Original research article

Comparison of Homocysteine (Hcy) levels and its association with pregnancy induced hypertension.

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Abstract

Aim: To study the Homocysteine (Hcy) levels in pregnancy induced hypertension. **Materials and Methods:** A Case control study was conducted in the Department of Obstetrics and Gynaecology, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India from 1 year. Total 200 pregnant female subjects in the age group of 16-50 yrs were selected. Out of them 100 were normotensive pregnant women (NPW) in their third trimester and were chosen as control Group 1 and 100 pregnancy induced hypertensive (PIH) patients in their third trimester were chosen as study Group 2. **Results:** The mean and standard deviation of Homocysteine, uric acid and magnesium levels of NPW and PIH groups. The Hcy level was significantly increased with a mean and standard deviation (SD) value of 20.14±5.87 µmol/l (p- value=0.001) and the uric acid level was also increased with a mean and SD of 6.05±0.67mg/dl (p-value= 0.003) in the PIH. The Hcy level was 9.07 ± 2.24 µmol/land the Uric acid level was 3.41 ± 0.84mg/dl in NPW group. The magnesium level was lower in the PIH compared to NPW (p -value=0.001).

Conclusion: The Hcy and uric acid levels were increased and Magnesium level was decreased in PIH women than the NPW. So these parameters should be part of the evaluation of the pregnant women presenting with hypertension. Thereby, we can reduce the maternal and fetal mortality rate.

Keywords: Homocysteine, Hyperhomocysteinemia, Uric acid, Magnesium and Pregnancy Induced Hypertension (PIH).

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Introduction

Since McCully[1] first hypothesized that elevated plasma homocysteine concentrations could cause atherosclerosis, a large body of evidence has validated this relationship.[2-4] Both retrospective and prospective studies have demonstrated that hyperhomocysteinemia is a risk factor for cardiovascular disease that is independent of classic risk factors, such as smoking, hypercholesterolemia, and hypertension.[5-7]

Hypertensive disorders are common in pregnancy and they cause serious complications like eclampsia, hemorrhage and infection leading to increased maternal and fetal mortality. Pregnancy induced hypertension is defined as a condition that results in persistent elevation of blood pressure of ≥140/90mm Hg or more (confirmed by two measurements in sitting posture at least six hours apart) or 30mm Hg systolic or ≥ 15mm Hg diastolic over base values arising denovo in pregnancy. Homocysteine, an essential amino acid is found in many animals and plant foods; it's formed from methionine, a sulphur containing amino acid. Elevated levels of homocysteine play an independent role for atherosclerosis and vascular thrombosis.[8] A derangement in the homocysteine-methionine metabolism leads to vascular damage causing hypertension and further to the classical clinical manifestations of preeclampsia. Elevated homocysteine is a risk factor for endothelial dysfunction and vascular disease such as atherosclerosis and occlusive vascular disorders.[9] The mean homocysteine levels normally decrease with gestation either due to physiological response to the pregnancy, increase in estrogen, hemodilution from increased plasma volume or increased demand for methionine by both the mother and fetus.[10] Homocysteine is a naturally occurring aminoacid derivative in the body. Increase in hormones

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such as estrogen and cortisol during pregnancy may also mediates, specific decrease in Hcy concentration. The mechanism behind the endothelial dysfunction had been demonstrated in experiments. Hcy decreases the expression of a wide range of antioxidant enzymes. This impairs endothelial nitric oxide (NO) bioavailability by decreasing Glutathione peroxidase activity which raises the possibility that Hcy sensitizes cells for reactive oxygen species (ROS).[11] During early pregnancy serum uric acid levels fall, often to 3 mg/dl or below, related to the uricosuric effects from estrogen and from the increase in renal blood flow. Uric acid levels then increase during the third trimester. However, it is known that subjects destined to develop preeclampsia show slightly higher serum uric acid levels during the first trimester in association with a relative reduction in urinary urate excretion.[12] Increasing evidence suggests that an elevated serum uric acid in pregnancy may not only be a valuable biomarker for preeclampsia but may also have a contributory role in the pathogenesis of the maternal and fetal manifestations. Uric acid is a potent inhibitor of endothelial function, induces systemic and glomerular hypertension in animals, and passes freely into the fetal circulation.[13] Uric acid has been found to block vascular endothelial growth factor (VEGF)-induced endothelial proliferation and thus may have a direct role in blocking fetal angiogenesis resulting in small for gestational age infants.[14] Uric acid can also block trophoblast invasion in vitro.[15] These studies suggest that measurement of serum uric acid is clinically useful and Serum calcium and magnesium are very important for metabolism at the cellular level and are vital for muscle contraction and cell death and neuronal activity making it very essential in pregnancy.[16] Magnesium plays an important role in peripheral vasodilatation. Homocysteine level causes injury to the vascular system of both maternal and fetal organs and increased uric acid level and decreased magnesium levels affects vascular and renal systems, thereby aggravating the process leading to eclampsia, resulting in increased maternal-fetal mortality and morbidity. So this study is taken up to assay the levels of Homocysteine, uric acid and magnesium in PIH and NPWgroup.

Material and Methods

A Case control study was conducted in the Department of Obstetrics and Gynaecology, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India from 1 year.

The study protocol was reviewed by the Ethical Committee.

Inclusion Criteria:

Control: Normotensive pregnant women in their third trimester with no complications.

Cases: Pregnant women with Pregnancy Induced Hypertension in their third trimester with persistent elevation of blood pressure 140/90 mmHg and more confirmed by two measurement (In the sitting posture, at least six hours apart) or increase of atleast 30mm of Hg systolic or 15mmHg diastolic over baseline value and both groups in age matched in the range 16 to 50yrs were included for the study.

Exclusion Criteria:

Women with previous history of Hypertension, Diabetes Mellitus, Renal or heart disease and other complications of pregnancy were excluded.

Methodology

Total 200 pregnant female subjects in the age group of 16-50 yrs was selected. Out of them 100 were normotensive pregnant women in their third trimester and were control. 100 pregnancy induced hypertensive (PIH) women in their third trimester were chosen as cases. Five ml blood sample was collected by venepuncture of the cubital vein after an overnight fast. Homocysteine was estimated by Axis Homocysteine enzyme Immunoassay [ELISA] method and uric acid was estimated by uricase method and magnesium estimated by colorimetric method.

Statistical Analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2010) and then exported to data editor page of SPSS version 19 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics included computation of Means and percentages. Test applied for the analysis were t-test and chi-square test. The confidence interval and p-value were set at 95% and 5%.

Results

Table 1: demographic profile of patients

	PIH (mean ± SD	NPW (mean± SD	P-value
Age	49± 1.83	48±2.61	0.681
BMI (kg/m2)	25.2 ± 0.4	24.2±0.5	0.419
Smoking status	28%	32%	0.274

Test applied: t-test and chi-square test

Table 2: Blood pressure (mm Hg)

Blood pressure (mm Hg)	PIH	NPW	P-value
Systolic	140 ±1.81	118±1.13	0.001
Diastolic	82±2.36	72±2.19	0.001

Test applied: t-test

Table3: Homocysteine, Uric acid and Magnesium levels in PIH & NPW

Parameter	Patients	Mean± SD	P value
Homocysteine (µmol/l)	PIH	20.14±5.87	0.001
	NPW	9.07 ± 2.24	
Uric acid level mg/dl	PIH	6.05±0.67	0.003
	NPW	3.11 ± 0.75	
Magnesium	PIH	1.41	0.001
	NPW	1.46	

Test applied: t-test

Discussion

In the present study, there was an increased Hcy level with a p value=0.001 and an increased uric acid level with a p value=0.003 in the PIH women when compared with NPW group.

In this study, we found homocysteine levels were higher in hypertensive patients as compared to a group of age, gender, and BMI-matched normotensive individuals. It has been shown that plasma homocysteine concentrations are higher in elderly isolated systolic hypertensive subjects than in normotensive controls.[17] Increased Hcy level had been proposed to explain endothelial cell dysfunction including direct cell injury in maternal circulation which causes a chronic inflammatory and endothelial damage and impairs synthesis of nitric oxide which causes uteroplacental insufficiency causing maternal vascular damage and increased reactive oxygen species (ROS), leading to hypertension.[18] Similar findings are reported by Sanchez et al.[19], Harma et al.[20] and Maruotti et al.[21] The interplay of various biological mechanism and effects of HHcy activates multiple processes leading to disorders. It enhances the production of several pro-inflammatory cytokines factors like Interlukin-8(IL-8).[22] It enhances the intracellular production of superoxide anions. Lopez et al. found an association between hyperhomocysteinemia and preeclampsia. In their study, the concentration of plasma homocysteine levels in patients with preeclampsia was higher than the NPW.[23]

The present study showed that serum magnesium level was significantly reduced in the PIH women than the NPW. These findings confirmed that hypomagnesemia may be one of the etiologies of preeclampsia. These results were consistent with earlier study by Zhao F and Frankel.Y et al, also showed mean serum magnesium was slightly lower in PIH women as compared to NPW group.[24] Lowered plasma or serum magnesium concentrations in pre-eclampsia may contribute to the development of hypertension in pregnancy.

Decreased renal excretion due to hypertension causes increased uric acid level in women with PIH initiating maternal and fetal complications. Similarly, in the present study, the Uric acid levels were increased in PIH women. In the study by Bellomo et al the results were remarkable, Uric acid conferred an 8–9 fold risk for preeclampsia and a 1.6 - 1.7 fold risk for small for gestational age infants.. These studies suggest that measurement of serum uric acid is clinically useful and should be part of the evaluation of the pregnant patient presenting with hypertension. Increasing evidence suggests that an elevated serum uric acid in pregnancy may not only be a valuable biomarker for preeclampsia but may also have a contributory role in the pathogenesis of the maternal and fetal manifestation.[25]

Conclusion

The Hcy and uric acid levels were increased and Magnesium level was decreased in PIH women than the NPW. So, early screening and diagnosis of PIH can be done by adding these parameters with other routine antenatal work-up in pregnant women.

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