Study the Role of Serum Leptin Level in the Detection of Preeclampsia and Its Severity

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Abstract: The aim of this study was to evaluate the serum leptin levels in preeclampsia patients and in normotensive pregnant women, as well as, to assess an association with the severity of the disease.

Design: In this prospective, cross-sectional, comparative, analytic study.

Materials and methods: A study carried out in Al-Zahra's Maternity and Pediatric Teaching Hospital in Al-Najaf city from April 2011 to September 2011. We measured serum leptin levels of 21 pregnant women having no hypertension (control group), 26 pregnant women with hypertension and no protein in urine, 20 pregnant women with mild pre-eclamptic group was the third group, and severe pre-eclamptic group 33 pregnant ladies. We also did blood and urine analysis for the evaluation of the severity of hypertensive disorder of pregnancy. The patients were followed until after delivery and information about labour was recorded. We analysed the difference and correlation between anthropometric measures, hormonal and biochemical parameters, and serum leptin levels in two groups.

Results: In the study group, serum leptin levels were determined to be higher in preeclamptic group than the control group (10.719±13.757), and there is further significant elevation in sever type (38.609±28.933) than in mild preeclampsia (14.885±14.786).

Conclusion: Serum leptin levels in sever preeclamptic pregnant women appear to be higher than mild preeclamptic one and the control group, so it may be used as a significant determinant of disease severity thereby it may be useful as a marker for predicting time of delivery or termination of pregnancy and pregnancy outcomes.

Keywords: Leptin, Hypertensive Disorder, Preeclampsia, Pregnancy.

I. INTRODUCTION

Preeclampsia is a multisystem disorder characterized by hypertension, proteinuria and non-dependent edema, which develops in late pregnancy, it can present in a wide variety of ways and not always in the classical fashion, it is a leading cause of maternal morbidity and mortality and common cause of prematurity and hospital admission and it remains a relatively common cause of death in pregnancy in the developed world.¹,² Although the precise mechanism of disorder remained elusive it is usually associated with placental hypoxia and dysfunction, 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.³ Several theoretical mechanisms have been proposed which result in uteroplacental insufficiency⁴ 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 activation⁵, especially neutrophils which releases superoxide and various cytokines.

All these are responsible for placental hypoxia and increase in plasma leptin concentration⁶ along with there is associated insulin resistance which is greatly influenced by adipocytokines characterizes preeclampsia maternal leptin rise⁷. Leptin is a product of ob/ob gene produced by adipose tissue and is synthesized by placenta during pregnancy⁸ resulting in increased serum leptin level with increasing gestational age particularly in preeclampsia and level declines in post partum period where by post-delivery the circulating levels fell sharply below pre-pregnant values⁹. An increasing number of biochemical agents were evaluated as markers for predicting pre-eclampsia. None of them has been proved to be of clinical value yet. Much effort has been put into assessing novel potential markers and their combination with other screening methods and as the leptin is a novel placenta-derived hormone in humans and suggested its significance in human pregnancy (2,9), we try to explore the changes in the leptin production level in the plasma of pregnant women with PE in our paper.

II. MATERIAL AND METHODS

This study was done in Al-Zahra'a Hospital Teaching center in Al-Najaf city between April 2011 and September 2011, total 100 pregnant women who were admitted at the
time of delivery or for termination of pregnancy due to complications of hypertension, all of them were of same age, weight. These women who participated in the study were divided into 4 groups: Control group consist of 21 pregnant women having no hypertension ,the second Hypertensive group consist of 26 pregnant ladies with hypertension and no protein in urine ,mild pre-eclamptic group was the third group consist of 20 pregnant ladies , and severe pre-eclamptic group 33 pregnant having sever preeclampsia. We exclude pre-existing chronic hypertension, diabetes, multiple pregnancies and any chronic renal or liver disease in the selected ladies. At time of admission a detailed obstetrical and medical history was taken from each subject with emphasis on her age, date of last menstrual cycle, family history, this is followed by a complete physical examination including an assessment of the lower extremity for edema and the weight of the patients and the blood pressure were measured.

After counselling and affordability of investigations their blood sample were drawn for serum leptin along with other biochemical and hematological investigations including renal function test, liver function test, and complete blood picture, in addition to Urine sample for estimation of albumin in urine. All analyses were performed using commercially available software (SPSS version 18). Significant differences of continuous variables were assessed by One Way Anova. Analysis (F-tests (P ≤ 0.01). Category data were assessed by Chi squared (χ²) test. A P-value ≤0.05 and ≤0.01 was considered as statistically significant and highly significant at 1% and 5% respectively.

III. RESULTS

TABLE I: Demonstrated Patients Characteristics Of Each Group

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Normal</th>
<th>Hypertensive</th>
<th>Mild Preeclampsia</th>
<th>Severe Preeclampsia</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>21</td>
<td>26</td>
<td>20</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>29.2±6.14</td>
<td>29.9±6.35*</td>
<td>26.9±6.67</td>
<td>24.6±5.968</td>
<td>0.211NS</td>
</tr>
<tr>
<td>Gestational Age</td>
<td>37.9±1.85</td>
<td>37.0±1.94</td>
<td>35.4±2.71</td>
<td>33.4±3.91</td>
<td>0.000**</td>
</tr>
<tr>
<td>Weight</td>
<td>86.24±9.37</td>
<td>90.58±11.73</td>
<td>88.80±8.76</td>
<td>85.48±10.07</td>
<td>0.236NS</td>
</tr>
<tr>
<td>Parity</td>
<td>1.43±1.28</td>
<td>1.40±1.61</td>
<td>1.15±1.60</td>
<td>1.24±1.44</td>
<td>0.817NS</td>
</tr>
<tr>
<td>Systolic BPmmHg</td>
<td>117.4±9.95</td>
<td>155.0±15.56</td>
<td>150.2±11.71</td>
<td>178.7±16.29</td>
<td>0.000**</td>
</tr>
<tr>
<td>Diastolic BPmmHg</td>
<td>76.7±9.13</td>
<td>96.9±9.70</td>
<td>103.5±6.71</td>
<td>114.5±5.65</td>
<td>0.000**</td>
</tr>
<tr>
<td>Birth weight kg</td>
<td>3.19±0.38</td>
<td>2.95±0.30</td>
<td>2.58±0.38</td>
<td>2.12±0.53</td>
<td>0.001**</td>
</tr>
<tr>
<td>Creatinin(mg/dL)</td>
<td>9.04±6.61</td>
<td>9.0±6.65</td>
<td>29.0±4.84</td>
<td>0.000**</td>
<td></td>
</tr>
</tbody>
</table>

**significant at P≤0.01, values of all characteristics are presented as mean ±SD; NS, not significant.

- No significant differences were observed in the age, weight and parity of hypertensive and pre-eclamptic groups in comparison with normal.
- Lower gestational age (P≤0.01) was recorded in the severe pre-eclamptic patients.

- Systolic and diastolic blood related significantly(P≤0.01) with severity of preeclampsia, higher blood pressure were recorded in the three studied groups in comparison with normal.
- Comparison of birth weight between patients groups showed that lowering of birth weight related to severity, mean that lower birth weight (P<0.01) was recorded in the women with severe preeclampsia.
- 84% of severe pre-eclamptic women delivered by C/S in comparison with 65% of mild preeclampsia and 34.6% of hypertensive and 14.28% of normal women.

TABLE II: Demonstrate Laboratory Results Of Each Group

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Normal</th>
<th>Hypertensive</th>
<th>Mild Preeclampsia</th>
<th>Severe Preeclampsia</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood urea mg/dl</td>
<td>27.6±3.248</td>
<td>31.0±3.908</td>
<td>31.0±4.979</td>
<td>39.3±5.822</td>
<td>0.000**</td>
</tr>
<tr>
<td>S.Creatinine Mg/dl</td>
<td>0.63±0.153</td>
<td>0.83±0.240</td>
<td>0.84±0.206</td>
<td>1.09±0.452</td>
<td>0.000**</td>
</tr>
<tr>
<td>S.Uric acid Mg/dl</td>
<td>4.84±0.76</td>
<td>4.49±1.231</td>
<td>5.62±1.947</td>
<td>6.34±1.447</td>
<td>0.000**</td>
</tr>
<tr>
<td>PCV %</td>
<td>34.04±2.418</td>
<td>34.00±2.083</td>
<td>33.54±2.018</td>
<td>30.50±4.148</td>
<td>0.032*</td>
</tr>
<tr>
<td>GPT IU/l</td>
<td>5.76±1.972</td>
<td>7.34±3.249</td>
<td>9.0±3.764</td>
<td>9.94±3.152</td>
<td>0.000**</td>
</tr>
<tr>
<td>GOT IU/l</td>
<td>14.33±3.947</td>
<td>15.40±6.303</td>
<td>23.40±11.325</td>
<td>33.00±13.610</td>
<td>0.014*</td>
</tr>
<tr>
<td>S.A.P. Mg/dl</td>
<td>1.75±1.327</td>
<td>1.86±1.299</td>
<td>1.87±2.398</td>
<td>2.05±1.920</td>
<td>0.000**</td>
</tr>
<tr>
<td>Platelets(10⁹)</td>
<td>232±15.0</td>
<td>222±18.1</td>
<td>192±15.1</td>
<td>120±38.2</td>
<td>0.000**</td>
</tr>
</tbody>
</table>

*significant at P≤0.05, **significant at P≤0.01, using ANOVA, values are presented as mean ±SD ; NS, not significant.

- Sever pre-eclamptic women showed higher (P≤0.01) blood urea, S. creatinine , and S. uric acid than other groups.
- PCV increased in relation with severity of preeclampsia, significant differences at (P≤0.05) were recorded for studied groups due to haemo-concentration.
- Liver function tests showed clear relationship with severity of preeclampsia, all enzymes titration elevated in the sever preeclamptic women. A decreasing of platelates count were observed in the sever preeclamptic women, that mean significant differences were recoded between groups.

Table II: The Level of S. Leptin In The Different Studied Groups

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Normal</th>
<th>Hypertensive</th>
<th>Mild Preeclampsia</th>
<th>Severe Preeclampsia</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. Leptin</td>
<td>10.71±15.75</td>
<td>11.77±15.89</td>
<td>14.08±14.78</td>
<td>30.60±28.933</td>
<td>0.000**</td>
</tr>
</tbody>
</table>

S. Leptin showed significant increment in sever preeclampsia (P≤0.01) group.
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IV. 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, in our study there is significant relation between severity of PE and low GA due to the risk of preterm labor, this risk is iatrogenic due to termination of pregnancy to prevent and decrease maternal and fetal complications. This agreed by Cruz, et al(10), who found that risk of preterm labor and pre maturity increase with severity of preeclampsia in their study. At the same time there is significant low birth weight in mild and severe PE group which is more significant in sever group and this is due to placental insufficiency and intra uterine growth retardation as a complication of PE and iatrogenic prematurity as the delivery is the only cure for PE, prematurity account 15% of all premature birth and one in five very low birth weight infant( less than 1500 gm)(11).

Regarding mode of delivery in our study 84% of patients in sever PE group and 65% of mild group was delivered by C/S due to increase maternal and fetal complications that need immediate delivery to decrease maternal and perinatal morbidity and mortality, which agree with Seong, et al study on 454 patients with pregnancy related hypertension they found that 71% of pre-eclamptic patients were delivered by C/S(12). In our study we demonstrate laboratory results of each group, and we found that there is significant deterioration in renal function test represented by increase B.urea, S. creatinine and S. uric acid, that all due to ischemic changes in origin, arterial constriction, endothelial swelling and intravasation fibrin deposition all that explain the deterioration of renal function which increase with severity of PE in comparison with control group which is within normal level also there is increase in PCV in sever PE group due to associated haemo-concentration, about platlate count there is markedly decrease in sever group due to platlate depletion as a complication of PE specially with HEELP syndrome.

In addition we found that there is marked elevation in the liver enzymes ( GPT ,GOT ,S.A.P.) in sever pre-eclamptic group, this results were confirmed with TAYLAR et al(13). 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 preeclampsia. The results of our study suggested that serum leptin level increases significantly in sever preeclampsia, Similar findings were seen in a study done by Firdous Muntazet al(14) who The results of our study suggested that serum leptin level increases with increase in blood pressure both systolic and diastolic, and the same was noticed in a study done by Sebiha Özkanet al(15) , serum leptin levels were determined to be higher in hypertensive pregnant women than the control group, they also found that Neonatal birth weight was significantly lower in the hypertensive group. While the serum uric acid, urea, aspartate amino-transferase, fibronectin, and fasting blood glucose levels were found to be higher, serum total protein and albumin levels were significantly lower among the hypertensive pregnant women.

Mise Het al(2) also demonstrated that placental production of leptin is augmented in severe PE, probably because of placental hypoxia, thereby suggesting the possible significance of leptin as a marker of placental hypoxia in severe PE, and a study done by Acromite Met al(16) which confirms that leptin levels are higher in women with preeclampsia than in controls and they demonstrates that serum leptin levels do not add to the prediction of preeclampsia after accounting for BMI, estrogen and SHBG levels of pre-eclamptic women. We found one study done by E. Martinez-Abundiset al(17) were they found that serum leptin levels were similar in the patients with different grades of pre-eclampsia and normotensive pregnant women.

V. CONCLUSION

It has been concluded from our study that plasma leptin level is increased in pre-eclampsia and further increased with sever preeclampsia for that it may be taken independently or along with other parameters as a marker for severity of preeclampsia, hence avoiding risk effects of pre-eclampsia to mother and foetus. Our study had some limitations such as smaller sample size, lacking some parameters hence our finding still needs some more interpretation for further study.

VI. ACKNOWLEDGMENTS

I gratefully thank all people who provide me with assistance in my study, especially all the staff in the laboratory of Al-Zahra’s Maternity and Pediatric Teaching Hospital in Al-Najaf city and Dr.Raheem Jabbar Hameed. We are grateful to all pregnant women who participated in this study. Special thanks are due to Dr Salam Jasim Mohammed for his help in data analyses.

VII. REFERENCES

[5]Masuyama H, Nakatsuksa H, Takamoto N, Hiramastu Y.Correlation between soluble endoglin, vascular endothelialgrowth factor receptor-1, and adipocytokines in