ORIGINAL RESEARCH PAPER

Volume-7 | Issue-6 | June-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

ROLE OF INSULIN RESISTANCE IN PREGNANCY INDUCED HYPERTENSION

Medical Science

Arshia Zeib — Osmania Medical College & 9-3-238/a/6, First Floor Khan Villa, Akberpura , Tolichowki, Hyderabad, Telangana

Arshiya fatima* — Osmania Medical College & 16-7-470,471. Flat No.302, Mythri Residency, Azampura, Chaderghat Hyderabad Telangana, *Corresponding Author

N.Vani — Osmania Medical College & Osmania Medical College , Koti, Hyderabad, Telangana.

ABSTRACT

Background & Objectives: Hypertension is one of the common medical complications of pregnancy and contributes significantly to maternal and perinatal morbidity and mortality. Preeclampsia is frequently described as a state of insulin resistance. Insulin resistance features like hypertension, hyperinsulinemia, glucose intolerance and lipid abnormalities are associated with pregnancy induced hypertension. Due to the effect of insulin on epithelium and smooth muscle, hyperinsulinemia causes vascular resistance by inducing endothelial dysfunction or smooth muscle hypertrophy. It also stimulates release of epinephrine and thus increasing blood pressure. Aim of the study is to evaluate insulin resistance as a causative pathogenesis factor of PIH.

Methods: A case control study was done with 90 patients divided into 2 groups (normotensive pregnant women as controls, pregnancy induced hypertension as cases). Fasting levels of Plasma Glucose and Serum Insulin were estimated. IR was calculated by HOMA-IR formula. Data was analyzed using unpaired t- test.

Results: In the present study women with PIH had significantly higher values of Serum Insulin (50.47 ± 24.59), IR(10.65 ± 5.22), , FBS(86.21 ±11.13,) as compared to normotensive pregnant women, Serum Insulin(10.28 ± 5.98), HOMA IR(1.97 ± 1.28), FBS(80.26 ± 8.69, p value 0.007) with p value of < 0.0001.

Interpretations & Conclusion: The PIH women exhibited significant increase in serum Insulin levels, HOMA IR, FBS. These observations suggest the possibility that insulin resistance may be involved in pathogenesis of PIH. Therapeutic approach to improve insulin sensitivity may help in prevention and treatment of PIH.

KEYWORDS

Pregnancy induced hypertension, Insulin resistance.

Introduction

Hypertension complicates 5% to 10% of pregnancies and contributes greatly to maternal morbidity and mortality. Hypertension is diagnosed empirically when blood pressure exceeds 140 mm Hg systolic or 90 mm Hg diastolic. Korotkoff phase V is used to define diastolic pressure.

According to World Health Organization (WHO), in developed countries 16 percent of maternal deaths were reported to be due to hypertensive disorders. More than half of these hypertension-related deaths were preventable.

The incidence is markedly influenced by race and ethnicity and thus by genetic predisposition. Young and primigravida women are vulnerable to develop preeclampsia, whereas older women are at greater risk for chronic hypertension with superimposed preeclampsia.[1] The cause of pregnancy-induced hypertension (PIH) is multifactorial, insulin resistance may be an important contributor to its development.[2]

Studies show thirty fold increase in human placental hormone plays role in increased secretion of insulin from pancreas in PIH women[4,5] The present study was under taken to evaluate role of insulin resistance in pregnancy induced hypertension.

METHODS:

Subject :

A case control study of 90 subjects was conducted in the Department of Biochemistry, Osmania General Hospital, Hyderabad after approval from the institutional ethics committee.

Inclusion criteria:

Group 1 included 45 normotensive pregnant women with gestational age >20weeks and BP< 140/90 mm of Hg as controls.

Group 2 included 45 pregnancy induced hypertension with gestational age > 20weeks and BP >140/90 mm of Hg as cases.

All the subjects under the study were in third trimester of pregnancy.

Exclusion criteria:

Women with gestational diabetes, twin gestation, diabetes mellitus, renal disease, heart disease, and other pregnancy related complications were excluded.

Data collection

After taking consent, fasting venous blood samples were collected from the subjects. Hemolysed and lipemic samples were discarded. Fasting plasma glucose estimation was done on the same day by Trinder`s method(GOD POD). Remaining sample was stored at -20^{0}C for insulin estimation Serum insulin levels were analyzed by ELISA method.

Homeostasis Model Assessment- Insulin Resistance (HOMA-IR) was used to measure insulin resistance

HOMA−IR[6] = [(fasting insulin (μU/ml)×(fasting glucose mg/dl)]

405

Statistical analysis

Data was analyzed using Graphpad prism software version 7.0. Analysis was performed using unpaired t test.

RESULT:

Table 1. MEAN + SD OF THE STUDY PARAMETERS AND THEIR SIGNIFICANCE

PARAMETERS	GROUP 1 (controls) n = 45	GROUP 2 (Cases) n=45	P value
Fasting glucose	80.26+ 8.69	86.21 + 11.13	<0.007
Insulin	10.28 + 5.98	50.47 + 24.59	<0.0001
HOMA-IR	1.97 + 1.28	10.65 + 5.22	<0.0001

TABLE 2.
UNPAIRED t TEST VALUES BETWEEN TWO GROUPS

PARAMETERS	t Value	P value	Degree of freedom
Fasting glucose	2.73	0.007	82
Insulin	10.29	0.0001	82
HOMA IR	10.46	0.0001	82

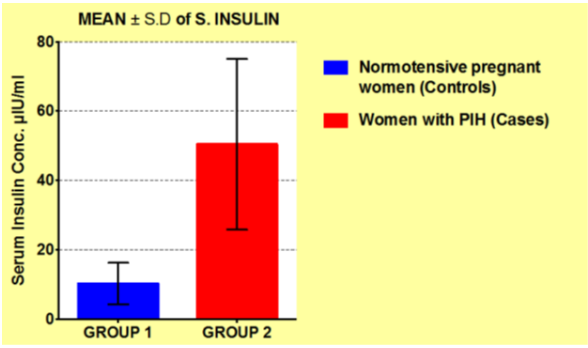

Figure 1. Comparison of Mean ± SD of Serum Insulin between PIH Women and nomotensive pregnant women

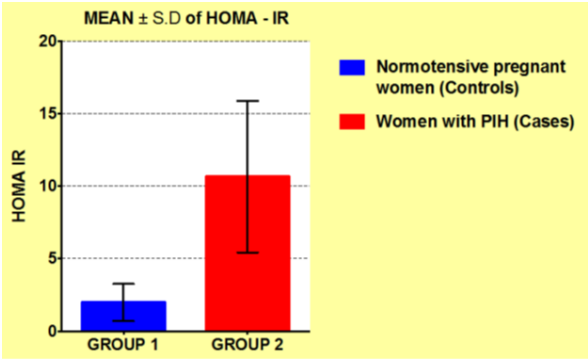

Figure 2. Comparison of Mean ± SD of HOMA -IR between PIH Women and nomotensive pregnant women

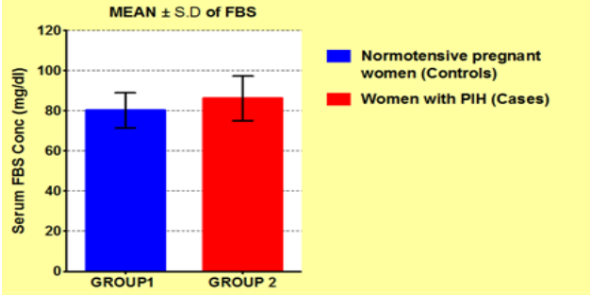

Figure 3. Comparison of Mean ± SD of Serum FBS between PIH Women and nomotensive pregnant women

Results are expressed in mean SD and unpaired t test .Comparison of mean + SD and p values of Group 1 and Group 2 is shown in table 1. Unpaired t values are shown in the table 2. P value <0.05 is considered significant. FBS, insulin and HOMA IR is significantly increased in the PIH women compared to normotensive pregnant women.

DISCUSSION:

Several studies have been done to indicate the role of insulin resistance in PIH. In this case control study, FBS and insulin levels were significantly increased in PIH women and insulin resistance which was calculated using the formula HOMA IR shows significant increase in the PIH women.

Mechanism that links hyperinsulinism and PIH remains unclear. Insulin has direct effects on vascular smooth muscle and epithelium. Hyperinsulinaemia increases vascular resistance by inducing smooth muscle cell hypertrophy or endothelial dysfunction leading to vasoconstriction and stiffening. It also acts on the sympathetic nervous system, and stimulate the release of epinephrine, thus increasing heart rate and systolic BP.[7,8]

According to ionic resistance model, resistance of Na-K ATPase to insulin, leads to increase in intracellular calcium and finally results in hypertension. Insulin might induce activation of Na-K ATPase and cause vasodilatation in normotensive pregnant women .[10,11]Reduction of Na-K ATPase activity in PIH women would increase intracellular sodium which reduce sodium/ calcium exchange and result in increased intracellular calcium and leads to increase in smooth muscle tone and hence blood pressure.[9]

Thus, in the present study the increased IR is probably mediated by placenta derived hormones, including human placental lactogen, progesterone, cortisol, estradiol, human placental growth hormone and prolactin. Pregnancy-associated insulin resistance has been also related to free fatty acids (FFAs), peroxisome proliferator-activated receptors, leptin, TNF-α, IL-6, adiponectin and resistin . Recently the role of adipokines has been highlighted.[12]

According to Farideh Rezaei Abhari et al Insulin-resistance in women with preeclampsia was higher in first trimester prior to diagnosis as well as in the third trimester after diagnosis compared to normal pregnancy under similar conditions.[4]

John C. Hauth, et al documented that midtrimester maternal insulin resistance is associated with subsequent preeclampsia and that maternal midtrimester insulin resistance increased significantly with increasing body mass index among Hispanic and African American women.[13]

V.M. Vinodhini observations indicate that insulin resistance may play a role in the pathogenesis of pregnancy induced hypertension. Measurement of insulin resistance in first trimester may be useful in predicting the risk of preeclampsia. Hyperinsulinemia which leads to increased renal sodium reabsorption and stimulation of sympathetic nervous system may directly predispose to hypertension. Insulin resistance may play a role in pathogenesis of PIH, which is characterized by sodium retention and increased level of catecholamine.[14]

CONCLUSION:

Our findings showed significant increase in insulin levels and insulin resistance in PIH women in comparison to normotensive women. Women with prior pre-eclampsia, especially those with early onset disease and recurring disease in subsequent pregnancies, carry an enhanced risk of future CVD. The risk of future cardiovascular events increases significantly if pregnancy has been complicated by both hypertensive disorders of pregnancy and GDM .[15] The association between pre eclampsia and insulin resistance may be significant in understanding the pathological process and may help in developing strategies for prevention and early diagnosis of pre-eclampsia.

References

1) Hypertensive Disorders. In :Cunningham, Lenovo, Bloom, Spong, Dashe, Hoffman, Casey, Shefield (eds). Williams obstetrics. 24th edition. McGraw-Hill Education; 2014. p: 1509
2) Caren G. and Ellen W. Seely Brief Review: Hypertension in Pregnancy : A Manifestation of the Insulin Resistance syndrome? Journal of the American heart association hypertension 2001;37:232-239
3) National High Blood Pressure Education Working Group Report on High Blood Pressure in Pregnancy. Am J Obstet Gynecol. 1990;163:1689–1712.
4) Farideh Rezaei Abhari, Maryam Ghanbari Andarieh, Asadollah Farokhfar, And Soleiman Ahmady: Estimating Rate Of Insulin Resistance In Patients With Preeclampsia Using Homa-Ir Index And Comparison With Nonpreeclampsia Pregnant Women : Biomed Research International Volume 2014. Available from: DOI :10.1155/2014/140851.
5) S. Handwerger and M. Freemark, "The roles of placental growth hormone and placental lactogen in the regulation of human fetal growth and development," Journal of Pediatric Endocrinology andMetabolism, vol. 13,no. 4, pp. 343– 356, 2000.
6) wikipedia
7) Matsuda Y, Hayashi K, Shiozaki A, Kawamichi Y, Satoh S, Saito S, 2011 Comparison of risk factors for placental abruption and placenta previa: case-cohort study. J Obstet Gynaecol Res 37: 538-546.
8) Mannisto T, Mendola P, Vaarasmaki M, et al, 2013 Elevated blood pressure in pregnancy and subsequent chronic disease risk. Circulation 127: 681-690
9) Shohreh Malek-Khosravi, MD; Bijan Kaboudi: Insulin changes in preeclamptic women during pregnancy: Ann Saudi Med 24(6) November-December 2004.
10) Well E, Sasson S, and Gutman Y. Mechanism of insulin induced activation of Na-K ATPase in isolated rat soleus muscle. Am J Physiol. 1991;261:C224-30.
11) Ang C, Hillier C, Mac Donald A, Cameron A, Greer I, Ann lumsden M. Insulin mediated vasorelaxiation in pregnancy. Br J Obstet Gynaecol. 2001;108:1088 - 1093.
12) Anna Tuuri Metabolic and Hormonal Factors Related to Hypertensive Pregnancy. Helsinki University Central Hospital, 2014 p:104.
13) Hauth JC, Clifton RG, Roberts JM, et al. Maternal insulin resistance and preeclampsia. Am J Obstet Gynecol 2011;204:327.e1-6.
14) V.M. Vinodhini, V. Devisri, W. Ebenezer William A Study On Insulin Levels In Pregnancy Induced Hypertension International Journal Of Pharmaceutical And Biological Research (Ijpbr) Vol 3 Issue 2 Apr-May 2012
15) Sullivan SD, Umans JG, Ratner R. Hypertension complicating diabetic pregnancies: pathophysiology, management, and controversies. J Clin Hypertens (Greenwich)2011;13(4):275-284.