A STUDY ON INSULIN LEVELS IN PREGNANCY INDUCED HYPERTENSION

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ABSTRACT:
Context: Pregnancy induced hypertension occurs in about 5-10% of pregnancies. Many features of insulin resistance syndrome like hyperinsulinemia and dyslipidemia have been identified in these patients.
Aim: To analyse the levels of insulin and lipid profile in patients with pregnancy induced hypertension.
Methods: We measured insulin levels and lipid profile in 50 patients with pregnancy induced hypertension in their 3rd trimester. 25 normotensive pregnant women in 3rd trimester 15 non pregnant non hypertensive females formed the control groups.
Results: Compared with controls, the patients with pregnancy induced hypertension had significantly elevated levels of insulin (p<0.01) and triglycerides (p<0.01).
Conclusion: These observations indicate that insulin resistance may play a role in the pathogenesis of pregnancy induced hypertension.
Key words: Dyslipidemia, Hyperinsulinemia, Insulin, Insulin resistance, Pregnancy induced hypertension.

INTRODUCTION:
Pregnancy induced hypertension which is one of the most common complications of pregnancy is a major cause of maternal and fetal morbidity and mortality. [1] Hypertensive disorders of pregnancy include i) new onset of hypertension in pregnancy (gestational hypertension and preeclampsia) ii) pre existing hypertension and iii) exacerbation of existing hypertension. [2] Preeclampsia is hypertension accompanied by significant proteinuria. [1] Preeclampsia is frequently described as a state of insulin resistance. [3] Many features of insulin resistance like hypertension, hyperinsulinemia, glucose intolerance and lipid abnormalities are associated with this condition. [2] Insulin resistance, inflammation and atherosclerosis appear to be linked via the metabolic syndrome. Insulin resistance is associated with elevated levels of various proinflammatory markers which cause endothelial dysfunction and initiate the atherosclerotic cascade. [4] Multiple studies have shown associations between markers of insulin resistance and hypertensive pregnancies. [2] The metabolic changes during pregnancy may provide an early means of assessing future risk for chronic diseases. [1] In several studies conducted postpartum, women with a history of preeclampsia have been shown to be more insulin resistant when compared with women with normotensive pregnancy. [5] The aim of the study was to assess the levels of fasting insulin and lipid profile in normotensive and hypertensive pregnancies.

SUBJECTS AND METHODS:
This was a case-control cross sectional study to compare the levels of fasting insulin and lipid profile in a group of 50 PIH patients and 40 controls. PIH was defined as persisting elevation of blood pressure ≥ 140/90 mm Hg confirmed by two measurements (in the sitting posture at least six hours apart) or an increase of at least 30mm Hg systolic or 15mm Hg diastolic over baseline values with or without significant proteinuria. Patients with twin pregnancy and gestational diabetes were excluded from the study. None of them had renal or heart disease. The control group 1 consisted of 25 normotensive pregnant women. All the subjects were primigravida in the age group of 20-32 years and in the 3rd trimester of pregnancy. The patients attended the Obstetrics department of Government General Hospital, Chennai. The control group 2 consisted of 15 healthy normotensive, non pregnant woman. Informed consent was obtained from all the subjects.
Methods:

5 ml of venous blood was collected from all the subjects after a 12-h fast. Plasma glucose and serum total cholesterol, triglycerides and HDL were analysed on the same day of collection using Erba autoanalyser and kits from the same company. LDL-C was calculated by Friedewald formula. The serum was stored at -20ºC and analysis of insulin was performed by sandwich type ELISA technique using Stat fax ELISA reader. Data analysis was performed using SPSS, version 17.0.

RESULTS:

The study group included 50 patients with pregnancy induced hypertension whereas the control group comprised of 25 normotensive pregnant females and 15 normotensive, non pregnant females. Both the study and the control groups were age matched.

The average fasting insulin levels were 53.4±13.65µU/ml in patients with PIH and 28.64±16.75µU/ml in the normotensive pregnant group. This difference was found to be statistically significant. Our study has also shown significant elevations in total cholesterol, triglyceride and LDL cholesterol in the hypertensive group.

Table 1.
Comparison of mean±SD of measured parameters between Normotensive pregnant and PIH groups and the statistical significance of the differences.

<table>
<thead>
<tr>
<th>PARAMETERS</th>
<th>NORMOTENSIVE PREGNANT (n=25)</th>
<th>PIH (n=50)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin (µU/ml)</td>
<td>28.64±16.75</td>
<td>53.4±13.65</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Fasting Plasma Glucose(mg/dl)</td>
<td>63.65±4.89</td>
<td>73.58±6.31</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>192.4±27.54</td>
<td>210.26±29</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)</td>
<td>173±28.04</td>
<td>211.5±49.17</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>LDL-C (mg/dl)</td>
<td>114±18.01</td>
<td>129.82±26.69</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>HDL-C (mg/dl)</td>
<td>40.2±5.68</td>
<td>38.82±5.2</td>
<td>NS</td>
</tr>
<tr>
<td>VLDL-C (mg/dl)</td>
<td>34.55±5.43</td>
<td>41.58±9.38</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

The values are considered to be statistically significant if the p value is less than or equal to 0.05 (p ≤ 0.05)

NS = not significant
DISCUSSION:

There is growing evidence to indicate that PIH is related to insulin resistance and may represent an early manifestation of insulin resistance syndrome. \[1\]

Insulin resistance and the resultant hyperinsulinemia are characteristic of normal pregnancy and are maximal in the third trimester. This is probably mediated by several hormonal changes including elevations in levels of human placental lactogen, progesterone, cortisol and estradiol. \[2\] Pregnancy also produces a relative hyperlipidemic state. \[1\]

Plasma levels of renin, angiotensin and aldosterone are increased. Despite these changes the blood pressure decreases slightly in normal pregnancy due to decreased systemic vascular resistance and increased resistance to angiotensin and other pressors. \[6\] In women whose pregnancies are complicated by hypertension, there appears to be an exaggeration of insulin resistance. \[2\]

In our study the fasting serum insulin levels were higher in women with pregnancy induced hypertension than in the controls. Mid pregnancy fasting hyperinsulinemia has been associated with subsequent development of pre eclampsia \[7\] Myles wolf et al, 2002 has identified through reduced sex hormone binding globulin [SHBG] levels, a significant association between 1st trimester insulin resistance and subsequent risk of pre eclampsia \[8\].
Hyperinsulinemia may directly predispose to hypertension by increasing the renal sodium reabsorption and stimulation of the sympathetic nervous system. [2] Since pregnancy induced hypertension is also characterised by sodium retention and increased level of catecholamines it is suggested that insulin resistance may play a role in the pathogenesis of hypertension in pregnancy. [1]

In this study, the lipid profile of patients with hypertensive pregnancy suggests a proatherogenic state. These findings are in accordance with the study by Belo et al, 2002 which reported that in females with established pre eclampsia the triglyceride and free fatty acid concentrations were higher than in women with normotensive pregnancies [9].

Ogura et al, 2002 has suggested that there is a predominance of the atherogenic small dense LDL in pre eclamptic women [10]. Similar to hyperinsulinemia, elevated total cholesterol, triglyceride and free fatty acid levels during pregnancy have preceded the development of pre eclampsia. [11,12]

Pregnancy induced hypertension has been associated with hyperinsulinemia in both cross sectional designs and cohort studies. Ichiro Yasuhi et al, 2001 has documented that mid pregnancy C-peptide concentrations were associated with later development of pregnancy induced hypertension independent of pre pregnancy obesity [13].

The results of a cohort study by Brenda et al, 2003 has found significant associations between hypertensive disease of pregnancy and the development of hypertension and other associated diseases in later life [14].

A retrospective study conducted by Gordon et al, 2001 has reported that women who had a diagnosis of pre eclampsia had a twofold risk of ischemic heart disease over the next 15-19 years [15]. The findings of the cohort study by Henrik U Irgens et al, 2001 indicates that the long term risk of death from cardiovascular causes is associated with a maternal genetic predisposition to eclampsia [16].

Thus pregnancy may be viewed as a stress test for glucose intolerance, hypertension and other abnormalities associated with insulin resistance syndrome. [1]

CONCLUSION:
In our study, features of insulin resistance such as hyperinsulinemia and hypertriglyceridemia have been observed in patients with pregnancy induced hypertension. These findings suggest that pregnancy induced hypertension may be an early manifestation of insulin resistance syndrome. Interventions to improve insulin sensitivity may be beneficial in these patients.

REFERENCES: