Original Article

A Study of Homocysteine and Uric Acid Levels in Pregnancy Induced Hypertension

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ABSTRACT

Introduction: Hypertensive disorders are common in pregnancy,they cause serious complications like eclampsia, hemorrhage and infection leading to maternal and fetal mortality. Hyperhomocystenemia (HHcy) is associated with hypertension and eclampsia. Uric acid have direct role in blocking fetal angiogenesis Magnesium plays an important role in vasodilatation. So by evaluating Homocysteine, uric acid and magnesium levels in blood , we can reduce the maternal and fetal mortality.

Aim &Objectives: To study the Homocysteine (Hcy), uric acid and magnesium levels in pregnancy induced hypertension.

Materials And Methods: Case control study of hundred female subjects of age group of 18-40 yrs. Out of them 50 were normotensive pregnant women (NPW) in their third trimester and were chosen as control Group 1 .50 pregnancy induced hypertensive (PIH) patients in their third trimester were chosen as study Group 2.

Results: The mean Hcy value was increased to18.24± 6.65µmol/l (pvalue=0.002) and there was an associated significant increase in Uric acid level of 5.25 ± 0.49mg/dl (pvalue=0.004) in the PIH women compared to homocysteine 8.41± 2.07 µmol/l and uric acid levels 3.41± 0.84mg/dl in NPW group. On the other hand, the serum Magnesium level was significantly reduced in PIH (1.41±.04mgs/dl) compared toNPW 1.46±.02mgs/dl (p=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)

INTRODUCTION:

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

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vascular thrombosis.[1] 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.[2] 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.[3]

Homocysteine is a naturally occurring aminoacid derivative in the body. Increase in hormones 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).[4] 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.[5] 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.[6] 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.[7] Uric acid can also block trophoblast invasion in vitro.[8] 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.[9] 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 NPW group.

MATERIALS AND METHODS:

Case control study of hundred pregnant female subjects in the age group of 18-40 yrs was selected. Out of them 50 were normotensive pregnant women in their third trimester and were control. 50 pregnancy induced hypertensive (PIH) women in their third trimester were chosen as cases. Five ml blood sample was collected by venepunture 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. Period of study: January to June, 2014 at Govt Kilpauk Medical College, Department of Obstetrics and Gynecology and Department Of Biochemistry, Chennai. Ethical committee clearance obtained.

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 18 to 40yrs 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.

Statistical Analysis:

Student's test was used to analyse the two groups.

RESULTS:

TABLE 1 shows 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 18.24±6.65µmol/l (p-value=0.002) and the uric acid level was also increased with a mean and SD of 5.25±0.49mg/dl (p-value= 0.004) in the PIH. The Hcy level was 8.41 ± 2.07µmol/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)

Table-1.Homocysteine, Uricacid and Magnesium levels in PIH & NPW

		Mean	Std. Deviation	p value
Homocysteine level (µmol/l)	PIH	18.24	6.65	0.002
	NPW	8.41	2.07	
Uricacid level (mg/dl)	PIH	5.25	0.49	0.004
	NPW	3.41	0.84	
Magnesium (mgs/dl)	PIH	1.41	0.04	0.001
	NPW	1.46	0.02	

DISCUSSION:

In the present study, there was an increased Hcy level with a p value=0.002 and an increased uric acid level with a p value=0.004 in the PIH women when compared with NPW group. 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[10]. Similar findings are reported by Sanchez et al.[11], Harma et al.[12] and Maruotti et al.[13] 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).[14] 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[15]. Power et al. found high levels of homocysteine in preeclamptic patients as compared to the NPW. 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.[16] 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.[17]

Limitations:

A larger sample size can be analyzed to confirm the effect of increased Hcy, uric acid and decreased Magnesium levels in pregnancy induced hypertensive women for early diagnosis and treatment and thereby averting the dreaded complications of eclampsia and other thrombotic disorders in pregnancy

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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