Original Research Paper MEDICAL SCIENCE

Homocysteine: Association with Preeclampsia and its Severity and Correlation with Maternal and Fetal Outcome of Preeclamptic Women

DR.S. ANURADHA ASSISTANT PROFESSOR, GOVT. RSRM LYING IN HOSPITAL, ROYAPURAM, CHENNAI-600001

DR. RIZWANA TAJ.T. ASSISTANT PROFESSOR, GOVT. RSRM LYING IN HOSPITAL, ROYAPURAM, CHENNAI-600001

ABSTRACT

OBJECTIVES: To study the homocysteine levels among normal, mild and severe preeclamptic pregnant women, its association with severity of preeclampsia, and Maternal and fetal outcome in pregnancy for any association with homocysteine levels.
METHODS: 120 pregnant women were tested for serum homocysteine levels and were followed until delivery for acute kidney injury, pulmonary edema, DIC, abruptio placenta. Similarly, birth weight, intrauterine growth restriction, intrauterine death, neonatal mortality was recorded.
RESULTS: In our study, mean homocysteine levels in : normal pregnancy:6.65 micromole/l, mild preeclampsia: 11.58+/-2.38 micromole/l,severe preeclampsia: 16.67+/-10.1 micromole/l. Maternal homocysteine levels more than 15micromole/l was associated with maternal and neonatal morbidities.
CONCLUSION: Preeclampsia is associated with hyperhomocysteinemia. Homocysteine levels are directly related to severity of preeclampsia. Elevated maternal homocysteine levels is associated with maternal and neonatal morbidities.

KEYWORDS Homocysteine, Pregnancy, Preeclampsia.

INTRODUCTION:
Preeclampsia is a pregnancy specific disorder which complicates 3-10% of all nulliparous pregnancies. It is characterized by the development hypertension with proteinuria after 20 weeks of gestation. Endothelial dysfunction has been considered central in the pathophysiology of preeclampsia.

Homocysteine is a sulfur containing amino acid primarily derived from the demethylation of dietary methionine required for the growth of cells and tissues in human body. Hyperhomocysteinemia leads to endothelial dysfunction and interferes with the fibrinolytic system adding to the pathophysiology of preeclampsia.

In normal pregnancy, homocysteine levels are decreased than the non-pregnant level. Maternal hyperhomocysteinemia has been associated with preeclampsia, placental abruption, recurrent pregnancy loss, still birth, deep vein thrombosis and neural tube defects in the newborn.

This study is mainly aimed to find the association between maternal homocysteine levels and preeclampsia and its severity and the correlation of maternal homocysteine level with maternal and fetal outcome of preeclamtic mothers.

MATERIALS AND METHODS:
This is a cross sectional case control study conducted in the Department of Obstetrics and Gynecology at RSRM Lying in Hospital, Chennai. Pregnant women attending the hospital were screened and those who were eligible according to the inclusion and exclusion criteria were included in the study.

INCLUSION CRITERIA:
Pregnant women in 28-40 weeks who were under regular checkup and who are under regular iron and folic acid prophylactic therapy were included in the study.

EXCLUSION CRITERIA:
Women with chronic hypertension, chronic kidney/liver disease, diabetes mellitus/gestational diabetes, under anti folate drugs(anti-epileptics), hypothyroid, megaloblastic or dimorphic anemia, multiple pregnancies. Women with history of deep vein thrombosis/recurrent miscarriage/neural tube defects.

120 women who came to RSRM are included in the study. These patients were categorized in to 3 groups as normal pregnancy (group 1) n=40, women with mild preeclampsia (group 2) n=40, women with severe preeclampsia (group 3) n=40 according to the American College of Obstetrics and Gynecology guidelines.

TABLE 1 : DIVISION OF PATIENTS INTO GROUPS

GROUP		CRITERIA AS
GROUP 1	Normal pregnant women with singleton pregnancy (28-40 weeks)	BP<140/90 mmhg
GROUP 2	Women with mild preeclampsia (28-40 weeks)	BP>140/90 But<160/110 with 1+ proteinuria
GROUP 3	Women with severe preeclampsia (28-40 weeks)	BP > or = 160/110 with 2+/3+ proteinuria or imminent signs.

Patients were subjected to complete hemogram, renal function test, liver function test, serum fibrinogen, uric acid, urine routine, 24 hours urine protein, fundus examination, CTG, ultrasonogram. Peripheral smear study was done for all patients to exclude megaloblastic and dimorphic anemia.

For the measurement of serum homocysteine, 5ml of blood was taken after overnight fasting and centrifugation was done at 3000rpm for 5-7 minutes and the clear serum obtained was used for measurement. Serum homocysteine was measured by Fluorescence Polarization Immunoassay(FPIA) run on Abbott's AxSYM machine using Abbott's kit. Patients were

followed up till delivery and watched for morbidities. Then their babies were followed up for neonatal morbidities.

To find out the statistical significance, one-way ANOVA (analysis of variance) test and student 't' test was done.

RESULTS AND OBSERVATION:

TABLE 2:CORRELATION OF MATERNAL HOMOCYSTEINE AMONG THE THREE GROUPS

GROUPS	HOMOCYSTEINE LEVELS(MEAN)	STANDARD DEVIATION	P VALUE
Group 1(n=40)	6.650	1.5785	<0.001
Group 2(n=40)	11.583	2.3770	<0.001
Group 3(n=40)	16.670	4.8181	<0.001

In our study there was a significant difference between the homocysteine levels in all 3 groups.

CORRELATION OF HOMOCYSTEINE LEVEL WITH PREECLAMPSIA:

On comparing group 1 with group 2 and group 1 with group 3, the serum homocysteine level differed significantly. So our study proves that serum homocysteine is raised in

preeclampsia and there is an association between preeclampsia and hyperhomocysteinemia.

CORRELATION OF HYPERHOMOCYSTEINEMIA WITH SEVERITY OF PREECLAMPSIA:

There was a significant difference in homocysteine level between mothers with mild and severe preeclampsia(p,<0.001). Our study showed that maternal homocysteine level is directly associated with the severity of preeclampsia.

TABLE 3: CORRELATION OF HOMOCYSTEINE LEVEL WITH FETAL MATURITY

GROUP	No of babies	AVERAGE HOMOCYSTEINE LEVEL
Preterm	21	15.95
Term	99	10.72

There is a significant association (p<0.001) between the maternal homocysteine level and fetal maturity. Most of the prematurity in the sever preeclamptic group (76%) was iatrogenic.

TABLE 4: CORRELATION BETWEEN MATERNAL HOMOCYSTEINE LEVEL AND BIRTH WEIGHT

BIRTH WEIGHT	NO OF BABIES	AVERAGE HOMOCYSTEINE LEVEL
<2.5kg	27	15.4
>2.5kg	93	10.54

In our study, there is a significant association(p<0.001) between maternal homocysteine level and neonatal birth weight.

TABLE 5: CORRELATION OF MATERNAL HOMOCYSTEINE LEVEL WITH PERINATAL MORTALITY

	NO OF BABIES	AVERAGE HOMOCYSTEINE LEVEL
Perinatal mortality	4	18.85
Normal	116	11.38

In our study, there is a significant association(p<0.001) between maternal homocysteine level and fetal perinatal mortality.

CORRELATION OF HOMOCYSTEINE WITH INTRAUTERINE GROWTH RESTRICTION:

In our study, there is a significant association(p<0.001) between maternal homocysteine level and neonatal intrauterine growth restriction. Average homocysteine levels in intrauterine growth restricted babies was 21.55 micromole/l compared to others (11.47micromole/l).

TABLE 6: CORRELATION OF HOMOCYSTEINE WITH MATERNAL MORBIDITY

HOMOCYSTEINE LEVEL (in Micromole/L)	0-4.9	5-9.9	10-14.9	15-19.9	20-24.9
MORBIDITY	0	0	0	6	1

In our study all the maternal morbidities occurred in mothers with homocysteine level of more than 15micromole/l.

DISCUSSION:

In our study, the homocysteine level among the normal pregnant women was 6.65+/-3.16micromole/l. This is similar to study by Stolkova et al (1), where the mean homocysteine was 6.24 micromole/l. In mild preeclamptic group, the homocysteine level was 11.58+/-4.76micromole/l and in severe preeclamptic group it was 16.67+/-6.7micromole/l. Women with severe preeclampsia gad the highest homocysteine level followed by mild preeclampsia and then normal pregnant women. All these values were statistically significant implying that homocysteine level differed significantly between women with and without preeclampsia and also correlated with the severity of preeclampsia. The large Hordaland homocysteine – a population based study (2) concluded that hyperhomocysteinemia is a risk factor for preeclampsia and this is also supported by several other studies (3-7)

With respect to the maternal and fetal outcome, elevated homocysteine levels correlated with all maternal morbidities and fetal conditions like preterm birth, low birth weight, intrauterine growth restriction and perinatal mortality. Both maternal and neonatal morbidities were common in mothers with homocysteine levels of more than 15micromole/l.

CONCLUSION:

Preeclampsia is associated with hyperhomocysteinemia. In preeclampsia, homocysteine levels are directly related to the severity of preeclampsia. A maternal homocysteine level of more than 15micromole/l can be used to expect poor maternal and fetal outcome. Maternal hyperhomocysteinemia is associated with preterm birth, low birth weight, and increased perinatal mortality. It also increases maternal morbidities especially placental abruption. Since nutritional deficiencies like B12, folate, B6 are known to produce hyperhomocysteinemia better nutritional care to the at risk mothers should be done.

REFERENCES:

1. Stolkova, Ivanov serum homocysteine level in pregnant women with preeclampsia Akush Ginekol 2005;44(6):16-9
2. The Hordaland Homocysteine study: Helga refsum, Eha nurk, David Smith: the journal of nutrition: American Society of Nutrition 2006.
3. Md.Mozammel Hoque, tani bulbul, serum homocysteine in preeclampsia and eclampsia Bangladesh med Res Counc Bull 2008;34:16-20
4. Mahal, yaesmin association of serum homocysteine and serum lipid with eclampsia JAFMC Bangladesh Vol15, no 1, June 2009.
5. Hasanzadeh, ayatollahi, farzadnia: elevated plasma total homocysteine in preeclampsia Saudi medical journal 2008 June;29:875-8
6. Makedos, papanicolloau, homocysteine, folic acid B12 serum levels in pregnancy complicated with preeclampsia. Archive Gynecol Obstet 2007 Feb;275(2):121-4
7. Bakshu, Taskin, goker Plasma homocysteine in late pregnancies complicated with preeclampsia and in new borns-Am J Perinatol 2006 Jan;23(1):31-5