-cerebroventricular leptin infusion increases arterial pressure, indicating its important role in development of hypertension.<sup>12</sup> The estimation of serum electrolytes in PE provides a useful index for the study of physiological and pathological changes in pregnancy. In the present study, mean serum calcium levels in preeclamptic women were significantly lower than in normal pregnant women. The present finding is similar to Kisters

*K et al* who showed that during cellular injury and cellular death in PE, there is influx of calcium ions into the cell leading to increased intracellular calcium ions and loss of calcium homeostasis.<sup>13</sup> However, Mohieldein *et al* showed a significant increase in the level of serum calcium in PE than normal pregnant women.<sup>14</sup> The Pearson correlation studies were done to find out the correlation between serum electrolytes and blood pressure. Fig. 1 showed an inverse relationship ( $r = -0.4$ ,  $p < 0.008$ ) between calcium and blood pressure values in PE. Low serum  $Ca^{2+}$  may cause high blood pressure by stimulating parathyroid hormone and rennin release which in turn increases intracellular  $Ca^{2+}$  in vascular smooth muscle and thus causing hypertension. Levels of serum  $Na^+$  were found to be significantly increased in patients of preeclampsia when compared with the normal pregnant women. PE may be an early sign of abnormality in the transport of sodium and potassium across the vascular smooth-muscle cell membrane, which is responsible for the maintenance of blood pressure.<sup>15,16</sup> The intra-renal productions of cyclic GMP, endothelin and PGE2 are all decreased in preeclampsia and this may have implications in the sodium retention, hypertension, intra-renal thrombosis and the vasospasm of preeclamptic pregnancy.<sup>17</sup> A positive correlation between sodium and blood pressure level in pre-eclamptic women was observed. Sodium and water retention in preeclampsia-eclampsia with endothelial damage, increases vascular sensitivity to angiotensin leading to hypertension, oedema and proteinuria. Serum potassium level was also significantly lower ( $p < 0.003$ ) in pre-eclamptic women than in normal pregnant women. This finding was similar to a study done by Manjareeka *et al*.<sup>18</sup> In an earlier study involving serum potassium on hypertensives, it was conclusively established that an inverse relationship existed between serum potassium level and the extent of hypertension.<sup>19</sup> Accordingly, there was a negative association between serum potassium and blood pressure levels in PE. Some investigators found that dietary potassium supplementation lowers blood pressure in established hypertension. This may result from natriuresis and from vasodilatation subsequent to stimulation of  $Na^+$ ,  $K^+$  ATPase in vascular smooth muscle and adrenergic nerve terminals. Table 2 shows no significant difference in serum chloride level between the study subjects. However, study by Barret *et al* observed that there was a significant difference in chloride level between the two groups.<sup>20</sup>

## CONCLUSION

From this comparative case control study, it was observed that Leptin levels were significantly elevated in PE than in normal pregnant women. Serum leptin was also

positively correlated with blood pressure. Thus, serum leptin level was increased with the severity of pre-eclampsia. The results also showed significant increase in sodium level and a significant decrease in calcium and potassium levels in pre-eclampsia. Thus, along with dietary restriction of sodium, dietary supplementation of calcium and potassium during pregnancy could result in reduction in the incidence of PE.

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