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The Assessment of Hyperinsulinemia in Hypertensive Disorders in Pregnancy

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OBJECTIVE - To determine whether hyperinsulinemia is present in hypertensive disorders in pregnancy. **METHOD** - A prospective analysis of the glucose and insulin responses to 75 gm oral glucose in 100 women with pregnancy induced hypertension (PIH) but normal glucose tolerance in comparison with the responses observed in a matched control group of 100 healthy pregnant women. **RESULT** - The glucose concentrations, both fasting and two hours after glucose ingestion, were similar in both the groups. Similarly, insulin concentrations, both fasting and postglucose, were also similar in the two groups. **CONCLUSION** - There is no definite evidence of the role of insulin resistance in the pathogenesis of hypertensive disorders in pregnancy. However, there was a subgroup of women with mild PIH and past history of PIH who demonstrated some evidence of insulin resistance in PIH.

Key words : insulin resistance, hyperinsulinemia, pregnancy induced hypertension

Introduction

Hypertensive disorders are the most common medical complications during pregnancy and are associated with high materno-fetal mortality and morbidity in both underdeveloped and developed countries. There is evidence that hyperinsulinemia and insulin resistance play a role in the development of hypertension[1]. It has also been suggested that insulin resistance is associated with severe preeclampsia[2]. Therefore, the present study was undertaken to determine whether hyperinsulinemia is present in hypertensive disorders in pregnancy.

Materials and Methods

The study was conducted over a period of one year in 100 consecutive pregnancy induced hypertensive women from 20 weeks of gestation onwards. For the control group, 100 healthy pregnant women matched to the study group by age, body mass index and gestational age were selected.

In all patients, laboratory investigations were done after an overnight fast of 10 to 12 hours. Blood samples were obtained before and two hours after 75 gm oral glucose according to WHO criteria. Measurement of blood glucose was done by Hexokinase method and insulin measurement by Microparticle Enzyme Immuno Assay Method.

Results

The two groups had similar mean age, body mass index, parity and gestational age, whereas systolic and diastolic blood pressure values were significantly higher in the preeclamptic group than in healthy pregnant women (Table I).

Table I : Clinical Characteristics

Characteristics	Normal Pregnancy N = 100	PIH N = 100	P Value
Age (years)	24.5 ± 3.5	24.09 ± 3.5	0.41
BMI (Kg/m2)	23.3 ± 2.5	23.0 ± 2.5	0.38
Parity Index	2.1 ± 1.6	1.73 ± 0.9	0.05
Gestational age (weeks)	34.4 ± 4.8	33.7 ± 5.0	0.31
Systolic Blood Pressure (mmHg)	117.5 ± 7.2	157.2 ± 17.5	<0.0001
Diastolic Blood Pressure (mmHg)	77.1 ± 6.5	109.7 ± 11.8	<0.0001

Fasting glucose concentrations were 81.6 mg/dl and 83.9 mg/dl in the control and the PIH group respectively. The difference is not significant. Post-load glucose concentrations were similar viz 110.2 µg/dl and 115.9 mg/d in the two groups. Even fasting insulin (11.4 µU/ml vs 12.9 µU/ml: P=NS) and post-load insulin concentrations (59.8 µU /ml vs 59.5 µU/ml; P=NS) were similar in the two groups.

However, the fasting and post-glucose insulin concentrations were higher in the mild PIH group compared to control or severe PIH groups (Table II) and the differences were statistically significant (P<0.05).

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Table II : Fasting and Post Load Insulin in PIH

Groups	Fasting Insulin (μU/ml)	Post load insulin (μU/ml)
Mild PIH	15.8	74.7
Severe PIH	10.4	49.8
Control	11.4	59.8

Fasting and post glucose insulin concentrations were also elevated in women with history of PIH in previous pregnancies as compared to controls, and the differences were statistically significant ($p<0.05$) (Table III). The means were compared across the groups using one way analysis of variance.

Table III : Fasting and Post-load Insulin in Women with Past History of PIH

Groups	Fasting Insulin (μ U/ml)	Post - load Insulin (μU/ml)
PIH in Previous Pregnancy	30.7	86.5
Control	10.0	48.3

In normotensive women, it was found that women with history of recurrent abortions, congenital anomalies in the fetus and medical complications, had higher mean post-glucose insulin concentrations as compared to that in the control group without high risk factors, both medical and obstetric, present or past (Table IV).

Table IV : Glucose and Insulin Concentrations in High Risk Women

Groups	Fasting blood glucose mg/dl	Post-load blood glucose mg/dl	Fasting Insulin μU/ml	Post-load Insulin μU/ml
Recurrent Abortions	78.6	112.1	12.19	145.99
Congenital anomalies in the fetus	81.2	115.5	9.49	62.99
Medical Complications	84.4	104.0	9.88	74.42
Control	79.5	105.3	9.96	48.3

Discussion

The incidence of hypertensive disorders in pregnancy in India is about 8-10%[3]. Despite numerous efforts at etiology, pathophysiology, early diagnosis, prevention and treatment, PIH remains a major cause for adverse maternal and perinatal outcome.

Insulin resistance appears to be a causative mechanism for the development of hypertension. Patients with high blood pressure as a group are resistant to insulin – mediated glucose uptake and are hyperinsulinemic. In this context, the study of women who become hypertensive during pregnancy provides additional insight into the relationship between insulin resistance hyperinsulinemia and blood pressure regulation.

The various hypotheses to explain hyperinsulinemia are as follows :

1. Hypertensive disorders in pregnancy are disorders of vasospasm with increased reactivity to angiotensin, catecholamine and vasopressin[4,11]. In addition, endothelial cells of these patients abnormally release pressor substances such as endodhelin – 1 which causes vasoconstriction and catecholamine release.
2. Insulin itself can stimulate endothelin – 1 from endodhelial cells[5].
3. Insulin stimulates sympathetic nervous system activity[6]. Sympathetic over activity may lead to insulin resistance.
4. Hyperinsulinemia may be associated with suppressed Ca^{2+} - ATPase activity with reduced intracellular Ca^{2+} efflux causing increased intracellular Ca^{2+} at the smooth muscle level[7]. This causes increased vascular tone and elevated vascular resistance.

A few studies in recent past have demonstrated that women with preeclampsia have higher insulin levels compared to matched healthy pregnant women[2,8-10]. However, the study by Jacober et al and our study were unable to confirm a relationship between hyperinsulinemia and PIH[11].

But there was a subgroup of women with mild PIH and history of PIH in previous pregnancies who demonstrated higher fasting and post-load insulin concentration with normal glucose tolerance, suggesting that a state of resistance to insulin action is present in these women and similar pathophysiology is manifested in later pregnancy.

The occurrence of insulin resistance in mild PIH and

of hyperinsulinemia in women with past history of PIH was significant in our study. We are unable to explain its cause.

The observation of post-glucose hyperinsulinemia in normotensive women with history of recurrent abortions, congenital anomalies in the fetus and with medical diseases, did not reach statistical significance in our study because of small size. Further research with large study sample may offer expected results.

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